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British Society of Gastroenterology position statement on the American Association for the Study of Liver Disease practice guidance on risk stratification and management of portal hypertension and varices in cirrhosis

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INTRODUCTION

The British Society of Gastroenterology (BSG) recognises that the current UK guideline on the management of variceal bleeding in cirrhotic patients (2015)[1] requires updating. Recent updates to similar international guidance including the American Association for the Study of Liver Disease (AASLD),[2] European Society of Gastrointestinal Endoscopy (ESGE)[3] and Baveno VII,[4] as well as updated NICE cirrhosis guidelines[5] are acknowledged by the Clinical Guidelines Development (CGD) group. However, the CGD are also mindful of the large-scale, multicentre UK studies recently completed or currently in progress addressing both primary and secondary prophylaxis of variceal bleeding, with results expected to significantly influence UK best practice. Therefore, the CGD has opted to produce a position statement on the latest international guidance, while these data are pending. This decision is supported by the BSG Clinical Services (CS) committee. Furthermore, prioritising the identification of clinically significant portal hypertension (CSPH), rather than the management of varices alone, was felt to be an important shift in practice. On review, the CGD agreed that the AASLD guidance was most consistent with UK clinical practice. Therefore, the BSG endorses the interim use of the AASLD guidance in the UK, with some important caveats. The individual AASLD guidance statements are reproduced below, with necessary caveats added where applicable. These caveats primarily pertain to the recommendations for diagnosis of CSPH including the role of non-invasive tests (NITs), defining indications for non-selective beta-blockers (NSBB) and use of pre-emptive transjugular intrahepatic portosystemic shunt (pTIPSS) following acute oesophageal variceal bleeding (OVB).

As the evidence base is evolving, it is important to involve patients in decisions around their care and to ensure they are aware that there is still uncertainty around best practice and the implementation of the guidance. Individual patients' circumstances (including likely concordance with medication, tolerability of medications and endoscopies) should be considered and they should be made aware that the guidance and approach may change with new emerging evidence. Patients should also be carefully counselled on how to recognise an acute variceal bleed. Vulnerable patients should be offered support to attend endoscopy/clinic appointments to facilitate engagement.

SCOPE AND PURPOSE

The aim is to provide a BSG position statement on AASLD guidance for the

prevention and management of variceal haemorrhage, while results of current studies are awaited. This is intended for use by clinicians and other healthcare professionals managing patients with liver cirrhosis in both the out-patient and acute setting. It also includes proposed future areas for research.

METHODOLOGY

This position statement was drafted after discussion with the liver section and CS committees of the BSG. The liver committee recognise that large sections of the prior 2015 BSG guidance on this topic were out of date,[1] particularly following recent publication of other international guidelines.[2–5] The CGD group was formed, including gastroenterologists, hepatologists, hepatology nurse practitioners and pharmacists. The CGD determined that an extensive rewrite of the BSG guidelines was inappropriate, while the results of several large UK multicentre randomised controlled trials on prevention and management of variceal bleeding are pending. Therefore, a full review of the relevant corresponding international guidelines and associated literature was undertaken, and a decision by vote to endorse the AASLD guidance was accepted, with some caveats applied.

After several online meetings, the position statement was drafted by the authors, and, where necessary, individual guidance statements were discussed to identify relevant caveats that best reflect UK practice and up-to-date evidence. A consensus was reached on all points. The draft document was submitted for review and approved by the CS, the BSG liver section committee and peer-reviewed for publication.

Cirrhosis and ACLD

With the increased use of NIT to stage and monitor liver disease, there has been a shift in the terminology away from using the term cirrhosis (which is a histological diagnosis) to advanced chronic liver disease (ACLD). The term ACLD encompasses advanced fibrosis, identifying people with liver disease (usually on NIT) who are at highest risk of developing complications. ACLD can be further stratified according to the absence or presence of complications into compensated ACLD (cACLD) and decompensated ACLD (dACLD), respectively.

THE IDENTIFICATION OF CLINICALLY SIGNIFICANT PORTAL HYPERTENSION IN ACLD

The development of CSPH is a milestone in the progression of chronic liver disease and is associated with higher risk of progressing from compensated to decompensated disease. Decompensated disease is clinically recognised by the development of complications such as ascites, variceal bleeding and hepatic encephalopathy and is the prequel to mortality.[4] Although the median survival in the compensated patient exceeds 12 years, once a decompensating event occurs, the median survival decreases to less than 1.5 years. Therefore, the identification of CSPH is imperative to improve management and outcomes for these patients.

→ Hepatic venous pressure gradient (HVPG) measurement is the gold-standard method to assess portal pressure in patients with ACLD. CSPH is defined as HVPG ≥10 mm Hg. HVPG may underestimate portal pressure in some patients with obesity and metabolic dysfunction associated steatohepatitis (MASH)-related ACLD.

BSG position = agree, with caveats: HVPG is not commonly used in the UK out-with the research setting and lacks UK wide clinical expertise and infrastructure. Therefore, the use of HVPG is not routinely recommended in the clinical environment to identify CSPH. In addition to MASH, HVPG may underestimate portal pressure in any aetiology of liver disease with a presinusoidal component such as primary biliary cholangitis, primary sclerosing cholangitis (PSC) and others.

→ The presence of clinical decompensation, or gastro-oesophageal varices on endoscopy, or portosystemic collaterals or hepato-fugal/reverse flow in the portal vein on imaging, is sufficient to diagnose CSPH.

BSG position = agree.

→ CSPH can be non-invasively identified by liver stiffness measurement (LSM) using vibration-controlled transient elastography (VCTE) and platelet count. CSPH is diagnosed at LSM ≥25 kPa irrespective of platelet count, LSM 20–24.9 kPa with platelet count <150 K/mm3 or LSM 15–19.9 kPa with platelet count <110 K/mm3—known as the 'rule of five' criteria.

BSG position = agree, with caveats (figure 1).

Owing to its wide availability, BSG recommends LSM with VCTE as the NIT of choice to determine the likelihood of CSPH. However, as VCTE can lead to false-positive results, any patient with an index LSM ≥10 kPa should have LSM measurement repeated in fasting conditions. For patients with alcohol-related liver disease (ArLD), LSM should be sought after a period of abstinence where possible, and caution applied when interpreting results in patients with active alcohol-related hepatitis or reduced platelet counts due to potential concurrent alcohol-related thrombocytopaenia.

In patients with ArLD, chronic viral hepatitis and lean metoabolic dysfunction assoicated steatotic liver disease (MASLD), CSPH can be ruled in by LSM ≥25 KPa with a positive predictive value ≥90%.[6] However, the positive predictive value falls to 63% in patients with obesity and MASH.[6] Caution should therefore be applied in patients with obesity/MASLD/alanine aminotransferase >3 x upper limit of normal and repeat measurements made following any significant weight loss.[7] The ANTICIPATE-NASH model may be adopted to further stratify risk of CSPH in patients with MASLD; however, specific cut-offs for initiation of therapy are not defined.[8 9] Caution is also advised

CSPH ruled out:	Possible CSPH "Grey zone":	CSPH highly probable:
LSM <15 KPa AND plt ≥150	LSM 20-25 KPa and plt >150 OR LSM 15-20 KPa and plt 110-150 OR LSM <15 KPa and plt <150	LSM ≥25 OR LSM 20-25 KPa and plt <150 OR LSM 15-20 KPa and plt <110 Portosystemic collaterals or hepato-fugal/reverse flow in the portal vein on imaging
No indication for NSBB Endoscopy can be avoided	If MASLD = consider ANTICIPATE-NASH model Endoscopic screening: NSBB indicated if varices present	NSBB indicated Endoscopy can be avoided

Figure 1 Rule in, rule out criteria for diagnosis of CSPH.**

in patients who have PSC with dominant strictures, as false positives can occur.

LSM ≤15 KPa plus platelets ≥150×10^9/L rules out CSPH with sensitivity and negative predictive value of ≥90%.[4 6] *However, the 'rule in', 'rule out' criteria results in an unfavourable number of patients (40%–50%) with indeterminate results—the so-called 'grey zone'.*[6 10 11] *Introduction of the 'rule of five' criteria with the incorporation of platelet count to specific LSM cut-offs, as outlined above, may only reduce the 'grey zone' to 37%, with no reduction in rates of decompensation or death when compared with patients in the non-rule of five grey zone (9% at 3 years, 11% at 5 years).*[12] *However, performing an endoscopy to screen for varices in patients with indeterminate results may reduce the 'grey zone' to 22%, with a PPV for CSPH of 84%, and is associated with an observed reduction in rates of decompensation or death (3% at 3 years, 3% at 5 years).*[12]

For patients with indeterminate results per the rule of five criteria, endoscopy to screen for varices should be considered to confirm/exclude CSPH. If varices are present, NSBBs should be commenced. If varices are not detected, the LSM and platelet count should be repeated in 1 year. Patients unwilling to undergo endoscopy should be counselled on the decompensation and mortality event rates noted above—annual LSM and platelet count may be considered an alternative strategy, particularly for those with inactive disease.

→Annual LSM by VCTE and serum platelet counts may provide prognostic information in patients with cACLD without baseline CSPH in whom the underlying aetiologies of ACLD remain active/uncontrolled.

BSG position: agree. Furthermore, data from MASLD and viral CLD populations suggests a 20% increase or decrease in LSM correlates with a respective change in risk of decompensation.[13 14] *When the underlying cause of liver disease has been removed and LSM/platelet count has subsequently improved, withdrawal from CSPH detection screening can be pragmatically considered on a case by case basis.*

PREFERRED NSBB FOR CSPH

→ Carvedilol is recommended as the preferred NSBB for the treatment of CSPH in patients with cACLD.

BSG position = agree.

→ The recommended maintenance dosage of carvedilol is 6.25–12.5 mg/day. Maintenance dosage can be given as a single daily dose or divided two times per day. In patients with concomitant arterial hypertension or cardiac disease, the dose of carvedilol may be further increased to address non-hepatic indications.

BSG position = agree. UK guidance suggests starting carvedilol at 6.25 mg OD and then increasing to 12.5 mg OD is optimal for reduction in portal pressure without increasing the risk of complications of systemic arterial hypotension.[5] *However, recent clinical trial data suggests split dosing (Carvedilol 6.25 mg BD) may improve compliance and reduce side effects.*[15] *Taking with food could also help reduce the risk of symptomatic postural hypotension. For patients who do not tolerate a total daily dose of 12.5 mg, a reduced total daily dosage of 6.25 mg may be effective in 50% of patients. Therefore, endoscopic screening for varices and EBL should be considered, and patient preferences determined in those who do not tolerate carvedilol at the recommended dose.*

STAGE-SPECIFIC MANAGEMENT OF PORTAL HYPERTENSION

cACLD without CSPH

→ Use of NSBBs in patients with ACLD without CSPH is not recommended for prevention of decompensation.

BSG position = agree. NSBBs have not been proven to reduce decompensating events, formation of new varices or variceal bleeding in this patient group.[16]

ABSOLUTE:
Asthma (confirmed)
2nd and 3rd degree atrioventricular block (in absence of implanted pacemaker)
Sick sinus syndrome
Extreme bradycardia (<50 bpm)
RELATIVE:
Psoriasis
Peripheral arterial disease
Chronic obstructive pulmonary disease
Pulmonary artery hypertension
Raynaud syndrome

Figure 2 Absolute and relative contraindications to NSBBs.

→ Lifestyle modification and treatment of underlying liver disease should be prioritised to prevent progression to CSPH and decompensation.

BSG position = agree.

cACLD with proven or suspected CSPH

→ In patients with cACLD and CSPH, the goal of therapy is to prevent the development of clinical decompensation.

BSG position = agree.

→ NSBBs (preferably carvedilol 12.5 mg/day) should be considered for patients with cACLD with CSPH to prevent decompensation.

BSG position = agree. See comment above regarding split dosing regimen.

→ NSBBs should not be administered to patients with cACLD and evidence of CSPH with asthma, advanced heart block and bradyarrhythmias, and caution should be used in patients with relative contraindications (figure 2).

BSG position = agree with caveats. When a patient has a historical diagnosis of asthma and is not symptomatic/not dependent on preventative (eg, steroid) inhalers, then the diagnosis may be challenged and discussed with patient and their general practitioner. If the patient is deemed non-asthmatic per British Thoracic Society guideline, NSBBs are not contraindicated. In addition, NSBBs are cautioned in patients with diabetes mellitus who have frequent hypoglycaemic episodes due to risk of suppression hypoglycaemic symptoms.

→ Patients with cACLD and evidence of CSPH (by endoscopy, TE, HVPG or imaging) who are candidates for NSBB should be considered for treatment with NSBB (in the absence of contraindications) to prevent hepatic decompensation, which would also obviate the need for further screening endoscopy.

BSG position = agree. The BOPPP study will provide data on whether NSBBs are beneficial for patients with small varices.

→ Where VCTE is not available to diagnose CSPH and when empiric NSBBs are contraindicated or not considered due to prior intolerance, endoscopic surveillance of all patients with ACLD is recommended. Patients with cACLD without varices on screening endoscopy should have endoscopy repeated every 2 years (with ongoing liver injury or associated conditions, such as obesity and alcohol use) or every 3 years (if liver injury is quiescent, eg, after viral elimination, alcohol abstinence). Patients with cACLD without varices who develop decompensation should have a repeat endoscopy when this occurs. The presence of varices of any size should prompt initiation of NSBB (in absence of contraindications).

BSG position = agree with caveats. For clarity, this statement pertains to patients with suspected but unconfirmed CSPH.

In reference to sentence 'the presence of varices of any size should prompt initiation of NSBB (in absence of contraindication)' note, a UK trial comparing carvedilol with placebo for small varices (BOPPP)[17] is ongoing and guidance may change accordingly. For advice on primary prevention of OVB in a newly decompensated patient, see relevant section below.

→ Where TE is not available, screening endoscopy is not necessary in patients on NSBB therapy; the need for screening endoscopy can be also obviated in

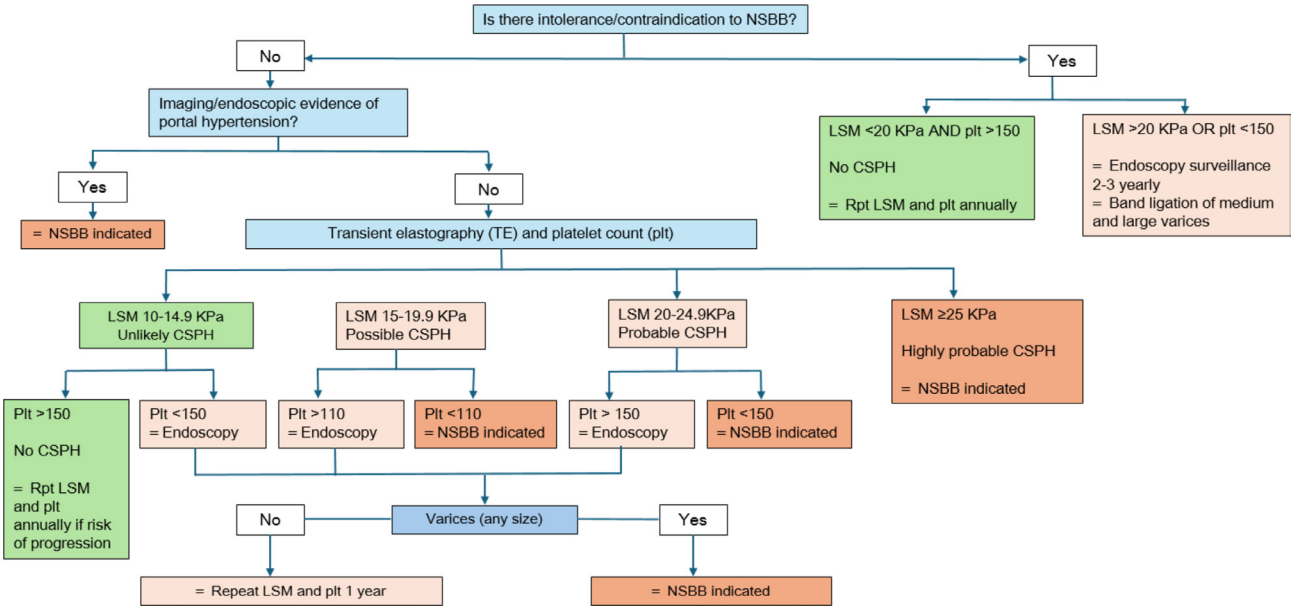

Figure 3 Management of portal hypertension in patients with compensated advanced chronic liver disease (cACLD) decision aid. CSPH, LSM,

some patients on a selective beta-blocker by switching therapy to a NSBB after discussion with the prescribing clinician.

BSG position = agree.

Note: A decision aid summarising the investigation and management of patients with cACLD who have CSPH excluded, included or indeed fall within the 'grey zone' has been provided (figure 3).

cACLD with contraindications to or intolerance of NSBB

→ Patients with cACLD and CSPH without varices who have contraindications or intolerance to beta-blockers should be screened for varices needing treatment with surveillance endoscopy every 2 years when the underlying disease remains uncontrolled and every 3 years when controlled.

BSG position = agree. Patients with cACLD and CSPH who have contraindications or intolerance to NSBB should have an initial screening endoscopy, with subsequent surveillance offered at the intervals outlined above. In the setting of inactive disease (with resolution of underlying aetiology) and negative serial endoscopies, cessation of endoscopic variceal surveillance should be considered.

→ Patients with cACLD and CSPH with varices that have not bled who have contraindications or intolerance to beta-blockers should be screened for varices needing treatment with surveillance endoscopy every year when the underlying disease remains uncontrolled and every 2 years when controlled.

BSG position = agree.

→ Primary prophylaxis with endoscopic band ligation (EBL) should be performed in patients with cACLD and CSPH and high-risk varices who cannot receive NSBBs.

BSG position = agree.

→ Band ligation should be repeated every 2–4 weeks until obliteration and then endoscopy repeated at 6 months and then every 12 months to assess for reappearance of varices requiring additional treatment.

BSG position = agree with caveats. Reduced EBL treatment intervals of 1–2 weeks have not shown superiority over intervals of 4–8 weeks in regard to bleeding, safety or mortality.[18 19] *A 4-week interval is therefore favoured; this may also allow time for banding ulcers to heal.*

→ TIPSS should not be used for the prevention of decompensation of cACLD or as primary prophylaxis for variceal haemorrhage.

BSG position = agree.

Strategies to prevent decompensation and first variceal bleed in dACLD

→ Patients with dACLD not taking NSBBs who have never bled from varices should undergo annual endoscopic screening.

BSG position = agree, with caveats. Patients who have decompensated disease, by definition, have CSPH. Therefore, it may seem reasonable to commence NSBBs. However, patients with dACLD have higher portal pressures and more developed hyperdynamic circulation compared with those with cACLD, thus being more at risk of hypotensive side effects. An individual patient data meta-analysis did not find a survival benefit of NSBBs over EBL in patients with dACLD.[20] *NSBBs can be poorly tolerated in dACLD and, while awaiting the outcome of the BOPPP trial,*[17] *overall data on the benefit of NSBBs in dACLD is lacking. There is some observational retrospective data suggesting a reduction in further decompensation or mortality in patients with dACLD without recurrent or refractory ascites with carvedilol vs other NSBBs.*[21]

Precedence is therefore given to individual case-by-case decision-making.

→ If high-risk varices are detected, NSBBs or EBL are recommended; preference is given to NSBBs (including carvedilol) because of benefits beyond prevention of variceal haemorrhage.

BSG position = agree. The CALIBRE trial did not find any statistical differences in clinical outcomes between carvedilol and EBL for the primary prevention of variceal bleeding in patients with medium and large varices; however, not all patients were decompensated and the study was terminated early, therefore underpowered. Carvedilol use was cheaper and resulted in slightly increased quality-adjusted life-years.[15]

'High-risk' varices pertain to grade II (moderate) or grade III (large) varices or any size varices with red wale marks or presence of any sized varices in a patient with Child-Pugh C disease. However, see note above regarding pragmatic decision to commence empirical NSBBs in all decompensated patients. This is an evidence-light area, particularly for Child-Pugh B disease with no or small varices. Therefore, the exclusion of 'high-risk' varices does not definitively preclude the use of NSBBs given the additional benefits of NSBBs in patients with CSPH, beyond the prevention of variceal bleeding.

NSBB use in patients with ascites and refractory ascites is safe and may even be beneficial, particularly with carvedilol.[22–24]

In patients with dACLD and G2/3 OV, a combination of carvedilol plus EBL was found to prevent variceal bleeding and improve survival over either single therapy alone (CAVARLY trial).[25] *Some of the results were unexpected and relevant correspondence in the literature is noted.*[26] *There is currently insufficient evidence to recommend combination therapy as standard of care.*

→ NSBBs should be dose reduced or discontinued in patients who develop persistently low systolic arterial pressure <90 mm Hg or severe adverse effects. NSBB discontinuation should prompt endoscopic evaluation for presence of high-risk varices requiring band ligation.

BSG position = agree. Low systolic blood pressure (<90 mm Hg) may attenuate the survival advantage associated with NSBB use potentially by reducing renal perfusion pressure, thus increasing the risk of hepatorenal syndrome or acute kidney injury.[27 28] *Note comment above regarding carvedilol split dose regimen.*

MANAGEMENT OF ACUTE OESOPHAGEAL VARICEAL BLEEDING

Definitions regarding variceal haemorrhage, time-frame of acute bleeding, failure to control bleeding, variceal rebleeding and early mortality remain unchanged from the 2015 BSG guidance on this topic.[1] So too is the recommendation for patients with suspected or proven variceal haemorrhage to be managed on a high dependency unit, or appropriately staffed acute bleeding unit. Haemodynamically unstable patients, patients with active hematemesis or patients suspected to have large volume of blood in the stomach should be intubated prior to endoscopy. Input from intensive care/anaesthesiologists to facilitate management of the acute bleed is felt to be of benefit.

→ All patients with known or suspected ACLD presenting with acute gastrointestinal bleeding should be initiated on vasoactive therapy (eg, somatostatin, octreotide or terlipressin if available) and intravenous antibacterial therapy as soon as possible.

BSG position = Agree. Terlipressin is the most commonly used vasoactive agent in the UK; however, data supporting the use of terlipressin is limited and historic. Terlipressin is associated with significant side effects including peripheral and cardiac ischaemia. The increasing number of patients with MASLD-related liver ACLD may compound these side effects further due to underlying arterial disease. Somatostatin is not available in the UK; therefore, octreotide (off licence) can be used in favour of terlipressin if there are concerns around side effects.

→ If portal hypertensive bleeding is confirmed at endoscopy, vasoactive therapy should be continued for 2–5 days.

BSG position = agree, with caveats. It is reasonable to discontinue terlipressin after 24 hours provided satisfactory achievement of endoscopic haemostasis and absence of clinical and biochemical signs of ongoing bleeding.[29] *NSBBs should be commenced thereafter, once adequate systemic haemodynamic status is confirmed.*

→ Intravenous antibacterial treatment should be given and tailored to local resistance patterns and patient allergies. Antimicrobial therapy can be discontinued once bleeding is controlled and in absence of an active infection.

BSG position = Agree.

→ Packed red blood cell (PRC) transfusions should target a haemoglobin of 70 g/L unless higher targets are required related to comorbid conditions.

BSG position = Agree. PRC transfusion may also be considered in severe bleeding requiring urgent resuscitation.

→ Fresh frozen plasma and platelet transfusions should not be administered based on international normalised ratio or platelet count targets, respectively, because there is no evidence of benefit of such transfusions in acute OVB, and in the case of fresh frozen plasma, there is evidence of potential harm.

BSG position = Agree.

→ Upper endoscopy should be performed within 12 hours of presentation with acute OVB.

BSG position = agree with caveats. In patients who are haemodynamically stable, it may be appropriate to extend the time to endoscopy to a maximum of 24 hours following presentation, depending on local resource.

→ If OVB is confirmed, EBL should be performed.

BSG position = Agree.

→ In patients with CTP class B score >7 and active bleeding on endoscopy or CTP class C score 10–13, pTIPSS creation (within 72 hours and ideally within 24 hours of initial upper endoscopy) should be recommended in the absence of absolute contraindications to TIPSS. If TIPSS is not locally available, transfer to a centre with the capacity to intervene should be considered.

BSG position: pre-emptive TIPSS following acute OVB is not currently recommended outside research settings. An individual patient data meta-analysis of all pTIPSS studies suggests a role for pTIPSS in reducing rebleeding and improving survival; however, there was significant heterogeneity of the studies included, particularly in relation to patient characteristics and standards of care used.[30] *A meta-analysis of RCT data alone suggested more studies are needed to confirm whether pTIPSS offers a positive effect.*[31] *In a UK RCT, no benefit of pTIPSS was observed over standard of care with carvedilol and EBL. The study was underpowered and highlighted the challenges of undertaking pTIPSS within the proposed time frame of 72 hours, even within specialised centres.*[32] *Currently, a large UK multicentre RCT investigating pre-emptive TIPSS versus standard of care (REACT-AVB)*[33] *is underway and will be imperative in informing UK practice.*

→ In patients presenting with acute OVB who do not undergo TIPSS, NSBB should be initiated at discontinuation of vasoactive therapy.

BSG position = agree. For UK purposes, 'TIPSS' in this regard pertains to salvage or rescue TIPSS, as pre-emptive TIPSS is not recommended, see above.

→ Covered expandable oesophageal stents (where available) or balloon tamponade should be considered in patients with uncontrolled acute OVB as a bridge to TIPSS.

BSG position = agree. Guidelines regarding the use of balloon tamponade (eg, Sengstaken-Blakemore tube) are unchanged. In addition, it may be used when patients are being transported long distances, and there is a concern OVB may occur during the journey. With respect to insertion, airway protection is mandated. Utilising the endoscope to 'drive' the tamponade tube into the stomach reduces the risk of oesophageal rupture, as balloon inflation is performed under direct vision.

Covered stents (eg, Danis stent) afford tamponade of oesophageal (but not gastric) varices.[34] *Placement is over a wire and stents can be left in situ for 7 days or more—this can potentially allow patients to clinically improve if they have a concomitant alcoholic hepatitis or an ischaemic hepatitis. A disadvantage is that stents frequently migrate; therefore, regular review and/or use of a fixation device is required.*

→ TIPSS should be considered in patients with uncontrolled OVB ('salvage' TIPSS) or who rebleed despite vasoactive therapy and EBL ('rescue' TIPSS).

BSG position = agree with caveats. The benefit of TIPSS is reduced in patients with advanced disease. A futility criterion may be applied to determine those not suitable for TIPSS, such as MELD >30, lactate >12 mmol/L or CPS>13.[35] *Discussion with local level 2/3 centre is recommended.*

→ Enteral feeding should be started once the OVB episode has been controlled. The presence of variceal bands does not contraindicate placement of a feeding tube if indicated.

BSG position = Agree.

→ Proton pump inhibitors (PPI) should be discontinued once OVB has been confirmed as the bleeding source in the absence of other specific indications.

BSG position = agree with caveats. Pre-endoscopic PPI is not recommended in UK GI bleeding guidelines.[36] *PPI in the setting of OVB is used in some centres to prevent banding ulcers; however, evidence is anecdotal and no well-designed, large trials have assessed this effect.*

STRATEGIES TO PREVENT RECURRENT HAEMORRHAGE AFTER INITIAL BLEED

→ Patients with variceal bleeding who do not fulfil the criteria for a pre-emptive TIPSS and/or do not undergo TIPSS during admission should undergo secondary prophylaxis with NSBB and EBL.

BSG position = agree with caveats. Pre-emptive TIPSS is not recommended. All patients should undergo secondary prophylaxis with NSBB and an EBL programme, provided a patent salvage or rescue TIPSS is not in situ. Intervals for EBL are as per above.

→ Use of TIPSS for secondary prophylaxis can be considered in patients with additional indications for TIPSS (eg, refractory ascites).

BSG position = agree. In addition, while pre-emptive TIPSS is not recommended after the first variceal bleed, it may be appropriate to consider TIPSS in patients with episodes of recurrent haemorrhage despite secondary prophylaxis with NSBB and EBL.

GASTRIC AND ECTOPIC VARICES

Prevention of bleeding

→ Patients with gastric or ectopic varices have CSPH, and therefore the use of NSBBs should be considered for prevention of rebleeding and decompensation. These patients should be investigated for the presence of portal vein thrombosis (PVT).

BSG position = agree. Investigation should also assess for the presence of splenic vein thrombosis. CT scanning is preferable to ultrasound given the better accuracy of detection for splenic vein thrombosis. Dedicated guidelines on the management of PVT should be consulted on detection.

→ Patients with high-risk cardio-fundal (GOV2 or IGV1) varices (≥10 mm, red wale signs, CTP class B/C) who have contraindications or intolerance to NSBBs may be considered for primary prophylaxis with endoscopic cyanoacrylate injection (ECI).

BSG position = agree with caveats. Low level evidence suggests thrombin injection may also be used. Thrombin is associated with fewer rebleeding events compared with ECI as well as fewer complications such as gastric ulcerations. Furthermore, thrombin injection requires simpler set-up compared with ECI. Endoscopic ultrasound guided coil embolisation is evolving as a technique and may be used in this setting; however, well-powered comparator trials are lacking.

→ Neither TIPSS nor BRTO (or related obliterative techniques) are recommended to prevent first haemorrhage in patients with fundal varices that have not bled.

BSG position = agree.

Management of initial and recurrent bleeding

→ Initial management of bleeding gastric or ectopic varices should be identical to the management of bleeding oesophageal varices, including vasoactive therapy, antimicrobials, conservative transfusion strategy and endoscopic evaluation, within 12 hours.

BSG position = agree with caveats. Endoscopy may be performed within 24 hours of presentation in haemodynamically stable patients.

→ Patients with confirmed bleeding gastric or ectopic varices should have contrast-enhanced cross-sectional imaging to define the anatomy of portosystemic collaterals or presence of venous thrombosis that would guide therapy.

BSG position = agree.

→ In patients with acute haemorrhage from gastric (GOV2/IGV1) or ectopic varices, either endoscopic cyanoacrylate therapy, TIPSS or retrograde transvenous variceal embolisation/obliteration can be considered first-line options. Retrograde obliteration is preferred when TIPSS is contraindicated.

BSG position = agree with caveats. Thrombin injection may also be considered as first-line endoscopic therapy. Trans-hepatic or trans-splenic embolisation can also be considered and indeed may be simpler to perform when these routes allow access to the bleeding source.

→ In patients who underwent ECI as the main therapy, the addition of NSBBs is recommended to prevent rebleeding, in absence of contraindications. Additionally, repeat endoscopic treatment at intervals every 2–4 weeks until obliteration and long-term surveillance should be performed.

BSG position = agree with caveats. Initiation of NSBBs also applies to patients treated with thrombin as the main therapy. There is a lack of evidence base regarding repeat endoscopic treatments, the relevant treatment goals and correlation with clinical outcomes. Therefore, repeat endoscopic treatments are not routinely recommended but may be considered on a case-by-case basis.

The role of pre-emptive TIPSS following gastric variceal bleeding has been studied.[37] However, aside from prevention of rebleeding, the benefits on other outcomes are inconclusive and the standard of care used differ from the guidance in this document. Further data are required, of note: REACT-AVB inclusion criteria allows for gastric variceal bleeding.

→ Patients with bleeding GV caused by isolated splenic vein thrombosis should be evaluated for splenectomy, splenic vein stenting or splenic artery embolisation

BSG position = agree.

PORTAL HYPERTENSIVE GASTROPATHY

→ Patients with greater than mild PHG should be presumed to have CSPH and should therefore be considered for prophylactic NSBB to prevent decompensation; this intervention may also prevent haemorrhagic complications or iron-deficiency anaemia from severe PHG.

BSG position = agree with caveats. There is likely variability regarding the interpretation of PHG severity among endoscopists. Furthermore, the direct correlation between PHG severity and CSPH is not well established. Therefore, other criteria to identify CSPH (per above) should be considered prior to commencing NSBBs. Endoscopic treatment should be considered in patients with anaemia thought to be secondary to PHG; however, this is an evidence-light area.

In relation to gastric antral vascular ectasia (GAVE), there are some data that suggest either EBL or argon plasma coagulation (APC) can be effective in reducing bleeding for anaemic patients. EBL is preferred for raised/nodular type GAVE as this may require fewer endoscopic sessions to achieve obliteration, as well as fewer transfusion requirements.[38]

→ In acute bleeding from severe PHG, vasoactive therapy (eg, somatostatin, somatostatin analogues such as octreotide or terlipressin if available) for 2–5 days at doses used for variceal bleeding should be considered.

BSG position = agree. Note, terlipressin is the most commonly used vasoactive agent in the UK and may be discontinued 24 hours after haemostasis.

→ NSBB are recommended to prevent rebleeding from PHG and PH-related polyps.

BSG position = agree.

→ If bleeding from PHG becomes transfusion-dependent despite NSBB, TIPSS placement should be considered.

BSG position = agree with caveats. Other therapies may be considered prior to TIPSS including endoscopic therapies (eg, argon plasma coagulation (APC)) or medical therapies such as lanreotide or thalidomide in selected cases. Of note, there is no role for TIPSS in bleeding GAVE.

VARICES AND HEPATOCELLULAR CARCINOMA

→ Prevention and treatment of OVB and hepatic decompensation in patients with HCC should follow the same principles as those for patients without HCC.

BSG position = agree with caveats. NITs have been shown to underestimate large varices and CSPH in patients with HCC[39] *but may be accurate to exclude CPSH in the absence of vascular invasion. Given the likelihood that cross-sectional imaging has been performed, radiological evidence of CSPH is sufficient to guide NSBB initiation. Otherwise, all patients with HCC and ACLD should undergo endoscopy. There is an increased rate of variceal bleeding in patients taking bevacizumab; therefore, screening for varices and commencing NSBBs if varices are present is recommended prior to treatment.*

→ In the absence of contraindications, NSBB therapy is recommended for the primary prophylaxis for variceal bleeding and prevention of decompensation in patients with HCC with CSPH (including varices).

BSG position = agree. EBL may be required for patients who do not tolerate NSBBs and for patients requiring secondary prophylaxis. For patients undergoing an EBL programme but require bevacizumab systemic therapy, we do not recommend significant delay in the initiation of systemic therapy—2 weeks after the initial banding procedure would be reasonable.

In the presence of occlusive bland or malignant PVT, upper GI endoscopy is recommended to investigate the presence of gastro-oesophageal varices. If varices are detected, NSBB or EBL is recommended; preference is given to NSBB (including carvedilol) because of benefits beyond prevention of variceal haemorrhage.

BSG position = agree. Data are limited for patients who require EBL (per above), and who require anticoagulation, and who require bevacizumab for systemic therapy. In this setting, low molecular weight heparin is recommended as their anti-coagulant of choice. Untreated PVT in these patients may cause worsening portal hypertension and increase variceal bleeding risk. Although anti-coagulated patients were excluded from initial atezolizumab/bevacizumab trial,[40] *anticoagulants have not been shown to increase variceal bleeding risk.*

PREGNANCY AND PORTAL HYPERTENSION

→ All patients with ACLD or non-cirrhotic PH planning pregnancy should undergo upper endoscopy within 1 year of conception.

BSG position = agree

→ Unscreened pregnant patients with ACLD or non-cirrhotic PH should undergo endoscopy early in the second trimester.

BSG position = agree; however, this is an evidence-light area. NSBBs are deemed to be safe in pregnancy therefore, patients who have either known or subsequently detected varices should have carvedilol initiated. Thereafter, post-delivery neonatal observations for bradycardia, hypotension and hypoglycaemia should be undertaken. In the presence of 'high-risk' varices (as defined above), EBL is the preferred treatment. Of note, in pregnant patients with acute variceal bleeding, use of terlipressin should be avoided and octreotide favoured.

PRE-OPERATIVE TIPSS FOR NON-HEPATIC SURGERY

→ Pre-operative TIPSS can be considered on a case-by-case basis after careful consideration of potential surgical benefits relative to potential harms related to the procedure (encephalopathy, worsening of liver failure).

BSG position = agree. A UK guidance document for risk assessment of patients with ACLD prior to elective non-hepatic surgery is available.[41]

AREAS FOR FUTURE RESEARCH

Validation of the CAVARLY trial[25] in a UK population is required and is of high priority. Combination therapy of carvedilol plus EBL may prevent variceal bleeding and reduce all-cause mortality in patients with decompensated disease and high-risk varices. The clinical and cost-effectiveness should be examined also.

well-powered study evaluating the potential benefit of adjuvant terlipressin in patients with variceal bleeding is required. Current data are limited to small, historic studies. The increasing risk of side effects particularly within the growing MASLD population needs evaluation also.

Other areas of future research outlined in the AASLD guidelines are noted below.

→ Prospective validation of the 'rule of 5' for the non-invasive selection of candidates for early initiation of NSBBs to prevent clinical decompensation and avoid screening endoscopy.

BSG position = agree with high priority. This needs to include validation across all aetiologies. Furthermore, assessment and validation of splenic stiffness measurement for the diagnosis of CSPH and its potential benefit in reducing patients within the 'grey zone'.

→ Systematic and cross-platform validation of cut-off points for magnetic resonance elastography, 2D shear wave elastography and point shear wave elastography for estimation of presence of clinically significant portal hypertension and high-risk varices.

BSG position = agree with moderate priority.

→ Identification and validation of non-invasive modalities to monitor 10%–20% changes in HVPG

BSG position = agree with low priority.

→ Confirmation of clinical, non-invasive liver disease assessment and/or HVPG thresholds for clinical recompensation after which screening endoscopy or NSBB therapy is no longer required, allowing de-escalation of monitoring and treatment for portal hypertension.

BSG position = agree with moderate priority. NITs should take preference over HVPG.

→ External validation of the PREDESCI trial in additional populations (patients with NASH)

BSG position = Agree with high priority.

→ Definition of patients with portal hypertension who might benefit from an earlier decision for TIPSS (ie, after first bleeding; before major operation).

BSG position = Agree with moderate priority.

→ Quantification of the benefit from nutritional intervention in patients with ACLD and sarcopenia and/or frailty for prevention of first or further decompensation and/or improvement in survival.

BSG position = agree with high priority.

→ Confirmation of the safety and effectiveness of statins in improving survival and/or preventing decompensation, further decompensation and acute-on-chronic liver failure when used alone or co-administered with NSBBs, rifaximin or other treatments.

BSG position = agree with low priority. Evidence is evolving in this area—note recent trial showed no benefit of statins plus rifaximin over placebo in improving outcomes for patients with dACLD.[42]

→ Larger prospective studies of self-expanding oesophageal stents to confirm role and refine utilisation in acute variceal haemorrhage

BSG position = agree with low priority.

CONCLUSIONS

The above guidance, endorsing the use, with caveats, of the AASLD guideline for risk stratification and management of portal hypertension and varices in ACLD, should be adopted in the UK on an interim basis until full BSG guidelines are published. This is anticipated to occur following the completion of several UK trials noted throughout the document. The caveats pertain to the diagnosis of CSPH using NITs and the clinical relevance, as well as in the management of acute OVB including the use of pTIPSS.

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