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ORIGINAL ARTICLE

Management of portal hypertensive upper gastrointestinal bleeding: Report of the Coorg Consensus workshop of the Indian Society of Gastroenterology Task Force on Upper Gastrointestinal Bleeding

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Abstract

Portal hypertensive bleeding is a major complication of portal hypertension (PHT) with high morbidity and mortality. A lot of advances have been made in our understanding of screening, risk stratification, and management strategies for portal hypertensive bleeding including acute variceal bleeding leading to improved overall outcomes in patients with PHT. A number of guidelines on variceal bleeding have been published by various societies in the past few years. The Indian Society of Gastroenterology (ISG) Task Force on Upper Gastrointestinal Bleeding (UGIB) felt that it was necessary to bring out a standard practice guidance document for the use of Indian health care providers especially physicians, gastroenterologists, and hepatologists. For this purpose, an expert group meeting was convened by the ISG Task Force to deliberate on this matter and write a consensus guidance document for Indian practice. The delegates including gastroenterologists, hepatologists, radiologists, and surgeons from different parts of the country participated in the consensus development meeting at Coorg in 2018. A core group was constituted which reviewed all published literature on portal hypertensive UGIB with special reference to the Indian scenario and prepared unambiguous statements on different aspects for voting and consensus in the whole group. This consensus was produced through a modified Delphi process and reflects our current understanding and recommendations for the diagnosis and management of portal hypertensive UGIB in Indians. Intended for use by the health care providers especially gastroenterologists and hepatologists, these consensus statements provide an evidence-based approach to risk stratification, diagnosis, and management of patients with portal hypertensive bleeding.

Keywords BRTO · Cirrhosis · Early TIPS · Endoscopy · Esophageal varices · Gastric varices · Gastrointestinal bleeding · Portal hypertension · Primary prophylaxis · Secondary prophylaxis

Introduction

Variceal bleeding is a common emergency encountered by physicians and surgeons, and constitutes 10.8% to 56% of upper gastrointestinal bleeding (UGIB) in India [1]. Portal hypertension (PHT)–related UGIB is associated with significant morbidity and a mortality rate of 10% to20% over a period of 6 weeks [2]. A number of recently published trials impact on the current management of portal hypertensive UGIB. An expert group meeting was conducted in June 2018 to deliberate on this matter and write a consensus guidance document for Indian practice. The expert group recognized the work published on this issue by the American Association for the Study of Liver Diseases (AASLD) [2] as well as in the Baveno VI consensus workshop [3] a few years back. The Indian Society of Gastroenterology (ISG) Task Force on UGIB felt it was necessary to bring out a standard practice guidance document for the use by Indian health care providers especially physicians, gastroenterologists, and

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hepatologists, and consequently developed a set of consensus statements for the diagnosis and management of portal hypertensive bleeding in Indians.

Methods

To develop a standard practice guidance document for diagnosis and management of portal hypertensive bleeding to be used by Indian health care providers, a core group was constituted by the ISG Task Force on UGIB which reviewed all published literature on portal hypertensive UGIB with special reference to the Indian studies, and prepared unambiguous statements on different aspects of portal hypertensive bleeding for voting and consensus. Subsequently, an expert group meeting was convened by the ISG Task Force on UGIB. The aim of this expert group meeting was to standardize the definitions of portal hypertensive UGIB in Indian context, to weigh the evidence regarding appropriate management, and to bring out a standard practice guidance document for the use of Indian physicians, gastroenterologists, and/or hepatologists. The delegates including gastroenterologists, hepatologists, radiologists, and surgeons from different parts of the country participated in the consensus development workshop at Coorg in 2018. The participants were provided all recently published literature and societal guidelines on portal hypertensive bleeding after a thorough search of Pubmed and other databases. The statements prepared by the core committee were allocated to different participants on the basis of their expertise and experience in their related field well in advance for presentation during the workshop. During the workshop, the statements were presented along with supporting evidence from published literature to enable an educated voting on the statements for developing a consensus. This consensus was produced through a modified Delphi process [4]. The statements were reviewed and considered for voting for any of the five options based on the available evidences. The statements were considered "accepted" when 80% of voting members voted for either *accept completely*, *or accept with some reservation.* The statements were "rejected" if 80% of voting members voted for either *reject with reservation or reject completely.* Statements on important issues which were unacceptable were modified for a final round of voting if the voting members felt so. The modified statements were again subjected to voting for either acceptance or rejection. After a consensus statement was finalized by voting, the quality of evidence and strength of recommendation was affixed to each statement on the basis of the evidence provided by the presenter. The template for rating of available evidence and recommendations was adapted from the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system for evaluating evidence [5]. The quality of evidence was rated as Level I, II-1, II-2, II-3, and III and the strength of recommendations as strong or weak (Table 1).

The consensus workshop was attended by a total of 23 experts and an additional 40 practicing gastroenterologists also participated in the discussion on the statements and voting. The statements are listed in Table 2.

Definitions and classifications

The premise for definitions and classifications is that they should be uniform, reproducible, and simple, for purpose of research and for easy applicability in the clinical settings.

Esophageal variceal classification Although a number of classification schemes have been published and used for classifying the grades of esophageal varices, ranging from 2 to 4 grades [6–8], the simplest and easiest to use is the one which uses two classifications categorizing the varices into low-risk and high-risk types (based on size, presence or absence of red colored signs [RCS]). The expert group recommends that esophageal varices should be classified as small (< 5 mm) and low-risk (without RCS) or large (>5 mm) and high-risk (with RCS) [3]. This helps in easy applicability of therapy and prognostication. Indeterminate category (small varices with RCS or large varices without RCS) should be treated as high-risk, unless more data are available. Also, any varices in Child-C cirrhosis patient are considered high-risk varices in view of increased risk of bleeding. The size of varices is best assessed at endoscopy by comparing these to the size of an opened biopsy forceps. The size of opened biopsy forceps is approximately 5 mm and hence can be used to classify the varices.

Gastric variceal classification Like esophageal varices, studies have shown that for gastric varices (GV) too the risk of bleeding depends on the size, presence or absence of red color signs, and the underlying liver functional reserve. The suggested classification to be followed is the one given by Sarin et al. [9] classifying GV as follows:

- Gastroesophageal varices type 1 (GOV1): it describes varices extending in continuity from the lower esophagus to lesser curvature of the stomach
- Gastroesophageal varices type 2 (GOV2): to describe varices in the fundus of the stomach in continuation with esophageal varices
- Isolated GV type 1 (IGV1): to describe varices in the fundus of the stomach in the absence of esophageal varices
- Isolated GV type 2 (IGV2): to describe varices in ectopic places (away from the gastroesophageal [GE] junction or

Table 1 Grade of recommendation and level of evidence

Quality of evidence	Criteria
I	Randomized control trials
II-1	Controlled trials without randomization
II-2	Cohort or case-control analytical studies
II-3	Multiple time series, uncontrolled experiments
III	Opinions of respected authorities, descriptive epidemiology
Strength of recommendation	**Criteria**
Strong	Factors influencing the strength of the recommendation including the quality of evidence, presumed patient important outcomes and cost
Weak	Variability in preferences and values, or more uncertainty. Recommendation is made with less certainty, higher cost or resource consumption

cardia or fundus of the stomach) like antrum of the stomach

Also, it was decided that the size and appearance of GV should be mentioned as F1, F2, or F3 to describe tortuous, nodular, or tumorous GV respectively [10]. RCS should also be mentioned as present or absent.

Acute variceal bleeding Bleeding within 120 hours (5 days) of presentation should be considered part of the same acute variceal bleed (AVB) episode. This is because the therapies for AVB (mainly vasopressors) are usually continued for 3–5 days. This is based on the fact that there is a rise in HVPG, which may persist up to 3–5 days (up to 10 days in some studies) after the initial endotherapy [11].

Control of AVB This was defined based on consensus as either cessation of acute bleeding with hemodynamic stability for 24 hours following therapy or demonstration of control of ongoing bleeding at endoscopy after endotherapy.

Failure to control bleeding Similar to the definition given in Baveno VI consensus and by the Asian Pacific Association for the Study of the Liver (APASL) consensus [12], failure to control the acute bleeding was defined as: > 2 hours after the start of specific therapy, if there is death or any of the following within 48 hours after initial endoscopy.

- Fresh hematemesis or more than 100 mL of fresh nasogastric (NG) aspirate
- Development of hypovolemic shock
- >2 g/dL drop in hemoglobin within any 24-h period

Rebleeding Although APASL has classified rebleeding as very early, early, and late rebleeding, it was decided in the current meeting to have just two time frames in order to reduce the ambiguity and confusion. So rebleeding was classified as early rebleeding (occurring after initial control of bleeding and between 2 to 5 days) and late rebleeding (after initial control of bleeding and after 5 days). The basis for this classification is that these two are distinct events; early rebleeding represents failure of primary therapy and late rebleeding represents failure of secondary prophylaxis. The expert group voted against the category of very early rebleeding as it would create confusion with the time frame used to define "acute variceal bleeding" and "failure to control bleeding." However, it was appreciated that there would be some overlap between failure to control bleed and early rebleeding.

Statements	Level	Grade
Varices should be classified as large/small (≥5 mm/ <5 mm) and high/low risk (with or without red color signs)	II-2	Strong
Large varices without red color signs and small varices with red color signs should also be considered as high risk until we have more data.	II-2	Strong
Time frame for presentation of acute bleed should be 5 days	III	Strong
Control of acute bleed refers to cessation of bleeding with hemodynamic stability for 24 hours after therapy	II-2	Strong
Rebleeding after initial bleed control should be classified as follows •Failure to control bleeding – Bleed within 48 hours of initial endoscopy •Early rebleeding – between 2-5 days of initial endoscopy •Late rebleeding – after 5 days of initial endoscopy	II-3	Weak
Rebleeding will be defined by any of the following criteria •Death •Fresh hematemesis or >100 mL of fresh red NG aspirate •Development of hypovolemic shock •> 2 g/dL drop in Hb within any 24 hour period (without transfusion)	II-3	Strong
Early rebleeding: Usually represents failure of initial or primary therapy	III	Weak
Late rebleeding: Usually represents failure of secondary prophylaxis	III	Weak

NG nasogastric, *Hb* hemoglobin

Table 2 Consensus statements of Indian Society of Gastroenterology Task Force on Upper Gastrointestinal Bleeding

Statements	Level	Grade
Varices should be classified as large/small (≥5 mm / <5 mm) and high/low risk (with or without red color signs)	II-2	Strong
Large varices without red color signs and small varices with red color signs should also be considered as high risk untill we have more data	II-2	Strong
Time frame for presentation of acute bleed should be 5 days	III	Strong
Control of acute bleed refers to cessation of bleeding with hemodynamic stability for 24 h after therapy	II-2	Strong
Rebleeding after initial bleed control should be classified as follows •Failure to control bleeding – Bleed within 48 hours of initial endoscopy •Early rebleeding – between 2-5 days of initial endoscopy •Late rebleeding – after 5 days	II-3	Weak
Rebleeding will be defined by any of the following criteria •Death •Fresh hematemesis or >100 mL of fresh red nasogastric (NG) aspirate •Development of hypovolemic shock •> 2 g/dL drop in hemoglobin (Hb) within any 24 hour period (without transfusion)	II-3	Strong
Early rebleeding: usually represents failure of initial or primary therapy	III	Weak
Late rebleeding: usually represents failure of secondary prophylaxis	III	Weak
Patients with acute variceal bleed should preferably be managed in an intensive care unit (ICU) or high dependency unit (HDU)	II-3	Strong
In the absence of availability of ICU or HDU, patients can be managed in the ward with dedicated staff and equipment	III	Strong
Assessment of severity of bleeding in a patient with acute variceal bleeding should be done based on the active bleeding, requirement of transfusion and severity of liver disease based on Child-Turcotte-Pugh (CTP) and model for end-stage liver disease (MELD) scores and presence of hemodynamic instability	II-2	Strong
In patients with acute variceal bleed, it is essential to assess and protect the circulatory and respiratory status of the patient.	II-3	Strong
Patients with high risk of aspiration need intubation	III	Strong
Immediate volume restitution should be initiated to restore and maintain hemodynamic stability preferably with crystalloids and by avoiding over infusion	II-2	Strong
A "restrictive" packed red blood cell (PRBC) transfusion strategy (PRBC transfusion at Hb < 7 g/dL and maintaining it at 7-9 g/dL) is recommended	I	Strong
Transfusion/volume expansion in an individual patient should take into account other factors, such as age, cardiovascular disorders, ongoing hemorrhage, and hemodynamic status	III	Strong
Correction of prothrombin time/international normalized ratio (INR) or platelet counts by the use of fresh frozen plasma and platelets is not required in every patient and needs to be individualized	I	Strong
Use of Factor VIIa is not recommended in patients with acute variceal bleed	I	Strong
Antibiotic prophylaxis should be given to patients with cirrhosis presenting with acute variceal bleed	I	Strong
Intravenous ceftriaxone (1 g/24 h) for a maximum of seven days is the preferable antibiotic	I	Strong
Combination of a vasoactive drug and endoscopic therapy is the treatment of choice for acute variceal bleed	I	Strong
There is no significant differences in hemostatic effects and survival benefits among terlipressin, somatostatin and octreotide as adjuvants to endoscopic treatment in patients with acute gastroesophageal variceal bleeding Choice should depend on availability and cost	I	Strong
Terlipressin is the preferred vasoactive agent in patients who have acute kidney injury (AKI) during an episode of variceal bleed	I	Strong
Vasoactive agents should be started as early as possible and continued for 2-5 days	III	Strong
Monitoring for adverse effects is necessary while using vasoactive agents	II-C	Strong
In a cirrhotic patient, screening endoscopy is recommended for assessment of varices	II-1	Strong
Survelliance endoscopy should be individualized based on: •No varix and no ongoing risk factor (3 yearly endoscopy) •No varix with ongoing risk factors (2 yearly endoscopy) • Small varices with no ongoing risk factor-2 yearly endoscopy •Small varices with ongoing risk factors - yearly endoscopy is recommended	II-1	Strong
In acute variceal bleeding, after resuscitation, upper gastrointestinal (UGI) UGI endoscopy should be done within 12 hours of presentation (preferably as soon as possible)	II-3	Strong
Use of propofol with proper monitoring is safe in a cirrhotic patient.	II-2	Strong
It is beneficial to use intravenous metoclopramide prior to endoscopy	II-3	Strong
Endoscopic variceal ligation (EVL) is preferred over endoscopic sclerotherapy (EST) for treating esophageal varices	I	Strong
EST should be done where EVL is not technically feasible	I	Strong

Table 2 (continued)

Statements	Level	Grade
Failure to control bleeding/rebleeding (with EVL+beta-blockers) may occur in 10 to 20% of patients with esophageal variceal bleed	I	Strong
More severe liver disease (presence of jaundice, ascites, higher CTP and MELD/MELD-Na scores) are predictive of variceal rebleeding	II-2	Strong
Presence of portal vein thrombosis (PVT) as well as hepatocellular carcinoma (HCC) are associated with a higher risk of rebleeding	II-2	Strong
Ongoing alcohol abuse is a predictor of variceal rebleeding	II-2	Strong
Large high risk varices, presence of active bleeding or white nipple sign/clot over varix are endoscopic predictors of failure to control bleeding/rebleeding.	II-2	Strong
Hepatic venous pressure gradient (HVPG) ≥20 mmHg is a good predictor of variceal rebleeding	I	Strong
EVL+Beta-blockers alone are associated with high risk of treatment failure in patients with HVPG ≥20 mmHg	I	Strong
In patients with a rebleed, HVPG is advisable to guide further therapy	II-2	Weak
Early transjugular intrahepatic portosystemic shunt (TIPS) is safe and effective in controlling acute variceal bleed in selected high risk patients	I	Strong
Early TIPS should be considered where available in acute variceal bleed in high risk patients: •HVPG >20 mmHg (where available) •Child C with CTP score -10-13 •Child B with active bleeding during endoscopy	I	Strong
Patients in whom there is failure to achieve hemostasis after initial endoscopic therapy are candidates for a second attempt at endoscopic therapy with EVL or glue injection.	II-2	Strong
Till definitive therapy can be organized, a bridging therapy with SX Ella-Danis stent (5-7 days) or Sengstaken-Blakemore tube (SBT) (24-48 hours) may be offered.	II-3	Strong
Definitive rescue therapy for failure of attempts at endoscopic therapy is TIPS for esophageal variceal bleed	I	Strong
Pre-primary prophylaxis for prevention of variceal development is currently not indicated	I	Strong
Non-selective beta blockers (NSBB) can be used as 1° prophylaxis for small/low risk esophageal varices	I	Strong
NSBB or EVL can be used as 1° prophylaxis for large/ high risk esophageal varices	I	Strong
Both propranolol and carvedilol are acceptable first line agents for 1° prophylaxis	I	Strong
HVPG measurement (baseline and post NSBB) provides an add-on information on prognosis	II-1	Strong
Use of NSBB in refractory ascites, spontaneous bacterial peritonitis (SBP) and AKI need to be carefully monitored and individualized.	II-C	Weak
NSBB (propranolol) + EVL combination is the preferred option for 2° prophylaxis of variceal bleed	I	Strong
Statements-Gastroesophageal varices-type 1 (GOV1)	**Level**	**Grade**
Primary prophylaxis		
NSSB may be used for primary prophylaxis of gastric varices (GV)	III	Weak
Endotherapy (EVL) for esophageal varices is the standard of care for primary prophylaxis for GOV1	II	Strong
Secondary prophylaxis		
NSBB with obliteration of esophageal varices is recommended for GOV1	III	Strong
Statements – Gastroesophageal varices type 2 (GOV2), and isolated gastric varices type 1 (IGV1)	**Level**	**Grade**
NSSB can be used for primary prophylaxis of GOV2 and IGV1	III	Weak
Use of glue injection for primary prophylaxis of high risk GV is acceptable	I	Strong
Endoscopic ultrasound (EUS) guided coiling in expert hands is also an option for primary prophylaxis for high risk GOV2/IGV1	III	Weak
Glue injection until eradication of GV is recommended for secondary prophylaxis of GOV2	I	Strong
Combination of EUS guided coiling with glue injection is a promising technique for treatment of bleeding GV	II-2	Strong
Surgery is not recommended for primary prophylaxis of GOV2/IGV1	III	Strong
In absence of cirrhosis, in patients with isolated GOV2/IGV1 with splenic vein thrombosis - splencectomy is recommended for secondary prophylaxis	III	Strong
In extrahepatic portal venous obstruction (EHPVO) with bleeding GOV2/IGV1, shunt surgery can be considered as a one-time treatment option	III	Weak
Statements - Interventional radiological treatment of GV	**Level**	**Grade**
Balloon-occluded retrograde transvenous obliteration (BRTO) and TIPS are safe and effective in the management of GV bleeding	I	Strong
BRTO should be considered in appropriate patients with GV bleeding not responding to endoscopic n-butyl cynoacrylate (glue) injection (in patients with gastrorenal shunt)	I	Strong
Eradication of esophageal varices should be done in all patients undergoing BRTO and such patients should be screened periodically for progression/appearance of esophageal varices	II-2	Strong
TIPS with embolisation of GV should be preferred in GV bleeding if gastrorenal shunt is absent or patient has high risk esophageal varices	II-2	Strong

Table 2 (continued)

Statements	Level	Grade
Statements - Ectopic varices	**Level**	**Grade**
Triple phase computed tomography (CT) of abdomen is the gold standard for planning treatment of ectopic varices	III	Strong
In view of absence of data, prophylactic treatment of ectopic varices is not recommended	III	Strong
Role of pharmacotherapy is undefined for control of ectopic variceal bleeding	III	Weak
There are insufficient data to recommend one endoscopic treatment modality over another for duodenal variceal bleeding However, glue may be the preferred modality	III	Strong
Radiological treatments are effective for ectopic varices, and include embolisation of the afferent vein alone, TIPS combined with embolisation, and BRTO. The choice of treatment modality should be carefully tailored in each case	II-2	Strong
In patients with ectopic varices, endoscopic treatment by standard ileo-colonoscopy, push-enteroscopy, or balloon assisted endoscopy is the first line treatment, if patient is hemodynamically stable	III	Strong
There is no study to suggest superior efficacy or safety among cyanoacrylate glue or sclerosant solutions	III	Strong
Individualized interventional radiological approach is preferred when endoscopic treatment is not feasible	II-2	Strong
Surgery remains an effective option for treating ectopic variceal bleeding in non-cirrhotic patients	II-2	Strong
Statements - Non cirrhotic portal hypertension (NCPH)	**Level**	**Grade**
Endoscopic therapy is effective in control of acute variceal bleeding in NCPH. EVL is preferable to EST	II	Weak
Although data on use of pharmacological agents for prophylaxis in NCPH are limited, it is reasonable to manage such patients on the lines of compensated cirrhosis	III	Weak
Shunt surgery may have a role in management of patients who fail endoscopic therapy, have symptomatic hypersplenism or portal cavernoma cholangiopathy or stay in remote locations with limited access to healthcare	III	Weak
Statements - Portal hypertensive gastropathy (PHG)	**Level**	**Grade**
Beta-blocker should be started in PHG or portal hypertensive colopathy with chronic blood loss	I	Strong
Beta-blockers are not effective for acute bleeding from PHG or portal hypertensive colopathy and gastric antral vascular ectasia (GAVE) related bleed	II-3	Weak

Esophageal variceal bleeding: Natural history

Esophageal varices are considered as the most important portosystemic collaterals from a clinical point of view. PHT is crucial in the transition from the preclinical to the clinical phase of cirrhosis [13]. Prevalence of esophageal varices in cirrhotic patients is variable, and it depends upon the degree of liver dysfunction. Pascal et al. [14] in a comprehensive review showed the prevalence of esophageal varices to be ranging between 24% and 80%, with a mean of about 60%. D'Amico and Luca [15] reported prevalence of varices as 30% among compensated and of 60% among decompensated cirrhotics. Knowledge of the rate of development and growth of esophageal varices is useful in defining the need and timing of endoscopic surveillance. Incidence and development of new varices is 8% per year as reported by Pagliaro et al. [16]. The rate of growth of varices from small to large is faster than the rate of de novo appearance of varices [13].

A meta-analysis by D'Amico et al. [17] revealed that the mean weighted bleeding rate of esophageal varices at 2 years was 24%. Several studies have shown that the HVPG is an independent predictor of variceal bleeding and death [15]. But once the threshold of 12 mmHg HVPG has been reached, there is no linear relationship between HVPG value and risk of bleeding. Also it must be noted that variceal bleeding is a stop-and-go phenomenon. Spontaneous cessation of bleeding may occur in 32% to 93% of patients, with an average of 52% [17]. The reported incidence of early re-bleeding ranges between 30% and 40% within the first 6 weeks [16]. The risk is greatest in the first 5 days, then declines slowly over the first 6 weeks, and becomes virtually equal to that before bleeding after the sixth week [18].

Recent studies show that the prevalence of varices and risk variceal bleeding are similar in NCPH patients and compensated cirrhotics. However, the rate of progression of varices is more rapid in NCPH compared to cirrhosis [19].

Severity assessment and ABC of acute variceal bleed

Maintenance of airway, breathing, and circulation (ABC) and assessment of severity are very important for the management of AVB. In this section, we discuss the place of management of such patients (intensive care unit [ICU] or high dependency unit [HDU] or ward), assessment of severity of bleed, indications for intubation, blood transfusion, fresh frozen plasma (FFP), platelets, recombinant factor VII transfusion, and use of prophylactic antibiotics.

Location of management

Patients with AVB need to be managed at a place where continuous pulse/blood pressure (BP) monitoring is possible with facilities for high flow oxygen and equipment for intubation and ventilation. Ideal place for such management would be an ICU or HDU, but a properly staffed and equipped "gastrointestinal bleeding bed" in the ward may also suffice in the absence of the ICU/HDU facilities.

Severity assessment

The following parameters would indicate a severe bleed; old age, male gender, presence of co-morbidities, active bleeding, systolic BP < 100 mmHg, requirement of > 4 units of packed red blood cells (PRBC), patients with Child status C, and model for end-stage liver disease (MELD) 19. In addition to these clinical parameters, various scoring systems (Glasgow-Blatchford, Rockall, and AIMS65) are available for the assessment of acute UGIB but are used predominantly for non-variceal UGIB.

Airway, breathing–intubation

In addition to the initial assessment, which would include quick history, physical examination and blood sampling, maintenance of airway and decision to intubate, is very crucial in patients with AVB. All patients should be given high flow oxygen. Intubation would be required to prevent aspiration in patients who are actively vomiting blood and have hepatic encephalopathy. A special mention was made about intubation before endoscopy in those patients who are hemodynamically unstable and are likely to have blood in the stomach. Patients can be extubated once they are stable in the ICU/HDU or ward.

Circulation

Blood volume restitution should be initiated promptly in all patients to restore and maintain hemodynamic stability and to ensure tissue perfusion and oxygen delivery. Peripheral intravenous (IV) access should be established preferably with two 16–18G cannulae. Central venous access may be required in patients with poor peripheral access, advanced liver disease, and associated renal failure. Fluid resuscitation can be done with crystalloids or colloids to maintain systolic BP of 100 mmHg. Care should be taken to avoid over-infusion.

Blood and blood product transfusion

PRBCs are used to improve oxygen delivery to tissues in case of severe anemia, but a restrictive transfusion strategy is adequate in most patients. Hemoglobin threshold for transfusion should be 7 g/dL with target range after transfusion of 7 to 9 g/dL [20]. A study comparing restrictive and liberal strategy for blood transfusion in patients with acute UGIB found better survival in those with restrictive strategy even among patients with AVB. Transfusion/volume expansion in an individual patient should take into account other factors, such as age, cardiovascular disorders, ongoing hemorrhage, and hemodynamic status. We recommend that the transfusion of FFP or platelets should be based on dynamic tests of coagulation like thromboelastography (TEG)/rotational thromboelastometry (ROTEM). In the absence of availability of viscoelastic tests, we recommend platelet transfusions when platelet count is <50,000/mm^3 and FFP if international normalized ratio (INR) >1.5 times the normal (although these cut-offs are not sacrosanct and can be guided by local experience). There is insufficient evidence to support the routine use of tranexamic acid or recombinant factor VIIa [21].

Prophylactic antibiotics

Since patients with AVB are prone to bacterial infections, prophylactic use of antibiotics is recommended to reduce infections, recurrent bleed, and mortality in all patients with cirrhosis. Earlier studies used oral norfloxacin or IV ciprofloxacin, but now the recommended antibiotic is IV ceftriaxone (1 g/24 h for 7 days) and has been shown to be more effective than norfloxacin in a comparative randomized controlled trial (RCT) [22]. However, the antibiotic choice should be based on local antibiotic susceptibility patterns.

Statements	Level	Grade
Patients with acute variceal bleed should preferably be managed in an intensive care unit (ICU) or high dependency unit (HDU)	II-3	Strong
In the absence of the availability of ICU or HDU, patients can be managed in the ward with dedicated staff and equipment	III	Strong
Assessment of severity of bleeding in a patient with acute variceal bleeding should be done based on the presence of active bleeding, requirement of transfusion and severity of liver disease based on Child-Turcotte-Pugh (CTP) and model for end-stage liver disease, (MELD) scores and presence of hemodynamic instability	II-2	Strong
In patients with acute variceal bleed, it is essential to assess and protect the circulatory and respiratory status of the patient.	II-3	Strong
Patients with high risk of aspiration need intubation	III	Strong
Immediate volume restitution should be initiated to restore and maintain hemodynamic stability preferably with crystalloids and by avoiding over-infusion.	II-2	Strong
A "restrictive" packed red blood cell (PRBC) transfusion strategy (PRBC transfusion at hemoglobin < 7 g/dL and maintaining it at 7-9 g/dL) is recommended	I	Strong
Transfusion/volume expansion in the individual patient should take into account other factors, such as age, cardiovascular disorders, ongoing hemorrhage, and hemodynamic status	III	Strong
Correction of prothrombin time/international normalized ratio (INR) or platelet counts by the use of fresh frozen	I	Strong

plasma and platelets is not required in every patient and needs to be individualized		
Use of factor VIIa is not recommended in patients with acute variceal bleed	I	Strong
Antibiotic prophylaxis should be given in patients with cirrhosis presenting with acute variceal bleed	I	Strong
Intravenous ceftriaxone (1 g/24 hrs) for a maximum of seven days is the preferable antibiotic	I	Strong

Initial management of variceal bleed

Vasoactive medication should be started as early as possible in a patient presenting with AVB. Vasoactive agents have been shown to significantly lower mortality, improve hemostasis, lower transfusion requirement, and lead to shorter hospital stay [23]. Pharmacological treatment along with endoscopic treatment is better than endoscopic treatment alone. A meta-analysis of 8 trials including 939 patients found that 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) [24]. A recent RCT showed no significant differences among vasoactive agents like somatostatin, terlipressin, and octreotide. Active bleed at first endoscopy, treatment success by day 5, need for rescue treatment, rebleeding, and mortality were similar among various vasoactive agents [25]. Choice of agent should therefore depend on availability and cost. Patients who present with variceal bleed and acute kidney injury (AKI) may benefit from use of terlipressin and it should therefore be preferred in patients with AKI [26, 27]. Vasopressin is associated with significant side effects and therefore should be avoided. The optimum duration of therapy with vasoactive agents extends from 2–5 days and must be individualized based on endoscopic assessment of risk of rebleeding, Child status, and the presence or absence of renal failure. While using vasoactive drugs, it is essential to monitor patients especially for vasoconstrictive side effects of these agents. Baseline electrocardiogram (ECG) and continuous hemodynamic monitoring are recommended. Caution should be exercised when use is required in elderly and hypertensive patients. Contraindications to usage of these agents such as peripheral vascular disease, arrhythmias, ischemic heart, or cerebral vascular disease should be looked for prior to initiation. Terlipressin causes hyponatremia and therefore sodium levels need to be monitored during therapy [25].

Statements	Level	Grade
Combination of a vasoactive drug and endoscopic therapy is the treatment of choice for acute variceal bleed	I	Strong
There is no significant difference in hemostatic effects and survival benefits among terlipressin, somatostatin and octreotide as adjuvants to endoscopic treatment in patients with acute gastroesophageal variceal bleeding. Choice should depend on availability and cost	I	Strong
Terlipressin is the preferred vasoactive agent in patients who have acute kidney injury during an episode of variceal bleed	I	Strong
Vasoactive agents should be started as early as possible and continued for 2-5 days	III	Strong
Monitoring for adverse effects is necessary while using vasoactive agents	II-C	Strong

Surveillance endoscopy in cirrhosis

Endoscopy is the investigation of choice for assessment of esophageal varices. Besides diagnosis, it also helps to identify predictors of bleed such as RCS and can be used for simultaneous therapy. Surveillance for esophageal varices in a cirrhosis depends on many factors: presence or absence of varices, size of varices, compensated or decompensated liver disease, and presence of ongoing insult or injury. In a patient with compensated cirrhosis with no varices and no ongoing injury, endoscopy can be repeated after 3 years. If a patient of compensated cirrhosis has ongoing insult or injury (continuous alcohol abuse for example), endoscopy should be performed every 2 years. In small varices with no ongoing injury, endoscopy can be repeated every 2 years. If ongoing injury is present, endoscopy should be performed yearly. If decompensation occurs in a previously stable cirrhotic, endoscopy should be performed even if there was no varix or small varices reported earlier.

Timing of endoscopy in acute variceal bleeding

It is advisable to perform early endoscopy for AVB (within 12 hours) once adequate resuscitation has been done [24]. Decompensation occurs rapidly if ongoing AVB is not adequately managed. Sedation is preferred for performing both diagnostic and therapeutic endoscopic procedures. Propofol sedation with proper monitoring carries no extra risk for endoscopy in cirrhotics [28]. Endoscopic management along with pharmacotherapy is the standard of care for managing AVB. Both EVL and endoscopic sclerotherapy (EST) have been used for managing esophageal variceal bleeds. EVL is the preferred modality for the management of variceal bleed, and EST should only be performed if EVL is not technically feasible [24, 29].

Statements	Level	Grade
In a cirrhotic patient, screening endoscopy is recommended for assessment of varices	II-1	Strong
Surveillance endoscopy should be individualized as follows: •No varix and no ongoing risk factors - 3 yearly •No varix with ongoing risk factors - 2 yearly •Small varices with no ongoing risk factor- 2 yearly	II-1	Strong

•Small varices with ongoing risk factros - one yearly endoscopy is recommended		
In an acute variceal bleeding, after resuscitation, upper gastrointestinal endoscopy should be done within 12 hours of presentation (preferably as soon as possible)	II-3	Strong
Use of propofol with proper monitoring is safe in a cirrhotic patient.	II-2	Strong
It is beneficial to use intravenous metoclopramide prior to endoscopy	II-3	Strong
Endoscopic variceal ligation (EVL) is preferred over endoscopic sclerotherapy (EST) for treating esophageal varices	I	Strong
EST should be performed when EVL is not technically feasible	I	Strong

Predictors of esophageal variceal rebleeding

Rebleeding of esophageal varices occurs in 10% to 20% of patients after initial bleed control (with EVL) [28]. Failure to control bleeding (within 48 hours) or early rebleeding (2–5 days) requires similar approach to management. Variceal rebleeding is seen more often in patients with advanced liver disease [30–35]. Predictors of rebleeding can be broadly divided into clinical, endoscopic, and others (HVPG, elastography). There is evidence that presence of jaundice as well as refractory ascites is predictive of rebleeding rates. Similarly, portal vein thrombosis and hepatocellular carcinoma patients have a higher portal pressures and higher rebleeding. Patients with higher Child-Turcotte-Pugh (CTP) and MELD scores have higher risk of rebleeding [36–38]. In a prospective cohort study, MELD-Na was shown to have best predictive value for rebleeding (compared to MELD and CTP score) (area under the curve [AUC] 0.83 vs. 0.77 and 0.70) [38]. Also there is higher rebleeding with ongoing alcohol abuse.

Endoscopic findings of active bleeding (spurt) and higher grades of varices as well as presence of white nipple sign or clot over varix have been associated with higher risk of rebleeding. Among other parameters, it has been suggested that elastography (ultrasound or magnetic resonance [MR]) may be able to predict rebleeding [39, 40]. The concept seems plausible (higher liver stiffness may reflect higher portal pressure), but these have not been evaluated as predictors. There is insufficient evidence to recommend elastography as predictor of rebleeding.

The single most important factor predictive of rebleeding is HVPG. Rebleeding in patients with HVPG >20 mmHg has been proven to be higher in an RCT [41], several prospective cohort, and retrospective studies [42–45]. Since HVPG has a good predictive value for rebleeding, it is suggested that in patients with rebleeding after initial control, HVPG is advisable (if available) to guide further therapy. Patients with HVPG > 20 mmHg may do better with transjugular intrahepatic portosystemic shunt (TIPS) compared to EVL with beta blockers. There are some data to suggest that in bleeders with HVPG >20 mmHg, pre-emptive therapy in the form of TIPS or percutaneous transhepatic variceal embolization (PTVE) early after bleed control may be considered instead of waiting for rebleeding. However, more data are required before this can be recommended as a standard of care. Also, in view of expenses as well as limited availability of TIPS or PTVE, these cannot be recommended as standard of care.

Statements	Level	Grade
Failure to control bleeding/rebleeding with endoscopic variceal ligation + beta blockers (EVL+BB) may occur in 10% to 20% of patients with esophageal variceal bleed	I	Strong
More severe liver disease (presence of jaundice, ascites, higher Child-Turcotte-Pugh [CTP] score, high model for end-stage liver disease [MELD]/MELD-Na score) are predictive of variceal rebleeding	II-2	Strong
Presence of portal vein thrombosis (PVT) as well as hepatocellular carcinoma (HCC) are associated with a higher risk of rebleeding	II-2	Strong
Ongoing alcohol abuse is a predictor of variceal rebleeding	II-2	Strong
Large high risk varices, presence of active bleeding or white nipple sign/clot over varix are endoscopic predictors of failure to control bleeding/rebleeding.	II-2	Strong
HVPG ≥20 mmHg is a good predictor of variceal rebleeding	I	Strong
EVL+BB are associated with high risk of treatment failure in patients with HVPG ≥20 mmHg	I	Strong
In patients with a rebleed, HVPG is advisable to guide further therapy	II-2	Weak

Early TIPS in acute variceal bleeding

TIPS is a flow-diversion procedure that can be used for uncontrolled variceal hemorrhage. It is a percutaneous imaging-guided procedure in which a channel is constructed within the liver with the intent of reducing portal pressure by diverting blood from the portal to the systemic circulation. This reduces the portosystemic pressure gradient by functioning as a side-to-side portacaval shunt. By creation of a TIPS, successful reduction of the portosystemic pressure gradient can be achieved in over 90% of the cases.

Early TIPS has been defined as TIPS procedure performed within 24–72 hours of initial endoscopy in a bleeder (with a risk of rebleeding). The role of TIPS in AVB has evolved from a conflicting role to an established treatment option for decreasing rebleeding and mortality in AVB. The first randomized study to evaluate the role of early TIPS showed that increased portal pressure estimated by early HVPG measurement is a reliable prognostic factor of treatment failure and survival after AVB. In this study, an HVPG cutoff value >20 mmHg showed poor survival and early portal decompression by TIPS placement in this high-risk group reduced treatment failure and improved short- and long-term survival [41]. Another RCT which assessed the efficacy of TIPS in AVB showed that patients with a high risk of bleeding with CTP score 10-13 and those with CTP 7–9 with active bleeding at the time of endoscopy showed a significant reduction in

treatment failure and mortality by early TIPS [46]. Subsequently in the post-RCT surveillance study, patients treated with early TIPS had a much lower incidence of failure to control bleeding or rebleeding than patients receiving drugs plus endoscopic treatment (3 vs. 15; p <0.001). The 1-year actuarial probability of remaining free of this composite end point was 93% vs. 53% (p <0.001) [47]. However, a study from France showed that early TIPS may not improve survival in patients with severe liver disease with high CTP and MELD scores though it may reduce rebleeding rates, suggesting that selection of candidates for TIPS has to be appropriate [48]. Two recent meta-analyses on the role of early TIPS in AVB have suggested that there is reduced rebleeding and mortality in this group; however, careful selection of the patients has to be done [49, 50]. In a multicentric real-life study, one-third of the patients with cirrhosis and variceal bleeding were eligible for early-TIPS. However, TIPS was restricted to 7% of patients displaying less severe cirrhosis suggesting that TIPS can be beneficial only in a small subgroup of patients in real-life [51]. Hence, early TIPS should be considered in patients with high risk of variceal bleeding with an HVPG >20 mmHg or CTP scores of 10-13 or class B with active bleeding during endoscopy. TIPS is safe and effective in controlling AVB and preventing rebleeding and reducing mortality. The role of early TIPS is not definitive in patients with Child status C cirrhosis with a CTP score >13.

Statements	Level	Grade
Early transjugular intrahepatic portosystemic shunt (TIPS) is safe and effective in controlling acute variceal bleed in selected high risk patients	I	Strong
Early TIPS should be considered where available, in acute variceal bleed in high risk patients • Hepatic venous pressure gradient (HVPG) >20 (where available) •Child B with active bleeding during endoscopy •Child C with CTP score of 10-13	I	Strong

Management of esophageal variceal rebleeding (failure to control bleeding and rebleeding)

Failure to control the acute bleeding is defined as follows: > 2 hours after the start of specific therapy, if there is death or any of the following within 48 hours after initial endoscopy.

- Fresh hematemesis or more than 100 mL of fresh NG aspirate
- Development of hypovolemic shock
- >2 g/dL drop in hemoglobin within any 24-h period

We classified rebleeding as early rebleeding (occurring after an initial control of bleeding and between 2 to 5 days) and late rebleeding (after an initial control of bleeding and after 5 days). However, the management of failure to control bleed and early rebleeding would remain similar.

Failure to control gastrointestinal hemorrhage or cases with rebleeding should be managed in the same manner as the index bleed with few differences. First step remains resuscitation with an aim to bring systolic BP >100 mmHg, Hb 7–8 g/dL, platelet support when count <50,000/mm^3, clotting factor support if INR >1.5, and to maintain adequate urine output. A second attempt at endoscopic therapy should be attempted within 12–24 h of presentation, once the patient has stabilized. As a bridge to the time when endoscopy can be arranged, several other measures can be taken.

Pharmacological treatment with either terlipressin, somatostatin or octreotide should be initiated. In desperate situations, a Sengstaken-Blakemore tube (SBT) can be used, which is an effective holding measure for a maximum of 24–48 hours. Success in controlling acute bleed is about 90%; however, more than 50% re-bleed when the gastric balloon is deflated. Severe complications such as ulceration, esophageal and tracheal rupture have been reported [52, 53].

Endoscopic therapy has several options such as hemostatic powder spray, SX Ella-Danis stent, EVL, EST, and, finally, endoscopic ultrasound (EUS)–guided therapies.

Dedicated fully covered self-expanding metal stent (Sx Ella Danis, Hradec Kralove, Czech Republic) is increasingly being used where balloon tamponade was considered earlier [54]. In a recent meta-analysis of 13 studies (mainly case series, n=2 to 34; 134 patients total) with refractory bleeding from esophageal varices, it was noted that stent was successfully placed in 95%, achieving hemostasis within 24 hours in 96%. Overall pooled estimate rate for failure to control bleeding during follow-up was 0.18 [55]. However, adverse events may occur: ulceration, rebleeding after removal (16%), and stent migration (28%) have been reported. Hence, retrieval of the stent is recommended within 5–7 days.

There are three types of hemostatic powders currently available for endoscopic usage: (a) hemostatic agent TC-325 (Hemospray; Cook Medical, Bloomington, Indiana), (b) EndoClot polysaccharide hemostatic system (EndoClot Plus, Santa Clara, CA, USA), and (c) Ankaferd blood stopper (Ankaferd Health Products Ltd, Istanbul, Turkey). By contact with moisture, the powder forms a stable mechanical barrier that covers the bleeding site, inducing hemostasis. Only the first one has been investigated in AVB management. After approximately 24 hours, the adherent layer subsequently sloughs off into the lumen from the mucosal wall and is eliminated from the gastrointestinal (GI) tract [56]. The timing of endoscopic hemostasis in use of powder is controversial. Currently it is used with medical treatment as bridging therapy till definitive endoscopic treatment is possible. It has only been studied on a small scale for such difficult bleeding situations as post-band ligation ulcer [57]. To date, the only

validated option in this situation is a high dose of proton pump inhibitors and injection of cyanoacrylate underneath the ulcer in conjunction with pharmacotherapy [58].

TIPS should possibly be considered as treatment of choice for rebleeding [3, 59]. Rebleeding during the first 5 days may be managed by a second attempt at endoscopic therapy, and if severe, polytetrafluoroethylene-covered TIPS is likely the best option [51]. TIPS (rescue TIPS) is considered as the definitive rescue for failure of endoscopic therapy (to control variceal bleeding). Even if clinical evidence exists for selected patients that TIPS is the treatment of choice after initial failure of endotherapy, its availability within the recommended time frame (48–72 h) remains a matter of concern in many places.

EUS-guided therapy is the new kid on the block. EUS provides real-time, high-quality images of both the GI wall and major arterial and venous vessels like the confluence, splenic artery, and hepatic artery that can be accessed and obliterated [60]. This technique may allow a rescue EUS-guided therapy via injection of cyanoacrylate or insertion of coils. The safety and efficacy of the EUS-guided sclerotherapy were shown in a RCT that compared endoscopic sclerotherapy with EUS-guided sclerotherapy in which 50 cirrhotic patients were randomized to undergo either endoscopic sclerotherapy or EUS-guided sclerotherapy. EUS-guided sclerotherapy was at least as effective as endoscopic sclerotherapy, with a lower recurrence rate [61].

Statements	Level	Grade
Patients who fail to stop bleeding after initial endoscopic therapy are candidates for a second attempt at endoscopic therapy with endoscopic variceal ligation (EVL) or glue injection.	II-2	Strong
Till definitive therapy can be organized, a bridging therapy with Sx Ella-Danis Stent (5-7 days) or Sengstaken-Blakemore tube (SBT) (24-48 h) may be offered.	II-3	Strong
Definitive rescue therapy for failure of second attempt at endoscopic therapy is TIPS for esophageal variceal bleed	I	Strong

Impact of acute variceal bleed on other organs

Acute variceal bleed leads to hemodynamic and systemic effects resulting in but not limited to increased risk of bacterial infections, renal failure, and precipitation of hepatic encephalopathy (HE).

Systemic bacterial infections

Variceal bleed is an established risk factor for bacterial infection in patients with cirrhosis [62]. Up to two-thirds of cirrhotic patients with UGIB may develop bacterial infection within the first 5–7 days of the bleeding episode [63]. In addition to being immunocompromised, cirrhotics also exhibit excessive activation of proinflammatory cytokines and are prone to spontaneous bacterial infections, hospital-acquired infections, and a variety of infections from uncommon pathogens [64]. Moreover, bacterial translocation from intestines is common as UGIB disturbs intestinal barrier function and local immune defense function [65]. The most frequent infections are spontaneous bacterial peritonitis and spontaneous bacteremia (50%), urinary tract infections (25%), and pneumonia (25%). Infections in bleeding cirrhotics are associated with failure to control bleeding, early rebleeding, abnormities in coagulation, and early mortality [66]. The administration of oral or systemic antibiotics (penicillins, cephalosporins, and/or quinolones) decreases the incidence of bacterial infections. A meta-analysis of 12 RCTs shows clear survival benefit for the early use of prophylactic antibiotics during an AVB (RR=0.79, 95%CI 0.63–0.98) [67].

Acute kidney injury

Gastrointestinal bleeding has a deleterious effect on kidney function due to various reasons. Reduced intravascular volume caused by the blood loss causes renal hypoperfusion leading to a reduction in glomerular filtration rate. Renal function also gets adversely affected by bacterial infections, which develop frequently in the setting of GI bleeding [68, 69]. Loss of blood volume also aggravates the already-reduced effective arterial blood volume in advanced cirrhosis and triggers the development of hepatorenal syndrome. Renal failure occurs frequently in these patients (10% to 40%), and its development is strongly associated with a very poor short-term prognosis. Management principles include supporting the renal function by adequate volume and electrolyte replacement and monitoring the urine output. Nephrotoxic drugs should be avoided, particularly aminoglycosides and non-steroidal anti-inflammatory drugs. Beta blockers need to be withdrawn. Vasoconstrictors (terlipressin or norepinephrine) in combination with IV albumin remain the preferred modality for treatment of modality for hepatorenal syndrome. In patients with AKI with variceal bleed, terlipressin is the vasoconstrictor of choice (preferred over somatostatin and octreotide [discussed in treatment section]).

Hepatic encephalopathy

Development of HE is a serious complication following variceal bleeding and is associated with increased morbidity and mortality [70]. Incidence of HE is lower in cirrhotic patients with upper UGIB treated with lactulose as compared those not

treated with lactulose [71]. Rifaximin is comparable to lactulose in treatment and prevention of HE [72].

Primary and secondary prophylaxis of esophageal varices

All cirrhotics should undergo screening endoscopy for assessment of varices. Pre-primary prophylaxis refers to the use on non-selective beta blockers (NSBBs) to prevent development of varices. A RCT on use of timolol to prevent development of varices did not show any effect on varix formation or bleeding [73]. The use of NSBBs for pre-primary prophylaxis is not recommended.

Primary prophylaxis refers to use of NSBBs in patients with varices. The utility of primary prophylaxis for small (low risk) esophageal varices is not very clear. A meta-analysis of 5 RCTs on this issue showed that the incidence of development of large varices and variceal bleeding and death were similar in beta-blockers group compared to placebo group [74]. However, as discussed before, small varices with red color signs should be considered high-risk varices and primary prophylaxis is recommended. There is enough evidence that primary prophylaxis should be offered for large varices (with or without RCS). The modalities of prophylaxis also have been extensively studied (NSBBs, EVL, combination). Two meta-analyses of RCTs on use of NSBBs vs. placebo showed a reduced incidence of bleeding and a trend towards less mortality in patients on beta-blockers [75, 76]. Both propranolol and carvedilol have been shown to be effective in reducing portal pressure and hence incidence of bleeding [77]. However, carvedilol should be avoided in Child C patients as it has potent hypotensive effects which may have deleterious effect in this subgroup of patients. EVL is the preferred method of variceal eradication (preferred over sclerotherapy). A meta-analysis of 5 RCTs showed EVL to be superior to no intervention in reducing bleeding as well as mortality in patients with high-risk varices [78]. The jury is still out on choice between NSBBs and EVL for primary prophylaxis. This has been a subject of various RCTs and meta-analysis with variable results. A recent Cochrane database review of 19 RCTs showed a reduced incidence of bleeding in EVL group, but the mortality rates (bleed related as well as overall) were not different between the two groups [79]. Use of NSBBs was associated higher incidence of hypotension, dizziness, and lethargy, whereas EVL patients had bleeding from post-EVL ulcers and significant pain. Post-banding ulcer bleeding is an uncommon but severe complication of EVL. Patients with HCC, poor liver function, and low beta blocker dose have higher risk of post-banding ulcer bleeding. Use of nitrates (with or without NSBB) or combination of EVL and NSBB is not recommended for primary prevention.

Secondary prevention refers to prevention of rebleeding after an episode of variceal bleeding. The evidence in this case is overwhelmingly in favor of a combination of EVL and NSBBs. Multiple RCTs as well as meta-analyses have shown that combination strategy is better than either alone in secondary prophylaxis [80–83].

The response to NSBBs can be accurately predicted by measuring HVPG. A good response is defined as a decrease in HVPG below 12 mmHg or by ≥ 20% from baseline [84]. However, HVPG is an invasive procedure with a definite risk of associated infection and other complications and not routinely available at all centers. Its use cannot be routinely recommended. However, when performed, it can help titrate the maximum dose of NSBBs as well as predict possible non-response to beta-blockers.

Statements	Level	Grade
Pre-primary prophylaxis for prevention of variceal development is currently not indicated	I	Strong
Non-selective beta blockers (NSBB) can be used as 1° prophylaxis for small/low risk esophageal varices	I	Strong
NSBB or endoscopic variceal ligation (EVL) can be used as 1° prophylaxis for large/ high risk esophageal varices	I	Strong
Both propranolol and carvedilol are acceptable first line agents for 1° prophylaxis	I	Strong
Hepatic venous pressure gradient (HVPG) measurement (baseline and post NSBB) provides an add-on information on prognosis	II-1	Strong
Use of NSBB in refractory ascites, spontaneous bacterial peritonitis (SBP) and acute kidney injury (AKI) needs to be carefully monitored and individualized	II-C	Weak
NSBB (propranolol) + EVL combination is the preferred option for 2° prophylaxis of variceal bleed	I	Strong

Gastric varices—prophylaxis and endoscopic management of bleeding

Gastric varices have been classified according to the classification suggested based on Sarin et al. [9]. Approximately 25% of patients with PHT have GV [85]. The prevalence of GV and GVB is lesser than that of esophageal varices and therefore high-quality RCTs which address management of GV have been difficult.

Gastric variceal bleed tends to be more severe, require more transfusions, and are associated with higher mortality. The main factors associated with a higher risk of GVB are large size >10 mm, presence of red spots, and severity of liver dysfunction. Location of the varices also determines risk of bleeding with IGV1 (78%) having the highest risk followed by GOV2 (55%) [86]. The current management strategies include pharmacotherapy, endoscopic therapies, interventional radiology techniques like TIPS and balloon-occluded

retrograde transvenous obliteration (BRTO), and surgical interventions.

In acute bleeding GV, the initial management including antibiotic use, vasoactive medications, and correction of hypovolemia is similar to esophageal varices outlined above. Endoscopic therapy mainly consists of cyanoacrylate injection to achieve hemostasis. A Cochrane review showed that cyanoacrylate injection is an effective modality to achieve hemostasis as compared with other modalities [87]. EUS-guided coil injection with or without cyanoacrylate injection may also be useful in AVB but needs more evidence. In varices that cannot be controlled by endoscopic therapy, interventional radiological methods like TIPS and BRTO may be considered (discussed below).

Gastroesophageal varices 1 are basically extensions of esophageal varices below the lesser curvature of stomach and are the most common (75% of GV) [3, 9]. Therefore, management of GOV1 is similar to that of esophageal varices. No RCT specific for primary prophylaxis for GOV1 is available. Pharmacotherapy with NSBB may be considered for primary prophylaxis of GOV1. Endotherapy for esophageal varices is the standard of care for primary prophylaxis in high-risk varices. For secondary prophylaxis of GOV1, NSBB along with obliteration of esophageal varices by EVL would be recommended similar to recommendations for treating esophageal varices.

Due to lack of studies, primary prophylaxis recommendations for GOV2 and IGV1 also rely on extrapolation from recommendations for esophageal varices. Reduction in HVPG following NSBB may therefore form a premise for recommending NSBB for primary prophylaxis, even though it is well known that GVB may not be entirely dependent on HVPG. Endoscopic therapy for GOV2 and IGV1 mainly comprises of injection of cyanoacrylate (glue) in the varix. Mishra et al. [88] included 89 patients with large (10 mm) GOV2 and IGV1 which had not bled. Patients were randomized to endoscopic injection of cyanoacrylate, NSBBs, and observation. Cyanoacrylate injection was associated with lower bleeding rates (10%) than NSBBs (38%) and observation (53%). Survival was higher in the cyanoacrylate group (93%) compared to observation (74%), but no different from those on NSBBs (83%). Cyanoacrylate injection of large GOV2 and IGV1 may thus be beneficial as primary prophylaxis. EUS-guided coiling is a new option available for endotherapy of GV. A study by Romero-Castro et al. [89] comparing EUS-guided coil placement with cyanoacrylate injection revealed less complications, reduced hospital stay, and decreased endoscopic sessions with coil placement compared to cyanoacrylate injection. Weilert et al. [90] reported coil deployment prior to glue injection appears to reduce the amount of glue to achieve varix obliteration and may prevent embolization. EUS-guided coiling with or without glue injection appears to be a reasonable alternative to glue injection only, but availability of this option is not widespread. TIPS or BRTO are currently not recommended for primary prevention of GVB.

For secondary prophylaxis in GOV2/IGV1, pharmacotherapy alone has shown no definite benefit. Beta blockers and nitrates do not decrease the risk of rebleeding and do not improve the overall survival in patients with GVB. Mishra et al. [91] conducted a RCT comparing endoscopic cyanoacrylate injection vs. beta-blocker for secondary prophylaxis of GVB. Probability of gastric variceal rebleeding rate in the cyanoacrylate group who underwent repeated injections was significantly lower than in the beta-blocker group and mortality was lower. Hung et al. [92] compared glue injection alone vs. glue injection plus propranolol. Forty-eight and 47 patients were included in each group, respectively. The study showed similar re-bleeding rates between both groups, 54% vs. 47%. Therefore, adding NSBB therapy to obliteration of GV provides no benefit as secondary prophylaxis.

Statements-Gastroesophageal varices type 1	Level	Grade
Primary prophylaxis		
Non-selective beta blockers (NSSB) may be used for primary prophylaxis of gastric varices.	III	Weak
Endotherapy (EVL) for esophageal varices is the standard of care for primary prophylaxis for gastroesophageal varices type 1 (GOV1)	II	Strong
Secondary prophylaxis		
NSBB with obliteration of esophageal varices is recommended for GOV1	III	Strong

Statements – Gastroesophageal varices type 1, Isolated gastric varices type 1	Level	Grade
Non-selective beta blockers (NSSB) can be used for primary prophylaxis of gastroesophageal varices type 2 (GOV2) and isolated gastric varices type 1 (IGV1)	III	Weak
Use of glue injection for primary prophylaxis of high risk gastric varices is acceptable	I	Strong
Endoscopic ultrasound (EUS) guided coiling in expert hands is also an option for primary prophylaxis for high risk GOV2/IGV1	III	Weak
Glue injection until eradication of gastric varices (GV) is recommended for secondary prophylaxis of GOV2	I	Strong
Combination of EUS guided coiling with glue injection is a promising technique in treatment of bleeding GV	II-2	Strong
Surgery is not recommended for primary prophylaxis of GOV2/IGV1	III	Strong
In absence of cirrhosis, patients with isolated GOV2/IGV1 with splenic vein thrombosis, - splencectomy is recommended for secondary prophylaxis	III	Strong
In extrahepatic portal venous obstruction (EHPVO) with bleeding GOV2/IGV1, shunt surgery can be considered as a one-time treatment option	III	Weak

Gastric varices—interventional radiology

Balloon-occluded retrograde transvenous obliteration and TIPS are safe and effective interventional treatments in the management of GVB [93–96]. These are however not recommended for the primary prophylaxis of GV. A RCT comparing TIPS with glue injection showed that TIPS was more effective in preventing rebleeding, albeit with a higher rate of encephalopathy. Thirty-five patients were allocated to TIPS and 37 to cyanoacrylate injections after acute bleeding was controlled. Re-bleeding from GV was lower in the TIPS group, 11% vs. 38%, $p = 0.014$ [97]. Another retrospective study comparing TIPS and cyanoacrylate therapy for GV bleeding found that the rebleeding and mortality rates were similar between the two groups [98].

In BRTO, obliteration of GV is done by accessing the varices by cannulating the gastro/lienorenal shunt. Thereafter, the shunt is occluded using a balloon catheter and sclerosant is injected into the shunt to completely fill the varix and lead to formation of thrombus. Hence, BRTO is technically possible in patients with GV and a gastro/lienorenal shunt. BRTO has shown to be effective in controlling GVB with lesser rebleed rate and it is considered in appropriate patients with GVB not responding endoscopic n-butyl cynoacrylate (glue) injection [99, 100]. In the past, ethanolamine oleate was the most commonly used sclerosant for BRTO but it was seen to be associated with various side effects. Sodium tetradecyl sulfate (STS) has lesser side effects and similar efficacy, so it is the preferred sclerosant for BRTO [101, 102]. Aggravation of esophageal varices is seen in patients undergoing BRTO [103], so it is recommended to eradicate esophageal varices prior to BRTO and periodic endoscopic screening should be done to look for any progression/appearance of esophageal varices. In patients having GVB with no gastro/lieno-renal shunt, TIPS should be considered along with embolization of GV for better and effective control of GVB [96, 104].

Statements	Level	Grade
Balloon-occluded retrograde transvenous obliteration (BRTO) and transjugular intrahepatic portosystemic shunt (TIPS) are safe and effective in the management of gastric variceal bleed	I	Strong
BRTO should be considered in appropriate patients with gastric varices (GV) bleed not responding to endoscopic n-butyl cynoacrylate (glue) injection (in patients having gastrorenal shunt)	I	Strong
Eradication of esophageal varices should be done in all patients undergoing BRTO and such patients should screened periodically for progression/appearance of esophageal varices	II-2	Strong
TIPS with embolisation of GV should be preferred in GV bleed if gastrorenal shunt is absent or patient has high risk esophageal varices	II-2	Strong

Management of ectopic varices

Ectopic varices include GV in the distal stomach, small bowel varices, and colorectal varices. Ectopic varices can also occur in the biliary tract, in the peritoneal or omental linings, peristomal area, and rarely in the pelvic organs including the ovaries, uterus, or urinary bladder.

The clinical approach to documented or suspected ectopic varices includes the following: (1) define the presence or absence of underlying cirrhosis; (2) define the anatomical extent of any underlying splanchnic venous occlusion (portal vein [PV], splenic vein [SV], superior mesenteric vein [SMV], or their tributaries); and (3) any local contributing factors, like surgically altered anatomy, adhesions or scarring form previous surgery, or local inflammatory process like pancreatitis or tuberculosis, etc. Doppler ultrasound is used to define the patency of PV (intra-hepatic branches as well as outside the liver), distal SMV, and SV. It can also define the direction of meso-portal blood flow (hepatopetal, hepatofugal, or alternating). Contrast-enhanced computed tomographic (CECT) scan with multi-planar reconstruction (MPR) remains the gold standard for treatment planning for ectopic varices.

Duodenal ectopic varices are usually part of porto-portal or portosystemic bypass, in the presence of underlying PV and/or SMV thrombosis. Jejunoileal varices are often seen in patients with underlying PHT, who have had prior segmental jejunal or ileal resections, at surgical anastomosis sites after pancreaticoduodenectomy, at hepaticojejunostomy site, inflammatory intra-abdominal scarring, or at ileal stoma site. Colorectal varices can be seen in the following clinical settings: splanchnic venous thrombosis (idiopathic, post-pancreatitis, or pancreatic cancer), cirrhosis, or Klippel-Trenaunay syndrome. There is an inconsistent relationship of colorectal varices with the etiology of underlying PHT, degree of liver dysfunction, or status of esophageal varices or GV [105, 106]. Rectal varices bleed in <5% of cirrhotic patients; however, the bleeding can be massive and fatal. Johansen et al. showed that the risk of rectal variceal bleeding increased with more advanced form (F3) and presence of RCS on the varices and was unrelated to the degree of liver dysfunction or prior treatment for esophageal varices [107].

There is no data to support routine prophylactic treatment of ectopic varices. Endoscopic treatments are applicable when the ectopic varices can be reached by gastroscopy, colonoscopy, echoendoscopy, or deep enteroscope. Cyanoacrylate glue injections, EST, EVL, mechanical clipping, thrombin injections, and EUS-guided endotherapy have been described in small series of patients.

Radiological treatment options are the cornerstone for treatment of ectopic varices. These include either meso-portal decompression or obliteration/sclerosis of the ectopic varices. Radiological meso-portal decompression by TIPS or recanalization of the PV occlusion may be very effective when

feasible. Sclerosis of the ectopic varices can be achieved by angiographic occlusion of the afferent vein, BRTO, balloon-occluded antegrade transvenous obliteration (BATO) via transhepatic or trans-TIPS route, or a combination of techniques [108].

Surgery remains an effective option for treating certain ectopic varices, especially jejunoileal varices in non-cirrhotic patients. Surgery may involve surgical ligation excision, and/or decompressive shunts.

Statements	Level	Grade
Triple phase computed tomography (CT) of abdomen is the gold standard for treatment planning for ectopic varices	III	Strong
In view of absence of data, prophylactic treatment of ectopic varices is not recommended	III	Strong
Role of pharmacotherapy is undefined for control of ectopic variceal bleeding.	III	Weak
There are insufficient data to recommend one endoscopic treatment modality over another for duodenal variceal bleeding. However, glue may be the preferred modality	III	Strong
Radiological treatments are effective for ectopic varices, and include embolization of the afferent vein alone, TIPS combined with embolization, and balloon-ccluded retrograde transvenous obliteration (BRTO). The choice of treatment modalities should be carefully tailored in each case	II-2	Strong
In patients with ectopic varices, endoscopic treatment by standard ileo-colonoscopy, push-enteroscopy, or balloon - assisted endoscopy is the first line treatment, if patient is hemodynamically stable	III	Strong
There is no data to suggest superior efficacy or safety among cyanoacrylate glue or sclerosant solutions	III	Strong
Individualized interventional radiological approach is preferred when endoscopic treatment is not feasible	II-2	Strong
Surgery remains an effective option for treating ectopic variceal bleeding in non-cirrhotic patients	II-2	Strong

Acute variceal bleeding in NCPH

There are limited data on the use of vasoactive agents in the management of AVB in the setting of NCPH. Endotherapy has replaced surgery as the preferred modality of therapy in AVB in NCPH. Dhiman et al. [109] reviewed 151 cases of non-cirrhotic portal fibrosis (NCPF) over 15 years. While surgery was the preferred modality for treatment of variceal bleeding in the earlier part of the study period, EST became the preferred mode of therapy in the latter part of the study.

Both EST and EVL have been shown to be effective in the control of AVB. Many authors have shown the efficacy of EST in extrahepatic portal venous obstruction (EHPVO) [110–114]. Chawla et al. [115] showed sclerotherapy with absolute alcohol and sodium tetradecyl sulfate (STD) to be effective in 72 patients with NCPF. Variceal obliteration was achieved in 65 (90.3%) patients with a mean of 5.7 ±3.0 (range 1 ± 14) sessions with rebleeding in 13 (17.3%). Bhargava et al. [116] showed comparable efficacy of emergency EST for active variceal bleeding due to cirrhosis of the liver, NCPF, and EHPVO. However, the results were influenced by the etiology of PHT and hepatic functional status. Their study on 202 patients with variceal bleeding included 123 with cirrhosis, 49 with NCPF, and 30 with EHPVO. EST was done with polidocanol and hemostasis was achieved in 177 (88%). Rebleeding occurred in 31 (17.5%) and was lower in EHPVO than cirrhosis or NCPF. The Child status influenced the rebleeding with lower rebleeding in Child A patients. Besides differences in active variceal bleed, success of eradication of varices with sclerotherapy has been shown to be greater in EHPVO (92%) and NCPF (87%) than cirrhotics (75%) [117]. However, in view of higher complication rates with sclerotherapy, it has largely been abandoned in favor of EVL.

Over a period of time, EVL has been shown to be more effective in initial control of bleeding and is associated with better survival than EST [118]. Zargar et al. [119] have shown that EVL is superior to EST, because it is less costly and achieves variceal eradication more quickly, with relatively lower frequencies of recurrent variceal bleeding and complications.

Prophylaxis

There are insufficient data on whether NSBBs or endoscopic therapy should be preferred for primary prophylaxis in EHPVO. While there are some data on the use of cyanoacrylate glue for the primary prophylaxis of GVB in patients with NCPH [120], the same need to be validated by other studies. Although the data on NSBBs in secondary prophylaxis are also limited, NSBBs are probably as effective as EVL for secondary prophylaxis. Sarin et al. [121] have shown equal efficacy of EVL and propranolol in secondary prophylaxis of variceal bleeding in patients with NCPH.

The Baveno VI guidelines have concluded that there are insufficient data on which therapy should be preferred for PHT prophylaxis in NCPH and such patients should be managed as Child A cirrhosis [122].

Role of shunt surgery

While shunt surgery was carried out routinely earlier, there have been concerns on shunt patency over long-term follow-up. Mishra et al. reported shunt patency rates of as low as 43% after 5 years of follow-up [123].

Conventionally, pharmacological and endoscopic management are recommended for management of variceal bleed and surgical therapy is used only for refractory bleeding. However, shunt surgery has certain advantages and unlike in

patients with cirrhosis, shunt surgery should be considered in the secondary prophylaxis of NCPH, especially patients with EHPVO. The availability of a physiological shunt (mesenteric-left-portal bypass or Rex shunt) brings to focus the role of primary shunt surgery in the management of EHPVO. Besides correcting PHT, this also improves the systemic manifestations of EHPVO such as improvement in liver functions, reversing growth retardation and normalization of coagulation parameters [124]. Moreover, early shunt surgery may possibly prevent portal cavernoma cholangiopathy (PCC) which occurs in 3.6% to 4% children with EHPVO after 12–15 years [125, 126]. Shunt surgery should be considered in patients who stay in remote areas with limited access to healthcare facilities. PCC is universal in adults and symptomatic biliary obstruction can be managed endoscopically, but shunt surgery followed by biliary bypass if necessary seems to be the best management strategy.

Prognosis

While the severity of the liver disease seems to be the primary determinant of outcome in cirrhotic patients with variceal bleeding (MELD values of 19 or greater have been shown to predict 20% or greater mortality, whereas MELD scores less than 11 predicted less than 5% mortality [127], EHPVO-related mortality is primarily determined by causes other than variceal bleeding [128].

Statements	Level	Grade
Endoscopic therapy is effective in control of acute variceal bleeding in non cirrhotic portal hypertension (NCPH). Endoscopic variceal ligation is preferable to endoscopic sclerotherapy	II	Weak
While data on use of pharmacological agents for prophylaxis in NCPH are limited, it is reasonable to manage them on the lines of compensated cirrhosis.	III	Weak
Shunt surgery may have a role in management of patients who fail endoscopic therapy, have symptomatic hypersplenism, or portal cavernoma cholangiopathy or stay in remote location with limited access to healthcare.	III	Weak

Portal hypertensive non-variceal bleed (NVB)

Gastric antral vascular ectasia vs. portal hypertensive gastropathy—diagnosis and management

Portal hypertensive gastropathy (PHG) is chracterized by changes in the gastric mucosa of patients with PHT due to vascular ectasia. PHG is recognized endoscopically as a mosaic-like pattern called snake-skin mucosa with or without red spots. Additionally, the terms portal hypertensive enteropathy and portal hypertensive colopathy are used to describe similar changes in the small bowel and colonic mucosa, respectively. PHG is classified as mild when the only change consists of a snakeskin mosaic pattern, and it is classified as severe when in addition to the mosaic pattern, flat or bulging red or black-brown spots are seen, and/or when there is active hemorrhage. Histologically PHG and gastric antral vascular ectasia (GAVE) are distinct entities. Full thickness mucosal biopsy in PHG shows dilated mucosal vessels without significant inflammation, while mucosal vascular ectasia, fibrin thrombi, and spindle cell proliferations are typical of GAVE [129].

NSBBs have been shown to be effective in controlling PHG bleeding but not for GAVE-associated bleeds. A RCT comparing propranolol vs. placebo for prevention recurrent bleed due to PHG showed that patients in the propranolol group were free of recurrent bleeding after 12 months (65% vs. 38%, $p< 0.05$) and at 30 months of follow-up (52% vs. 7%, $p< 0.05$) [130]. Another small trial showed control of acute bleed in 13 out of 14 patients (93%) of PHG with NSBB [131].

Vasoactive drugs like octreotide and terlipressin have also been shown to be useful in controlling PHG bleeding. In a trial of 68 subjects with PHG, patients were assigned to receive octreotide, vasopressin, or omeprazole [132]. Bleeding was controlled in all 24 of the patients who received octreotide, in 14 of 22 (64%) of the patients who received vasopressin, and in 13 of 22 (59%) of patients who received omeprazole. In another trial with 86 patients with bleeding from PHG or varices, those who received higher doses of terlipressin had better bleeding control and lower recurrence rates than patients who received lower doses [133]. In a series of 40 cirrhotic patients, TIPS placement was associated with decrease in transfusion requirement in 75% of patients with severe PHG [134].

In contrast, GAVE bleeding correlates poorly with PHT and hence is not controlled by NSBBs or vasoactive drugs [135]. Multiple studies have demonstrated usefulness of palliative endoscopic treatment with argon plasma coagulation (APC), laser or radiofrequency ablation (RFA) in GAVE with improvement in hematocrit and a decrease in the need for blood transfusion, re-bleeding or hospitalization [136–141]. An open pilot study in patient with chronic blood loss due to GAVE showed improvement in re-bleeding and decreased in need for transfusion from 4 units/month to 1.4 unit/month over a follow-up period of 11 months with estrogen-progesterone treatment [142].

Fourteen patients with GAVE who underwent TIPS had neither endoscopic resolution nor a decrease in transfusion requirements after TIPS [141].

Literature on role of antrectomy in GAVE is limited. A series of 3 patients with persistent iron deficiency anemia due to GAVE, treated with antrectomy and Billroth I anastomosis, showed stable hemoglobin levels over the follow-up period of 2 year [135, 143].

Role of NSBBs in portal hypertensive NVB

Primary prophylaxis of GI bleeding in patients with PHG has not been assessed, and it is usually not recommended. However, management in these situations needs to be done on an individual basis. The severity of PHG is an important factor taken into consideration. Mild PHG alone usually does not require primary prophylaxis. If the patient has small esophageal varices and mild PHG, the use of NSBBs may be considered because theoretically it can be of benefit for PHG [143]. In patients with severe PHG and no varices, prophylaxis with NSBBs can be considered. However, this approach is controversial and more research is needed to clarify if NSBBs should be implemented as primary prophylaxis for bleeding from PHG.

The use of NSBBs reduces bleeding secondary to PHG in RCTs [130, 131]. Thus, it is recommended to start propranolol (up to 160 mg) orally twice a day or to the maximum tolerated dose with goal heart rate (HR) of 50–55 beats per minute (bpm). Propranolol therapy should be continued as long as the patient continues to have PHT.

Secondary prophylaxis of bleeding in PHG should be with a NSBB. A study assessed the occurrence of PHG after endoscopic variceal ligation in 77 patients who were randomized to EVL alone (40 patients) or combined with propranolol (37 patients). Patients who received propranolol had a lower occurrence of PHG than patients who had only EVL [144].

Portal hypertensive colopathy and enteropathy

The evidence with which to base treatment strategies in portal hypertensive colopathy (PHC) is limited. Indeed, there is no established standard treatment of PHC or enteropathy. Most of the available recommendations are based on case reports or small series reports. In patients with chronic lower GI bleeding secondary to PHC, treatment with a NSBBs has been reported to be effective [145]. Another study demonstrated that there was a decreased risk of bleeding from PHC in patients with PHT who were taking B-blockers [146].

Statements	Level	Grade
Beta-blocker should be started in portal hypertensive gastropathy or colopathy with chronic blood loss	I	Strong
Beta-blocker is not an effective therapy for acute bleeding from portal hypertensive gastropathy or colopathy and gastric antral vascular ectasia (GAVE) related bleed	II-3	Weak

Epilogue

This is the first consensus on portal hypertensive UGIB from India. These recommendations provide a data-supported approach to risk stratification, diagnosis, and management of patients with portal hypertensive UGIB. These are based on a formal review and analysis of recently published Indian and world literature on portal hypertensive bleeding, outcomes of past consensus conferences, and the authors' years of experience caring for patients with PHT and bleeding. The consensus was formalized at a conference with use of modified Delphi process taking into account various quality control measures and validated grading system. Intended for use by healthcare providers, these recommendations suggest preferred approaches to the diagnostic, therapeutic, and preventive aspects of care and are intended to be flexible in their application. These guidelines cannot replace clinical judgment; they are only intended to offer general guidance applicable to the majority of patients with portal hypertensive bleeding. At times, clinical considerations may even justify a course of action that differs from this guideline. On the other hand, despite the existence of multiple guidelines, there is considerable variation in the care of patients with variceal bleeding, and consequently there is considerable room for quality improvement in compliance to these guidelines. Hence, just making guidelines for our patients alone may not be sufficient; we must also initiate programs to implement guideline-based care by standardizing care using checklists, appointing bleeding nurse-coordinators, or even developing dedicated variceal bleeding units, besides addressing the causes for guideline noncompliance [147–150].

Author's contribution SPS, SKA, MW, SB, and KM generated the initial list of statements. SPS and SKA constituted the core committee and coordinated with the participants for the consensus meeting/voting. MW, SB, KM, MKS, NB, SPM, AD, AM, ACA, AG, BSS, JV, MKP, MT, MKM, PP, PMR, RPW, ST, VT, and VB presented the statements with the evidence in the consensus meeting. All of these members and other delegate members of the ISG Task Force voted in the consensus meeting. All authors approved the manuscript.

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Compliance with ethical standards

Conflict of interest MW, SKA, SB, KM, MKS, NB, SPM, AD, AM, ACA, AG, BSS, JV, KKP, MT, MKM, PP, PMR, RPW, ST, VT, VB, and ISG-TSFUGIB declare that they have no conflict of interest.

SPS owns stock for Sun Pharmaceutical Industries Ltd., Torrent Pharmaceuticals Ltd., Dr. Reddy's Laboratories, and Panacea Biotec.

Ethical statement The study was performed in a manner to conform with the Helsinki Declaration of 1975, as revised in 2000 and 2008 concerning human and animal rights, and the authors followed the policy concerning informed consent as shown on Springer.com.

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