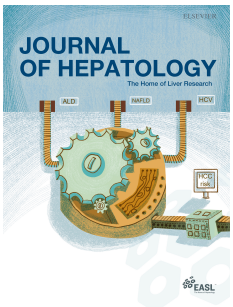


BAVENO VII - RENEWING CONSENSUS IN PORTAL HYPERTENSION

Roberto de Franchis, Jaime Bosch, Guadalupe Garcia-Tsao, Thomas Reiberger, Cristina Ripoll, on behalf of the Baveno VII Faculty

PII: S0168-8278(21)02299-6

DOI: https://doi.org/10.1016/j.jhep.2021.12.022

Reference: JHEPAT 8550

To appear in: *Journal of Hepatology*

Received Date: 18 November 2021

Revised Date: 10 December 2021

Accepted Date: 17 December 2021

Please cite this article as: de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C, on behalf of the Baveno VII Faculty, BAVENO VII - RENEWING CONSENSUS IN PORTAL HYPERTENSION, *Journal of Hepatology* (2022), doi: https://doi.org/10.1016/j.jhep.2021.12.022.

BAVENO VII - RENEWING CONSENSUS IN PORTAL HYPERTENSION

Report of the Baveno VII Consensus Workshop: personalized care in portal hypertension

Roberto de Franchis[1]*, Jaime Bosch[2,3], Guadalupe Garcia-Tsao[4,5], Thomas Reiberger[6,7], Cristina Ripoll[8], on behalf of the Baveno VII Faculty§

Short title: Renewing consensus in portal hypertension

Affiliations:
1. Department of Biomedical and Clinical Sciences, University of Milan
2. Department of Visceral Surgery and Medicine, Inselspital, Bern University Hospital, University of Bern, Switzerland
3. Instituts d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) and CIBERehd, University of Barcelona, Spain
4. Yale University , New Haven, USA
5. VA-CT Healthcare System, West Haven, USA
6. Division of Gastroenterology and Hepatology, Department of Medicine III, Medical University of Vienna, Vienna, Austria
7. Vienna Hepatic Hemodynamic Lab, Medical University of Vienna, Vienna, Austria
8. Internal Medicine IV, Universitätsklinikum, Friedrich Schiller University, Jena, Germany

Short title: Renewing consensus in portal hypertension

Keywords: Cirrhosis, diagnosis, decompensation, treatment, recommendations

*Corresponding Author:
Roberto de Franchis, MD, AGAF
Department of Biomedical and Clinical Sciences, University of Milan
e-mail: roberto.defranchis@unimi.it

§The members of the Baveno VII Faculty are given before the references

Word count: this paper contains 12,632 words

Acknowledgments: JB is supported by the Stiftung für Leberkrankheiten, Bern (Switzerland)

Disclosures: None relating to this manuscript. JB has been a consultant for Zydus, Surrozen and Actelion. TR is a consultant for and/or receives research support from Abbvie, Bayer, Boehringer-Ingelheim, Gilead, Intercept, MSD, Philips, Pliant Pharmaceuticals, Roche, and Siemens. RdF, CR and GGT have no disclosures to report

Portal hypertension is a major consequence of cirrhosis and is responsible for its most severe complications, including ascites, bleeding from gastroesophageal varices and encephalopathy. The evaluation of diagnostic tools and the design and conduct of high-quality clinical trials for the treatment of portal hypertension and its complications have always been difficult. Awareness of these difficulties has led to the organisation of a series of consensus meetings. The first one was organized by Andrew Burroughs in Groningen, the Netherlands in 1986[1]. After Groningen, other meetings followed, in Baveno, Italy in 1990 (Baveno I)[2], and in 1995 (Baveno II)[3,4], in Milan, Italy in 1992 [5], in Reston, U.S.A.[6], in 1996, in Stresa, Italy, in 2000 (Baveno III)[7,8], in Baveno in 2005 (Baveno IV) [9,10], in Atlanta, U.S.A. in 2007 [11], in Stresa in 2010 (Baveno V)[12,13] and in Baveno in 2015 (Baveno VI) [14,15]

The aims of these meetings were to develop definitions of key events in portal hypertension, to review the existing evidence on the natural history, the diagnosis, and the therapeutic modalities of portal hypertension, and to issue evidence-based recommendations for the conduct of clinical trials and the management of patients. All these meetings were successful and produced consensus recommendations that referred mostly to the management of varices and variceal hemorrhage.

To continue and expand the work of the previous meetings, a Baveno VII workshop was planned for March 20-21, 2020. This would also include recommendations on other complications of cirrhosis and portal hypertension besides variceal hemorrhage. However, the COVID 19 pandemic and the consequent lockdown forced the organizers to postpone the workshop until the end of October 2021 and to change the format from face-to-face to a virtual meeting. Despite these limitations, many of the experts responsible for the major achievements over the last years in the field of portal hypertension and its complications participated in the workshop. Many of them had attended the previous meetings.

Importantly, following the spirit of the Baveno meetings, the Baveno Cooperation was formed in 2016 with the aim to expand the scope towards a continuous effort of collaborating experts in portal hypertension, aiming to establish a continuous, high-quality research agenda. In, 2019 the European Association for the Study of the Liver (EASL) has endorsed the Baveno Cooperation as an official EASL consortium.

Patients with cirrhosis transition through different prognostic stages, the main ones being the compensated and decompensated stages. Transition from the compensated to the decompensated stage is clinically marked by the development of complications such as ascites, variceal hemorrhage and overt hepatic encephalopathy. Because “cirrhosis” implies a pathological (invasive) diagnosis, at the Baveno VI conference, the concept of compensated advanced chronic liver disease (cACLD) was

put forward based on non-invasive tests that would predict the development of complications of cirrhosis. Among patients with compensated cirrhosis or cACLD, at least two different stages have been identified, those with and without clinically significant portal hypertension (CSPH). The various disease stages differ in outcomes, including death, and therefore patients in different stages have different diagnostic and therapeutic needs. Accordingly, the Baveno VII workshop was entitled "Personalized Care for Portal Hypertension". The main fields of discussion were the relevance and indications for measuring the hepatic venous pressure gradient (HVPG) as a gold standard, the use of non-invasive tools for the diagnosis of cACLD and CSPH, the impact of etiological and of non-etiological therapies in the course of cirrhosis, the prevention of the first episode of decompensation, the management of the acute bleeding episode, the prevention of further decompensation, as well as the diagnosis and management of splanchnic vein thrombosis and other vascular disorders of the liver. For each of these nine topics, a thorough review of the medical literature was made, and a series of consensus statements/recommendations were discussed and agreed upon. Whenever applicable, the level of existing evidence was evaluated, and the recommendations were ranked according to the GRADE System [16], according to which the scientific evidence was graded from A (high) to D (very low). The strength of the recommendations was graded 1 (strong) and 2 (weak). The presentations made during the workshop are reported 'in extenso' in the Baveno VII proceedings book [17]. A summary of the most important conclusions/recommendations derived from the workshop is reported here. The statements are classified as unchanged, changed, and new in relation to Baveno VI.

1) HVPG AS A GOLD STANDARD

Description of HVPG measurement

1.1. The use of an end-hole, compliant balloon occlusion catheter reduces the random error of wedged hepatic vein pressure (WHVP) measurements and is preferred over the use of a conventional straight catheter (A.1). (New)

1.2. A small volume of contrast medium should be injected when the occlusion balloon is inflated to confirm a satisfactory occluded position and to exclude the presence of hepatic venous-to-venous communications (A.1) (New)

1.3. Hepatic venous-to-venous communications may result in underestimation of the WHVP and must be reported (A.1). (New)

1.4. Deep sedation during liver hemodynamic measurement may cause inaccurate HVPG values (B.1). If light sedation is required, low dose midazolam (0.02 mg/kg) does not modify the HVPG and is acceptable (B.1) (New)

1.5. Slow speed (up to 7.5 mm/s) permanent tracings of pressures, recorded either on paper or electronically, are recommended. Digital, on-screen readings are much less accurate and should not be used (A.1). (New)

1.6. To properly reflect portal venous pressure, WHVP requires a stabilization time. Recording of WHVP requires a minimum of 1 minute, with particular attention to stability during the last 20-30 seconds. WHVP should be recorded in triplicate (D,1) (New)

1.7. The wedged to free hepatic vein pressure gradient has superior clinical prognostic value than wedged to right atrial pressure gradient and should be used as the standard reference (B.1). Right atrial pressure can be measured to rule-out a post-hepatic component of portal hypertension. (B.1) (New)

1.8. Free hepatic vein pressure (FHVP) must be measured in the hepatic vein (HV) within 2-3 cm from HV-Inferior vena cava (IVC) confluence. IVC pressure should be measured as an internal control, at the level of the hepatic vein ostium. If the FHVP is more than 2 mmHg above IVC pressures, the presence of a hepatic vein outflow obstruction should be ruled-out with the injection of a small amount of contrast medium (A.1). (New)

Diagnosis of CSPH in patients with cirrhosis

1.9. Hepatic venous pressure gradient (HVPG) measurement values >5 mmHg indicate sinusoidal portal hypertension (A.1). ” (Unchanged)

1.10. In patients with viral and alcohol-related cirrhosis, HVPG measurement is the gold-standard method to assess the presence of “clinically significant portal hypertension” (CSPH), which is defined as an HVPG ≥10 mmHg (A.1). (Changed)

1.11. In patients with primary biliary cholangitis, there may be an additional pre-sinusoidal component of portal hypertension that cannot be assessed by HVPG (B.1). As such, in these patients, HVPG may underestimate the prevalence and severity of PH.(B.1)(New)

1.12. In patients with NASH cirrhosis, although an HVPG ≥10mmHg remains strongly associated with presence of clinical signs of portal hypertension, these signs can also be present in a small proportion of patients with HVPG values <10 mmHg. ” (C.2) (New)

1.13 In patients with chronic liver disease and clinical signs of portal hypertension (gastroesophageal varices, ascites, portosystemic collateral vessels) but with HVPG <10 mmHg, porto-sinusoidal vascular disorder (PSVD) must be ruled-out. (B.1) (New)

1.14 . In alcohol-related or viral cirrhosis, a decrease in HVPG in response to NSBB is associated with a significant reduction in the risk of variceal bleeding or of other decompensating events. (A.1) (Changed)

Inclusion of HVPG assessment in trial design

1.15 HVPG measurements should be encouraged in clinical trials investigating novel therapies but are not essential if portal hypertension-associated endpoints are well defined (B.1). (Unchanged)

1.16 In viral, alcohol-related, and reasonably in NASH cirrhosis, HVPG response assessment is recommended as a surrogate endpoint in phase II clinical trials where a low rate of events is expected. (D.2) (Changed)

1.17 Test-retest reliability of HVPG measurement is excellent but influenced by the stage of liver disease (lower in decompensated patients) and its etiology (higher in alcoholic patients). This should be taken into consideration in designing clinical trials based on HVPG assessment. (C.1). (New)

Assessment of surgical risks

1.18 Presence of CSPH, determined either by HVPG ≥10 mmHg or by clinical manifestations of portal hypertension, is associated with higher risk of decompensation and mortality in patients with cirrhosis undergoing liver resection for HCC. (A.1). (New)

1.19. In candidates for non-hepatic abdominal surgery, a HVPG ≥16 mmHg is associated with increased risk of short-term mortality after surgery (C.1) (New)

Portal pressure gradient (PPG) in the setting of TIPS

1.20. PPG should be measured before and after TIPS insertion (A.1). (New)

1.21. Anatomic locations for post-TIPS PPG measurement should include the main portal vein and the IVC (at the shunt outflow) (B.1). (New)

1.22 The immediate post-TIPS PPG may be influenced by various factors, such as general anesthesia, use of vasoactive agents or hemodynamic instability and therefore immediate post-TIPS PPG may not represent long-term PPG (B.1). PPG measurements in hemodynamically stable, non-sedated patients better reflect post-TIPS PPG values and are recommended (B.1). (New)

1.23 .In patients with variceal bleeding undergoing TIPS, reduction of absolute PPG to < 12 mmHg is associated with near complete protection from portal hypertensive bleeding and is the preferred target for TIPS hemodynamic success (A.1). Relative reduction of PPG, by at least 50% from pre-TIPS baseline, may also be useful (B.2) (New)

1.24 PPG re-measurement is indicated if there is clinical or Doppler-ultrasonographic suspicion of TIPS dysfunction, to evaluate the need for TIPS revision (B.1). (New)

Research Agenda

- The usefulness, safety, and accuracy of direct portal pressure measurement by endoscopic-US requires further evaluation.
- The prognostic role of HVPG and definition of specific cut-offs in patients with NASH-cirrhosis requires further investigation.
- The utility of HVPG-guided therapy needs further confirmation in randomized clinical trials.
- The prognostic role of HVPG in patients undergoing extra-hepatic surgery needs further investigation in prospective cohorts that should compare HVPG with non-invasive tests.
- Test-retest HVPG reliability at an individual level and factors that determine variability should be examined.
- Further investigations evaluating portocaval versus porto-atrial measured PPG and clinical outcomes after TIPS (e.g., rebleeding) are warranted.
- The optimal PPG decrease to control medically recurrent/refractory ascites is unclear. Further investigation correlating TIPS hemodynamic outcomes and ascites clinical response is necessary.
- The optimal PPG increase (in the context of TIPS reduction) needed to ameliorate adverse events related to over-shunting should be investigated.

2) NON-INVASIVE TOOLS FOR CACLD AND PORTAL HYPERTENSION

Definition of Compensated Advanced Chronic Liver Disease (cACLD)

2.1 The use of elastography in clinical practice has allowed the early identification of patients with untreated/active chronic liver disease (CLD) at risk of having clinically significant portal hypertension (CSPH) and consequently, at risk of developing decompensation and liver-related death (A.1) (Changed).

2.2 The term "compensated advanced chronic liver disease (cACLD)" had been proposed to reflect the continuum of severe fibrosis and cirrhosis in patients with ongoing CLD. A pragmatic definition of cACLD based on liver stiffness measurement (LSM) is aimed at stratifying the risk of CSPH and decompensation at point of care, irrespective of histological stage or the ability of LSM to identify these stages. (B.1) (Changed).

2.3 Currently, both terms "cACLD" and "compensated cirrhosis" are acceptable, but not equal (B.1) (Changed).

Criteria to identify cACLD

2.4 LSM values by transient elastography (TE) <10 kPa in the absence of other known clinical/imaging signs rule out cACLD; values between 10 and 15 kPa are suggestive of cACLD; values >15 kPa are highly suggestive of cACLD (B.1). (Changed)

2.5 CLD patients with LSM<10 kPa by TE have a negligible 3-year risk (≤1%) of decompensation and liver-related death (A.1) (New)

2.6 Patients with cACLD should be referred to a liver disease specialist for further work-up (B.1). (Changed)

2.7 Invasive methods (liver biopsy, hepatic venous pressure gradient-HVPG) can be used for further work-up in an individualized manner at referral centers (B.1). (Changed)

Outcome and Prognosis

2.8 LSM (irrespective of the technique used for its measurement) holds prognostic information in cACLD, both at index investigation and during follow-up (A.1) (New).

2.9 A rule of five for LSM by TE (10-15-20-25 kPa) should be used to denote progressively higher relative risks of decompensation and liver-related death independently of the etiology of CLD (B.1) (New).

How to monitor

2.10 Patients with LSM values 7-10 kPa and ongoing liver injury should be monitored on a case-by-case basis for changes indicating progression to cACLD (C.2) (New).

2.11 TE could have false positive results, therefore an index LSM ≥10 kPa should be repeated in fasting conditions as soon as feasible or complemented with an established serum marker of fibrosis (FIB-4 ≥2.67, ELF test ≥9.8, FibroTest ≥ 0.58 for ALD/viral, FibroTest≥0.48 for NAFLD) (B.2) (New).

2.12 In cACLD patients, LSM could be repeated every 12 months to monitor changes (B.2) (New).

2.13 A clinically significant decrease in LSM, which is associated with substantially reduced risk of decompensation and liver-related death, can be defined as a decrease in LSM of ≥20% associated with LSM<20 kPa or any decrease to a LSM <10 kPa (C.2) (New).

Diagnosis of CSPH in patients with cACLD

2.14 Although the concept of CSPH is HVPG-driven, non-invasive tests are sufficiently accurate for estimating CSPH in clinical practice (A.1) (New)

2.15 LSM by TE ≤15 kPa plus platelet count ≥150x10^9/L rules out CSPH (sensitivity and negative predictive value >90%) in cACLD patients (B.2). (New)

2.16 In patients with virus and/or alcohol related cACLD and non-obese (BMI <30 kg/m^2) NASH cACLD, a LSM value by TE ≥25 kPa is sufficient to rule in CSPH (specificity and positive predictive value >90%), defining the group of patients at risk of having endoscopic signs of PH and at higher risk of decompensation (B.1). (Changed)

2.17 In patients with virus and/or alcohol related and non-obese NASH cACLD with LSM values <25 kPa, the ANTICIPATE model can be used to predict the risk of CSPH. Based on this model, patients with LSM values between 20-25 kPa and platelet count <150x10^9/L or LSM values between 15-20 kPa and platelet count < 110x10^9/L have a CSPH risk of at least 60% (B.2). (New)

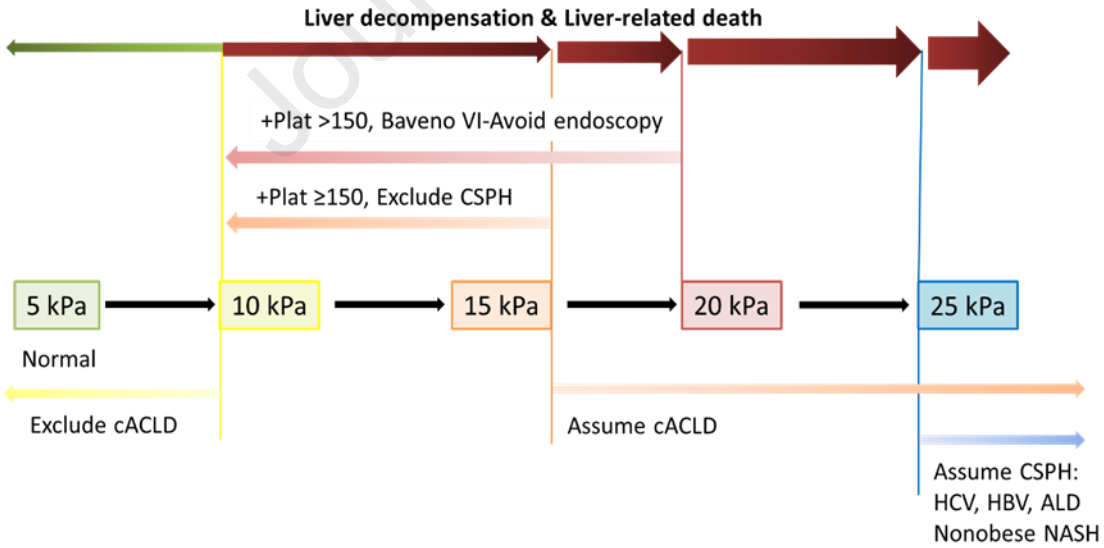
2.18 In patients with NASH cACLD, the ANTICIPATE-NASH model (including LSM, platelet count and BMI) may be used to predict the risk of CSPH, but further validation is needed (C.2). (New)

Varices and screening endoscopy in patients that cannot be treated with NSSB

2.19 Patients with compensated cirrhosis not candidates for initiating NSBB (contraindication/intolerance) for the prevention of decompensation should undergo an endoscopy for variceal screening if LSM by TE ≥20 kPa or platelet count ≤150x10^{9}L (A.1). (New)

2.20 Patients avoiding screening endoscopy can be followed up by yearly repetition of TE and platelet count. If LSM increases (≥20 kPa) or platelet count declines (≤150x10^{9}L), these patients should undergo screening endoscopy (D.1). (Unchanged)

FIGURE 1



Spleen stiffness

2.21 SSM using TE can be used in cACLD due to viral hepatitis (untreated HCV; untreated and treated HBV) to rule-out and rule-in CSPH (SSM <21 kPa and SSM >50 kPa, respectively).

Validation of the best cut-off using a 100 Hz specific TE-probe, as well as using pSWE and 2D-SWE is needed (B.2) (New).

2.22 In patients not candidates for initiating NSBB (contraindication/intolerance) for the prevention of decompensation and in whom endoscopy would be required according to the Baveno VI criteria (LSM by TE ≥20 kPa or platelet count ≤150x10^9L), SSM ≤40 kPa by TE can be used to identify subjects at low probability of high-risk varices, in whom endoscopy can be avoided. (C.2) (New).

Research agenda

- Define risk of decompensation associated with different LSM cut-offs in different etiologies of cACLD.
- Validation and refinement of non-invasive tools for CSPH in NASH patients.
- Evaluate the diagnostic value of LSM for CSPH in etiologies other than viral/alcohol/NASH.
- Establish whether gender and age require specific calibration of NITs for CSPH.
- Validation of circulating biomarkers for prediction of decompensation in all etiologies.
- Validation of LSM thresholds for CSPH, high-risk varices and decompensation obtained from devices other that TE.
- Validation of what constitutes a clinically significant improvement or worsening of LSM in all etiologies.
- Validation of SSM in non-viral etiologies.
- Evaluation of emerging methods to diagnose CSPH and determine response to NSBB, such as contrast-enhanced ultrasound-based methods (SHAPE), magnetic resonance imaging methods, combination of elastography, novel imaging methods and tests addressing liver function

3) MANAGEMENT OF ACLD AFTER REMOVAL/SUPPRESSION OF THE PRIMARY ETIOLOGICAL FACTOR

3.1 Removal/suppression of the primary aetiological factor includes sustained virological response (SVR) in patients with hepatitis C virus (HCV) infection, hepatitis B virus (HBV) suppression in the absence of hepatitis D virus (HDV) coinfection in patients with chronic HBV infection, and long-term abstinence from alcohol in patients with alcohol-related liver disease (ALD). (A.1) (New)

3.2 The definition and impact of the removal/suppression of the primary aetiological factor in other ACLDs is less well established. (A.1) (New)

3.3 Overweight/obesity, diabetes, and alcohol consumption are important contributors to liver disease progression even after removal/suppression of the primary aetiological factor and should be addressed. (A.1) (Changed)

3.4 Removal/suppression of the primary aetiological factor leads to potentially meaningful decreases in HVPG in the majority of patients and substantially reduces the risk of hepatic decompensation. (A.1) (Changed)

3.5 Absence/resolution of CSPH following removal/suppression of the primary aetiological factor prevents hepatic decompensation. (B.1) (Changed)

3.6 The optimal percent/absolute decrease in HVPG associated with a reduction in hepatic decompensation following the removal/suppression of the primary aetiological factor in cACLD patients with CSPH has yet to be established. (B.1) (New)

3.7 In the absence of co-factors, patients with HCV-induced cACLD who achieve SVR and show consistent post-treatment improvements with LSM values of <12kPa and PLT >150x10^9/L can be discharged from portal hypertension surveillance (LSM and endoscopy), as they do not have CSPH and are at negligible risk of hepatic decompensation. In these patients, hepatocellular carcinoma surveillance should continue until further data is available. (B.1) (New)

3.8 The Baveno VI criteria (i.e., LSM <20kPa and PLT >150x10^9/L) can be used to rule-out high-risk varices in patients with HCV- and HBV-induced cACLD who achieved SVR and viral suppression, respectively. (B.1) (New)

3.9 cACLD patients on NSBB therapy with no evident CSPH (LSM <25kPa) after removal/suppression of the primary aetiological factor, should be considered for repeat endoscopy, preferably after 1-2 years. In the absence of varices, NSBB therapy can be discontinued. (C.2) (New)

Research Agenda

- Establish the definition and impact of the removal/suppression of the primary aetiological factor in cACLD other than HCV and HBV infection and ALD, particularly in non-alcoholic fatty liver disease (NAFLD).
- Identification of factors responsible for liver disease progression despite removal/suppression of the primary aetiological factor.
- Establish the optimal percent/absolute decrease in HVPG associated with a reduction in hepatic decompensation following the removal/suppression of the primary aetiological factor in cACLD patients with CSPH.

- Diagnostic ability of NIT in monitoring disease regression and determining the presence of CSPH after removal/suppression of a non-viral primary aetiological factor.
- Evaluation and validation of other non-invasive risk stratification algorithms (e.g., LSM/VITRO and SSM) in patients in whom the primary aetiological factor has been removed/suppressed.
- Estimates of the regression of varices after removal/suppression of the primary aetiological factor and long-term data on the risk of hepatic decompensation (and more specifically, variceal bleeding) and its evolution over time in patients with cACLD.

4) IMPACT OF NON-ETIOLOGICAL THERAPIES

4.1 The use of statins should be encouraged in patients with cirrhosis and an approved indication for statins since these agents may decrease portal pressure (A.1) and improve overall survival. (B.1) (Changed)

4.2 In patients with Child B and C cirrhosis, statins should be used at a lower dose (simvastatin at max. 20mg/d) and patients should be followed closely for muscle and liver toxicity. (A,1). In Child C cirrhosis the benefit of statins has not been proven yet and their use should be more restrictive (D.1). (Changed)

4.3 The use of aspirin should not be discouraged in patients with cirrhosis and an approved indication for aspirin, since it may reduce the risk of hepatocellular carcinoma, liver-related complications, and death. (B.2) (New)

4.4 Long-term albumin administration may reduce complications of cirrhosis and improve transplant-free survival in patients with uncomplicated ascites, but a formal recommendation cannot be given until further data become available. (B.2) (New)

4.5 Short-term albumin administration is indicated for SBP (A,1), AKI > stage 1A (C.1), large volume paracentesis (A,1) and HRS-AKI combined with terlipressin (B.1). (New)

4.6 Primary antibiotic prophylaxis is recommended in selected patients (i.e., GI hemorrhage, Child-C cirrhosis with low protein ascites) at high-risk for SBP (B.1) (New)

4.7 Secondary antibiotic prophylaxis is indicated in patients with previous SBP. (A.1) (New)

4.8 Rifaximin is indicated for the secondary prophylaxis of hepatic encephalopathy (A,1) (New)

4.9 Rifaximin should be considered for prophylaxis of overt hepatic encephalopathy in patients with previous overt hepatic encephalopathy undergoing elective TIPS (B.2) (New)

4.10 Rifaximin is not indicated beyond these indications, including primary or secondary prophylaxis of spontaneous bacterial peritonitis. (C.1) (New)

4.11 Anticoagulation should not be discouraged in patients with cirrhosis and an approved indication for anticoagulation, since anticoagulation may reduce liver-related outcomes in patients with and without portal vein thrombosis and may improve overall survival (B.1) (Changed)

4.12 The safety and efficacy of DOACs to prevent cardiovascular events in patients with Child A and B cirrhosis are equivalent to those in patients without cirrhosis (B.2). DOACs are not recommended in patients with Child C cirrhosis outside study protocols (B.2) (New)

Research agenda

- The gut microbiome can be targeted by several means including pre-, pro-, syn- and post biotics, diet, FMT, phage therapy, drugs, bioengineered bacteria, and antibiotics. There is a need for interventional trials with outcome assessments that includes functional aspects and clinical outcomes.
- The composition of the gut microbiome (e.g., high relative abundance of Enterobacteriaceae) in various body fluids (stool, saliva, blood, bile, intestinal mucosa, skin) is associated with severity of cirrhosis, complications, and presence of organ failures and ACLF. Components of the gut microbiome should be explored for biomarkers to inform stage of disease (diagnostic), to predict the risk of progression (prognostic), likelihood to benefit from intervention (predictive) and efficacy of intervention.
- Faecal microbiota transplant (by enema or by the oral route) seems to be safe in patients with cirrhosis and hepatic encephalopathy but efficacy studies are pending.
- Anti-fibrotic strategies including the FXR-pathway, the renin-angiotensin system, and angiogenesis should be further explored in cirrhosis and portal hypertension.

5) PREVENTION OF (FIRST) DECOMPENSATION

5.1 Compensated cirrhosis is defined by the absence of present or past complications of cirrhosis. The transition from compensated to decompensated cirrhosis leads to an increased mortality risk." (A.1) (New)

5.2 Compensated cirrhosis can be divided in 2 stages, based on the absence or presence of clinically significant portal hypertension (CSPH). Patients with CSPH have increased risk of decompensation. The goal of treatment in compensated cirrhosis is to prevent complications that define decompensation. (A.1) (Changed)

5.3 Prevention of decompensation is especially relevant in compensated patients with CSPH and/or esophageal or gastric varices due to their higher risk of developing decompensation. (B.1) (New)

5.4 The events that define decompensation in a compensated patient are overt ascites (or pleural effusion with increased SAAG (> 1.1 g/dL), overt hepatic encephalopathy (West Haven grading >=II) and variceal bleeding. (B.1) (New)

5.5 Other relevant liver related events in compensated cirrhosis are the development of superimposed liver injury (see statement 5.12)/ACLF and hepatocellular carcinoma (B1) (New)

5.6 Insufficient data are available regarding whether a minimal amount of ascites only detected in imaging procedures, minimal hepatic encephalopathy, and occult bleeding from portal hypertensive gastroenteropathy can be considered as decompensation. (D.1) (New)

5.7 Limited data suggests that jaundice alone (in non-cholestatic etiologies) may be the first manifestation of cirrhosis in a minority of patients; however, its definition, whether it should be considered true first decompensation or if it reflects superimposed liver injury/ACLF in compensated cirrhosis requires further research. (D.1) (New)

5.8 Non hepatic comorbidities are frequent in patients with compensated cirrhosis, can adversely impact prognosis, and should be specifically dealt with. (A.1) (Changed)

5.9 There is insufficient data to draw definitive conclusions on the impact of sarcopenia and frailty on the natural history of compensated cirrhosis. (D.1) (New)

5.10 Bacterial infections are frequent in compensated patients with CSPH, can lead to decompensation (ascites, variceal bleeding, hepatic encephalopathy) and, consequently, adversely affect natural history (B.1) (New)

5.11 There is insufficient data as to whether infections are frequent in compensated cirrhosis without CSPH and whether they may per se impact prognosis (D.1) (New)

5.12 Superimposed liver damage, such as (acute) alcoholic hepatitis, acute viral hepatitis (HEV, HAV), HBV flares or drug induced liver injury can precipitate decompensation. (A.1) (New)

5.13 Other factors such as HCC and major surgery can precipitate decompensation of cirrhosis in patients with CSPH (B.1) (New)

5.14 Treatment with non-selective beta-blockers (NSBBs) (propranolol, nadolol or carvedilol) should be considered for the prevention of decompensation in patients with CSPH (B.1) (New).

5.15 Carvedilol is the preferred NSBB in compensated cirrhosis, since it is more effective in reducing HVPG (A.1), has a tendency towards greater benefit to prevent decompensation and

towards better tolerance than traditional NSBBs and has shown an improvement in survival (B.1) compared to no active therapy in compensated patients with CSPH. (Changed)

5.16 The decision to treat with NSBBs should be taken when clinically indicated, independent of the possibility of measuring HVPG (B.2) (Unchanged)

5.17 Patients with compensated cirrhosis who are on NSBB for the prevention of decompensation do not need a screening endoscopy for the detection of varices since endoscopy will not change management (B.2). (New)

5.18 There is no evidence that endoscopic therapies such as EBL or glue might prevent ascites or hepatic encephalopathy. (D.1) (New)

5.19 In compensated patients with high-risk varices who have contraindications or intolerance to NSBB, endoscopic band ligation is recommended to prevent first variceal bleeding. (A.1) (Changed)

5.20 There is no indication at present to use NSBB in patients without CSPH. (A.1) (Unchanged)

5.21 Although a single study suggested that cyanoacrylate injection is more effective than propranolol in preventing first bleeding in patients with large gastroesophageal varices type 2 or isolated gastric varices type 1, there were no differences in survival. However, NSBB are indicated in these patients to prevent decompensation (B.1). Further studies are required in these patients using new therapeutic approaches in addition to NSBBs. (D.1) (Changed)

5.22 There is no indication at present for BRTO/BATO/BARTO/TIPS in primary prophylaxis of gastric variceal bleeding in compensated patients (D.1) (New)

Research agenda

- Competing risks from comorbidities should be taken into account in future studies in compensated cirrhosis. Impact of early detection and treatment of comorbidities.
- Impact of sarcopenia and frailty (and of its treatment) on prognosis and mortality of compensated cirrhosis.
- Prognostic significance of the sole presence of minimal ascites only detected in imaging procedures, minimal hepatic encephalopathy, and chronic bleeding from portal hypertensive gastroenteropathy.
- Prognostic significance of the sole presence of jaundice in compensated cirrhosis, and its definition.
- Role of statins to prevent decompensation.
- Impact of sole bacterial infection in compensated cirrhosis on natural history. Impact of non-bacterial infections in compensated cirrhosis.

- Impact of vaccination (pneumococcal, haemophilus, influenza, coronavirus) on the natural history of compensated cirrhosis.
- Prevention of bacterial infections in patients with CSPH and its impact on the incidence of decompensation.
- Factors predicting which infections will give rise to decompensation and/or worsen prognosis.

6) ACUTE VARICEAL BLEEDING

6.1 The goal of resuscitation is to preserve tissue perfusion. Volume restitution should be initiated to restore and maintain hemodynamic stability (D.2) (Unchanged)

6.2 PRBC transfusion should be done conservatively at a target hemoglobin level between 7-8 g/dl., although transfusion policy in individual patients should also consider other factors such as cardiovascular disorders, age, hemodynamic status and ongoing bleeding (A.1) (Unchanged)

6.3 Intubation is recommended before endoscopy in patients with altered consciousness and those actively vomiting blood (D.1) (New)

6.4 Extubation should be performed as quickly as possible after endoscopy (D.2) (New)

6.5 In suspected variceal bleeding, vasoactive drugs (terlipressin, somatostatin, octreotide) should be started as soon as possible and continued for 2-5 days (A.1) (Changed)

6.6 Hyponatremia has been described in patients on terlipressin, especially in patients with preserved liver function. Therefore, sodium levels should be monitored (B.1) (Unchanged)

6.7 Antibiotic prophylaxis is an integral part of therapy for patients with cirrhosis presenting with upper gastrointestinal bleeding and should be instituted from admission. (A.1) (Unchanged)

6.8 The risk of bacterial infection and mortality are very low in patients with Child Pugh A cirrhosis, but more prospective studies are still needed to assess whether antibiotic prophylaxis can be avoided in this subgroup of patients (B.2) (Unchanged)

6.9 Intravenous ceftriaxone 1 g/24 h should be considered in patients with advanced cirrhosis (A.1) in hospital settings with high prevalence of quinolone-resistant bacterial infections and in patients on previous quinolone prophylaxis, and should always be in accordance to local resistance patterns and antimicrobial policies (D.2) (Changed)

6.10 Malnutrition increases the risk of adverse outcomes in patients with cirrhosis and AVB and oral nutrition should be started as soon as possible (D.2) (New)

6.11 Manipulation of airway, including use of nasogastric tube, should be performed with caution because of the risk of pulmonary infection (D.2) (New)

6.12 PPIs, when started before endoscopy, should be stopped immediately after the procedure unless there is a strict indication to continue them (D.2) (New))

6.13 Six-week mortality should be the primary endpoint for studies for treatment of acute variceal bleeding. (D.1) (Unchanged)

6.14 Five-day treatment failure is defined either by absence of control of bleeding or by rebleeding within the first 5 days (D.1) (Changed)

6.15 Child-Pugh class C, the updated MELD score, and failure to achieve primary haemostasis are the variables most consistently found to predict 6-week mortality (B.2) (Unchanged)

6.16 Child-Pugh and MELD scores are currently the most utilized severity scoring systems (D.2). (Unchanged)

6.17 Following hemodynamic resuscitation, patients with suspected AVB should undergo upper endoscopy within 12 hrs of presentation (B.1). If the patient is unstable, endoscopy should be performed as soon as safely possible (D.1) (Changed)

6.18 The availability of an on-call GI endoscopist proficient in endoscopic haemostasis and on-call support staff with technical expertise in the usage of endoscopic devices, enabling performance of endoscopy on a 24/7 basis, is recommended. Trainees performing the procedure must always be closely supervised by the GI endoscopist (D.1) (Changed)

6.19 In the absence of contraindications (QT prolongation), pre-endoscopy infusion of erythromycin (250 mg IV 30-120 minutes before endoscopy) should be considered (B.1) (Unchanged)

6.20 Patients with acute variceal bleeding should be managed in intensive or intermediate care units (D.1) (Unchanged)

6.21 Ligation is the recommended form of endoscopic therapy for acute esophageal variceal bleeding (A.1) (Unchanged)

6.22 Endoscopic therapy with tissue adhesives (e. g. N-butyl-cyanoacrylate/thrombin) is recommended for acute bleeding from isolated gastric varices (IGV) (A.1), gastroesophageal varices type 2 (GOV2) that extend beyond the cardia (D.2) (Unchanged)

6.23 EVL or tissue adhesive can be used in bleeding from gastroesophageal varices type 1 (GOV1) (D.1) (Unchanged)

6.24 Based on current evidence, haemostatic powder cannot be recommended as first-line endoscopic therapy for acute variceal bleeding (D.1) (New)

6.25 Endoscopic therapy (argon plasma coagulation, radiofrequency ablation or band ligation for PHG-GAVE) may be used for local treatment of PHG bleeding (C.2) (New)

6.26 All patients with AVB should undergo abdominal imaging, preferably contrast-enhanced cross-sectional imaging (CT or MRI) to exclude splanchnic vein thrombosis, hepatocellular carcinoma and to map portosystemic collaterals in order to guide treatment (D.1) (New)

6.27 Pre-emptive TIPS with PTFE-covered stents within 72 hours (ideally <24hours) is indicated in patients bleeding from EV, GOV1 and GOV2 who meet any of the following criteria: Child Pugh class C<14 points or Child class B >7 with active bleeding at initial endoscopy or HVPG >20 mmHg at time of hemorrhage (A.1) (Changed)

6.28 In patients fulfilling pre-emptive TIPS criteria, ACLF, HE at admission and hyperbilirubinemia at admission should not be considered as contra-indications to pTIPS (B.1) (New)

6.29 In refractory variceal bleeding, balloon tamponade (BT) or self-expandable metal stents (SEMS) should be used as a bridge therapy to a more definite treatment such as PTFE-covered TIPS. SEMS are as efficacious as BT and a safer option (B.1) (Changed)

6.30 Failure to control variceal bleeding despite combined pharmacological and endoscopic therapy is best managed by salvage PTFE-covered TIPS (B.1) (Changed)

6.31 TIPS may be futile in patients with Child-Pugh ≥14 cirrhosis, or with a MELD score >30 and lactate >12 mmol/L, unless liver transplantation is envisioned in the short-term (B.1) The decision to perform TIPS in such patients should be taken on a case-by-case basis (D.1) (New)

6.32 In patients with AVB and HE, HE bouts should be treated by lactulose (oral or enemas) (D.1) (New)

6.33 In patients presenting with AVB, rapid removal of blood from the gastro-intestinal tract (lactulose oral or enemas) should be used to prevent HE (B.1) (New)

6.34 Variceal bleeding is due to PHT, and the aim of the treatment should be focused on lowering portal pressure rather than correcting coagulation abnormalities (B.1) (New)

6.35 Conventional coagulation tests, namely, prothrombin time (PT/INR) and activated partial thromboplastin time (aPTT), do not accurately reflect the hemostatic status of patients with advanced liver diseases (B.1). (Changed)

6.36 In the acute variceal bleeding episode, transfusion of fresh frozen plasma is not recommended as it will not correct coagulopathy and may lead to volume overload and worsening of portal hypertension. (B.1) (New)

6.37 In the setting of acute variceal bleeding, there is no evidence that platelet count and fibrinogen levels are correlated with the risk of failure to control bleeding or rebleeding. However, in case of failure to control bleeding, the decision to correct the haemostatic abnormalities should be considered on a case-by-case basis (D.2) (New)

6.38 Recombinant factor VIIa and tranexamic acid are not recommended in acute variceal bleeding (A.1) (New)

6.39 In patients with AVB who are on anticoagulants, these should be temporarily discontinued until the hemorrhage is under control. Length of discontinuation should be individualized based on the strength of the indication for anticoagulation (D.2) (New)

6.40 In patients with GOV2, IGV1, and ectopic varices, BRTO could be considered as an alternative to endoscopic treatment or TIPS, provided it is feasible (type and diameter of shunt) and local expertise is available, as it has demonstrated to be safe and effective (D.2) (New)

6.41 Either endovascular or endoscopic treatment should be considered in patients with ectopic varices (D.1) (New)

6.42 TIPS may be combined with embolization to control bleeding or to reduce the risk of recurrent variceal bleeding from gastric or ectopic varices, particularly in cases when, despite a decrease in portosystemic pressure gradient, portal flow remains diverted to collaterals (D.2) (New)

6.43 In patients with cirrhosis and PVT, management of AVB should be performed according to the guidelines for patients without PVT, when possible. (D.1) (New)

- ***Research Agenda***
    - Role of vasoactive drugs and antibiotics in Child-Pugh A patients
    - Optimal shorter time frame limit for vasoactive drug therapy?
    - Definition of active bleeding at endoscopy, assessment of its subjectivity, and prognostic value
    - Identifying the clinical role of non-invasive markers of portal pressure
    - Role of hemostatic powder in acute and refractory variceal bleeding
    - Role of thrombin in gastric variceal bleeding
    - Pre-emptive TIPS in patients with gastric varices

- Management of high risk in patients not fulfilling the high-risk criteria used for pre-emptive TIPS
- Cost effectiveness data regarding the use of SEMSs
- Alternatives other than Blakemore/Linton should be developed as they are in shortage
- The role of global hemostasis tests, such as viscoelastic tests and thrombin generation assays, to assess and correct hemostasis abnormalities in decompensated cirrhosis and acute variceal bleeding (using clinical endpoints).
- The potential role of prothrombin complex concentrates, fibrinogen, or cryoprecipitate in bleeding patients with cirrhosis.
- Is there any relation between low platelet count (up to which level?) or fibrinogen and the risk of variceal bleeding, failure to control bleeding, or bleeding after endoscopic band ligation?
- Identification of patients that will benefit from variceal embolization during TIPS
- Role of EUS-guided therapy with tissue adhesive with or without coils
- The impact of PVT on the prognosis of cirrhotic patients with AVB
- The optimal duration of vasoactive therapy in cirrhotic patients with PVT and AVB
- Role of pre-emptive TIPS in cirrhotic patients with PVT presenting with AVB
- Management of AVB in patients with cirrhosis and PVT, including management of anticoagulation and timing of endoscopic/invasive procedures.

7) PREVENTION OF FURTHER DECOMPENSATION

Definition of "further decompensation"

7.1 Further decompensation in cirrhosis represents a prognostic stage associated with an even higher mortality than that associated with first decompensation. Specific events that define further decompensation are any of the following (B.1) (New):

a) Development of a second portal hypertension-driven decompensating event (ascites, variceal hemorrhage or hepatic encephalopathy) and/or jaundice
b) Development of recurrent variceal bleeding, recurrent ascites (requirement of ≥3 large-volume paracenteses within one year), recurrent encephalopathy, development of spontaneous bacterial peritonitis (SBP) and/or hepatorenal syndrome (HRS-AKI)
c) In patients presenting with bleeding alone, development of ascites, encephalopathy, or

jaundice after recovery from bleeding but not if these events occur around the time of bleeding

Preventing further decompensation in patients with ascites

7.2 Patients with decompensated cirrhosis should be considered for liver transplantation. (A.1) (New)

7.3 Patients with ascites who are not on non-selective beta-blockers (NSBB, i.e., propranolol or nadolol) or carvedilol should undergo screening endoscopy. (B.1) (New)

7.4 TIPS should be considered in patients with recurrent ascites (requirement of ≥3 large-volume paracenteses within one year) irrespective of the presence or absence of varices or history of variceal hemorrhage. (A.1) (New)

7.5 In patients with ascites and low-risk varices (small [<5mm], no red signs, not Child C), NSBB or carvedilol may be used to prevent first variceal hemorrhage. (B.2) (Changed)

7.6 In patients with ascites and high-risk varices (large varices [≥5 mm]), or red spot signs, or Child C), prevention of first variceal hemorrhage is indicated, with NSBB or carvedilol being preferred over endoscopic variceal ligation (EVL). (B.1) (Changed)

7.7 In patients with ascites, NSBBs or carvedilol should be dose-reduced or discontinued in case of persistently low blood pressure (systolic blood pressure <90 mmHg or mean arterial pressure <65 mmHg) and/or HRS-AKI (B.1). Once blood pressure returns to baseline and/or HRS-AKI resolves, NSBB can be re-initiated or re-titrated. (B.1). If a patient remains intolerant to NSBB, EVL is then recommended to prevent variceal hemorrhage (Changed)

Preventing recurrent variceal hemorrhage (Secondary prophylaxis)

7.8 First line therapy for the prevention of recurrent variceal hemorrhage is the combination of NSBB or carvedilol and EVL (A.1). (Changed)

7.9 TIPS is the treatment of choice in patients who rebleed despite NSBB or carvedilol and EVL. (B.1) (Unchanged)

7.10 In patients who cannot get/tolerate EVL or carvedilol or NSBB, any of these therapies can be maintained alone (A1) and TIPS should be considered in patients with recurrent ascites. (B.1) (Changed)

7.11 In patients who bleed despite adherence to NSBB or carvedilol as primary prophylaxis, the combination of NSBB or carvedilol and EVL is recommended, and TIPS should be considered in those with recurrent ascites. (B.1) (New)

Preventing Recurrent Bleeding from Portal Hypertensive Gastropathy (PHG)

7.12 PHG and portal hypertension-associated gastric or small intestinal polypoid lesions (PHP) have to be distinguished from gastric antral vascular ectasia (GAVE) because treatments are different. (B.1) (Changed)

7.13 NSBB are first line therapy in preventing recurrent bleeding from PHG. (A.1) (Unchanged)

7.14 Endoscopic therapy (e.g., argon plasma coagulation or hemospray) may be used to treat recurrent bleeding from PHG. (D.1) (New)

7.15 TIPS should be considered for transfusion dependent PHG despite NSBB or carvedilol and endoscopic therapy. (C.1) (Changed)

Role of Infections in decompensated cirrhosis

7.16 Bacterial infections are common in patients with decompensated cirrhosis and may cause further decompensation. (A.1) (New)

7.17 In all patients hospitalized with decompensation, bacterial infections should be ruled out. The minimal work up for infections should include diagnostic paracentesis, chest X-ray, cultures of blood, ascites and urine, and skin examination. (A.1) (New)

7.18 Patients with bacterial infections should be promptly treated with antibiotics. The empirical antibiotic treatment should be tailored to local epidemiology, risk factors for multidrug-resistant bacteria and severity of infection. (A.1). If no response to antibiotics is observed, consider viral and fungal infections. (C.1) (Changed)

The Role of Sarcopenia and Frailty in Further Decompensation

7.19 Frailty, malnutrition, and sarcopenia have an impact on survival in patients with decompensated cirrhosis. They should be evaluated with available standardized tools (B.1) (New)

7.20 All patients with decompensated cirrhosis should receive nutrition consultation and be advised regarding the benefits of regular exercise (B.1) (New)

7.21 While sarcopenia improves in some patients after TIPS, pre-procedural sarcopenia has also been associated with poor outcomes (e.g., encephalopathy, slower resolution of ascites) and a higher mortality. Therefore sarcopenia by itself should not be an indication tor TIPS.

Definition of cirrhosis recompensation

7.22 The concept of recompensation implies that there is at least partial regression of the structural and functional changes of cirrhosis after removal of the etiology of cirrhosis. (A.1) (New)

7.23 Clinically, the definition of “recompensation” is based on expert consensus and requires fulfilment of all the following criteria: (C.2) (New)

a. Removal/suppression/cure of the primary etiology of cirrhosis (viral elimination for hepatitis C, sustained viral suppression for hepatitis B, sustained alcohol abstinence for alcohol-induced cirrhosis)

b. Resolution of ascites (off diuretics), encephalopathy (off lactulose/rifaximin) and absence of recurrent variceal hemorrhage (for at least 12 months)

c. Stable improvement of liver function tests (albumin, INR, bilirubin)

7.24 Because clinically significant portal hypertension (CSPH) may persist despite recompensation, NSBB should not be discontinued unless CSPH resolves. (B.1) (New)

7.25 Resolution of ascites (while on diuretics or after TIPS) and/or lack of recurrent variceal hemorrhage (while on NSBB + EVL or carvedilol + EVL or after TIPS) without removal/suppression/cure of the primary etiologic factor and without improvement in liver synthetic function, is not evidence of recompensation. (B.1) (New)

Research agenda

Further Decompensation and Re-Compensation

- Investigate the effect of time to further decompensation on prognosis
- Obtain data to support the suggested concept of cirrhosis recompensation, particularly on the timeframe necessary to consider a patient truly recompensated
- Association between re-compensation and resolution of CSPH.
- Impact of etiological therapy other than alcohol abstinence and antiviral therapy on re-compensation

NSBB and Further Decompensation

- Prospective studies should assess if NSBB treatment prevents further (non-rebleeding) decompensation in decompensated patients
- Prospective studies should assess if HVPG-guided (NSBB/Carvedilol) therapy is more efficient to prevent further decompensation over non-HVPG guided strategies
- Optimal blood pressure cut-offs (MAP/SAP) to define safe use of NSBB/Carvedilol therapy and whether does reduction (vs. discontinuation) is safe
- The impact of NSBB discontinuation on the natural history of decompensated cirrhosis
- Assessment of the benefit of carvedilol over traditional NSBBs in secondary prophylaxis of variceal hemorrhage

TIPS and Further Decompensation

- The benefit of TIPS in secondary prophylaxis in patients with NSBB intolerance/NSBB non-response should be assessed in patients with ascites not meeting strict criteria for recurrent ascites
- Establish whether TIPS placement past the 72-hour preemptive TIPS window is still beneficial
- Hemodynamic and non-hemodynamic effects of NSBB in patients after TIPS

Sarcopenia, Frailty and Nutrition and Further Decompensation

- Impact of nutritional interventions on the natural history of decompensation.
- Impact of therapies targeting sarcopenia and frailty on the natural history of decompensation.
- Define the role of sarcopenia in the selection of patients for TIPS.

8) SPLANCHNIC VEIN THROMBOSIS

Aetiological work up in primary thrombosis of the portal venous system or hepatic venous outflow tract

8.1 For patients with primary thrombosis of the splanchnic veins in the absence of cirrhosis, close collaboration with subspecialists is recommended for complete work-up for prothrombotic factors and systemic diseases (A.1). (Changed)

8.2 Various combinations of risk factors for thrombosis can be present, so that identification of one risk factor does not deter from a complete work-up (A.1). (New)

8.3 In all adult patients, myeloproliferative neoplasia (MPN) should be searched for by testing for V617F JAK2 mutation in peripheral blood (A.1). (Unchanged)

8.4 In patients with undetectable JAK2 V617F mutation, consider additional investigations for MPN, including somatic calreticulin and JAK2-exon12 mutations, and next-generation sequencing (A.1). (Changed)

8.5 In all adult patients with primary thrombosis of the splanchnic veins without MPN driver mutation, bone marrow biopsy should be discussed in collaboration with hematologists to rule out MPN, irrespective of blood cell counts. Bone marrow biopsy should be considered particularly in patients without major risk factors for thrombosis (B.2). (Changed)

Budd-Chiari Syndrome-Definition

8.6 Budd-Chiari syndrome (BCS) is the consequence of an obstruction to the hepatic venous outflow. Obstruction can be located from the level of the small hepatic veins to the level of the entrance of the inferior vena cava into the right atrium (A.1) (Unchanged)

8.7 BCS is the preferred designation for any primary hepatic venous outflow tract obstruction (HVOTO) (D.1) (New)

8.8 BCS is considered secondary when the mechanism for venous obstruction is an extrinsic compression for example by a benign or malignant tumour. BCS is considered primary otherwise (A.1). (Changed)

Budd-Chiari Syndrome-Diagnosis

8.9 BCS presentation and manifestations are extremely diverse, so that the diagnosis must be considered in any patient with acute, acute-on-chronic, or chronic liver disease (A.1). (Changed)

8.10 BCS is diagnosed by the demonstration of an obstruction of the venous lumen, or by the presence of hepatic vein collaterals together with the absence of patent hepatic veins (A.1) (Unchanged)

8.11 Liver biopsy should not be performed to diagnose BCS when vascular imaging demonstrates obstruction of the hepatic venous outflow tract (B.1). (Unchanged)

8.12 Liver biopsy is necessary to diagnose BCS if obstruction of the small hepatic veins is not seen on imaging (B.1) (Changed)

8.13 In patients with BCS, hepatic nodules are frequent and most often benign. However, HCC may occur and therefore patients should be monitored with periodic imaging and alpha-fetoprotein measurements. (B.1). (Changed)

8.14 A 6-month interval can be proposed for periodic imaging (C.1). (New)

8.15 It is still unclear which of ultrasonography or magnetic resonance imaging should be used for periodical imaging screening. (C.1) (New)

8.16 Patients developing nodules should be referred to centers experienced in managing BCS (D.1) (Unchanged)

8.17 Characterization of the nodule may first include magnetic resonance imaging using hepatobiliary contrast agents (C.1). Biopsy of the lesion is indicated for a definitive diagnosis of hepatocellular carcinoma (C.1). (New)

Budd-Chiari Syndrome- Management

8.18 Management of BCS should be undertaken using a stepwise approach including anticoagulation, angioplasty/stent/thrombectomy/thrombolysis, TIPS and orthotopic liver transplantation, at experienced centres (B.1) (Unchanged)

8.19 Long-term anticoagulation should be given to all patients with primary BCS (B.1) (Changed)

8.20 Because of the increased risk of heparin induced thrombocytopenia, the use of unfractionated heparin is generally not recommended and may only be reserved for special situations (e.g., glomerular filtration rate < 30 mL/min, pending invasive procedures) (D.2). (New)

8.21 Stenoses that are amenable to percutaneous angioplasty/stenting (short length stenoses) should be actively looked for, and treated accordingly (B.1) (Unchanged)

8.22 TIPS insertion should be attempted by operators with specific experience in BCS when angioplasty/stenting/thrombectomy/thrombolysis is not feasible, and when the patient does not improve on medical therapy including anticoagulants (B.1) (Unchanged)

8.23 Consider improvement as a combination of several of the following outcomes: decreasing rate of ascites formation, decreasing serum bilirubin, serum creatinine and INR when elevated (or increasing factor V in patients receiving vitamin K antagonists) (D.1). (New)

8.24 BCS-TIPS Prognostic Index score can be used to predict outcome in patients in whom TIPS insertion is considered (B.1). (Changed)

8.25 Liver transplantation should be considered in patients with uncontrolled clinical manifestation despite stepwise approach, or in patients with high BCS-TIPS Prognostic Index score (> 7) before TIPS placement (C.1) (Changed)

8.26 In patients with BCS presenting as acute liver failure, urgent liver transplantation should be considered. Emergency TIPS should be performed, if possible, independently of listing for liver transplantation (C.1). (New)

Portal vein thrombosis and portal cavernoma in the absence of cirrhosis- Definition

8.27 Portal vein thrombosis is characterized by the presence of a thrombus in the portal vein trunk or its branches. Portal cavernoma is a network of porto portal collaterals which develops as a consequence of prior portal vein obstruction (D.1). Obstruction leading to cavernoma is mostly related to thrombosis in adults, but less likely so in children and young adults (B.1). (Changed)

8.28 Portal vein thrombosis should be distinguished by imaging tools from the extravascular compression of the venous lumen by a neighbouring space-occupying formation (D.1) (New)

8.29 Cirrhosis and/or malignancy should be ruled out and other underlying liver diseases (e.g., PSVD or other chronic liver disease) should be investigated (D.1). (Changed)

Portal vein thrombosis and portal cavernoma in the absence of cirrhosis- Diagnosis

8.30 For diagnosis of portal vein thrombosis or cavernoma, Doppler ultrasound, CT- or MR angiography should demonstrate solid intraluminal material not showing enhancement after injection of vascular contrast agents; or a network of porto-portal collaterals, respectively.

(B.1). If diagnosed by Doppler ultrasound, confirmation with contrast enhanced CT or MR angiography is needed (D.1). (Changed)

8.31 A standardized documentation (as proposed in Table 1) of initial site, extent degree of luminal obstruction, and chronicity of clot formation is required to allow subsequent evaluation of the spontaneous course and/or response to treatment (D.1) (New)

Table 1: Recommended standardised nomenclature for the description of portal vein thrombosis and portal cavernoma in both the clinical and research setting [18]

FEATURE	DEFINITION
Time Course	
Recent	PVT presumed to be present for <6 months
Chronic	PVT present or persistent for >6 months
Percent occlusion of main PV	
Completely occlusive	No persistent lumen
Partially occlusive	Clot obstructing >50% of original vessel lumen
Minimally occlusive	Clot obstructing <50% of original vessel lumen
Cavernous transformation	Gross porto portal collaterals without original PV seen
Response to treatment or interval change	
Progressive	Thrombus increases in size or progresses to more complete occlusion
Stable	No appreciable change in size or occlusion
Regressive	Thrombus decreases in size or degree of occlusion

8.32 Portal vein thrombosis and portal cavernoma in adults is frequently associated with one or more risk factors for thrombosis, which may be occult at presentation and should be investigated (B.1). (Unchanged)

8.33 In patients with portal vein thrombosis following abdominal surgery or pancreatitis, invasive procedures (e.g., bone marrow biopsy and liver biopsy) should be discussed on an individual basis considering the expected low diagnostic yield in such populations and the risk of morbidity associated with these procedures. (C.2) (New)

8.34 If the liver is dysmorphic on imaging or liver tests are persistently abnormal, liver biopsy and HVPG measurement are recommended to rule out cirrhosis or PSVD (B.1). Liver stiffness by TE may be useful to exclude cirrhosis although precise cut-offs cannot be proposed yet (C.2) (Changed)

Portal vein thrombosis and portal cavernoma in the absence of cirrhosis- Management

8.35 In the absence of cirrhosis, recent portal vein thrombosis rarely resolves spontaneously. Therefore, anticoagulation should be started at therapeutic dosage immediately at diagnosis (B.1). (Changed)

8.36 Because of the increased risk of heparin induced thrombocytopenia, the use of unfractionated heparin is not generally recommended and may only be reserved for special situations (e. g. glomerular filtration rate < 30 mL/min, pending invasive procedures) (D.2). (New)

8.37 As a primary treatment option for recent portal vein thrombosis in the absence of cirrhosis, start with low molecular weight heparin and switch to vitamin K antagonists when possible (B.1) (Changed) DOACS can be considered as primary option in selected cases in the absence of so-called "triple positive" anti-phospholipid syndrome, although data are limited (C.2). (New)

8.38 Anticoagulation should be given for at least six months in all patients with recent portal vein thrombosis in the absence of cirrhosis (B.1). (Unchanged)

Recent portal vein thrombosis in the absence of cirrhosis- Management

8.39 After 6 months, long term anticoagulation is recommended in patients with a permanent underlying prothrombotic state (B.1) and should also be considered in patients without an underlying prothrombotic state (B.2) (New)

8.40 If anticoagulation is discontinued, D-dimers < 500 ng/mL one month after discontinuation may be used to predict a low risk of recurrence (C.2). (New)

8.41 In patients without cirrhosis who do not develop complications of recent portal vein thrombosis despite absence of portal vein recanalization, interventions other than anticoagulation are not required (B.2) (Changed)

8.42 A follow-up contrast-enhanced CT-scan should be performed 6 months after recent portal vein thrombosis. (C.1) (New)

8.43 Because of the risk of recurrence of splanchnic vein thrombosis, patients need to be followed up, irrespective of anticoagulation discontinuation (C.1) (New)

8.44 The risk of intestinal infarction and organ failure is increased in patients with recent portal vein thrombosis and (i) persistent severe abdominal pain despite anticoagulation therapy, (ii) bloody diarrhea, (iii) lactic acidosis, (iv) bowel loop distention, or (v) occlusion of second order radicles of the superior mesenteric vein, Therefore, a multidisciplinary approach with early image-guided intervention, thrombolysis and surgical intervention should be considered in referral centers (C.2) (New)

Past portal vein thrombosis or cavernoma in the absence of cirrhosis- Management

8.45 In patients with past portal vein thrombosis or cavernoma, including those with incomplete resolution of recent portal vein thrombosis at 6 months, long term anticoagulation is recommended in patients with a permanent underlying prothrombotic state (B.1) and should also be considered in patients without an underlying prothrombotic state (B.2) (New)

8.46 No data are available to recommend or discourage anticoagulation in childhood-onset past portal vein thrombosis or cavernoma in the absence of an underlying prothrombotic state (C.1). (New)

8,47 In patients with past portal vein thrombosis or cavernoma not yet receiving anticoagulants, anticoagulation should be started after adequate portal hypertensive bleeding prophylaxis has been initiated in patients with high-risk varices (C.2). (Changed)

8.48 Mesenteric-left portal vein bypass (Meso-Rex operation) should be considered in all children with complications of portal cavernoma, and these patients should be referred to centres with experience in treating this condition (B.1) (Unchanged)

8,49 Patients with refractory complications of portal vein thrombosis or cavernoma should be referred to expert centers to consider percutaneous recanalization of the portal vein or other vascular interventional procedures (C.1) (New)

Treatment of portal hypertension in EHPVO

8.50 There is insufficient data on whether beta blockers or endoscopic therapy could be preferred for primary prophylaxis of portal hypertension related bleeding in patients with past portal vein thrombosis or cavernoma. Guidelines for cirrhosis should be applied (C.2). (Changed)

8.51 Esophageal variceal band ligation can be performed safely without withdrawing vitamin K antagonists (C.2). (New)

8.52 All patients in whom thrombosis has not been recanalized should be screened for gastroesophageal varices within six months of the acute episode. In the absence of varices, endoscopy should be repeated at 12 months and two years thereafter (B.1) (Unchanged)

8.53 In patients with acute portal hypertension related bleeding, recommendations for patients with cirrhosis may be applied (D.1) (Changed)

8.54 Based on recommendations for cirrhosis, combination of non-selective beta-blockers and band ligation is recommended for secondary prophylaxis (D.1). (New)

Research agenda

Budd- Chiari Syndrome:

- Risk factors for hepatocellular carcinoma in patients with BCS
- Non-invasive diagnosis of hepatocellular carcinoma in patients with BCS
- Short-term (8 days) evolution criteria predicting a good mid-long-term outcome (i.e., criteria for "treatment response") in patients with BCS

Portal Vein Thrombosis without cirrhosis

- Predictors of development, progression, and spontaneous resolution of PVT
- Influence of beta-blockers on natural history of PVT
- Effect of early recanalization using interventional radiology or TIPS *vs.* fibrinolytic agents and/or anticoagulants in patients with recent PVT
- Efficacy of anticoagulation on recanalization and on prevention of progression of PVT in children/young adults with PVT
- Pathophysiology and management of cytopenia in patients with non-cirrhotic portal hypertension

9) OTHER ISSUES IN VASCULAR LIVER DISORDERS

Use of anticoagulants in non-cirrhotic vascular liver diseases

9.1 Low Molecular Weight Heparin and Vitamin K Antagonists are widely accepted and used in primary thrombosis of the portal venous system or hepatic venous outflow tract (A.1). (Unchanged)

9.2 There are no major concerns with safety of DOACs in patients with non-cirrhotic vascular liver diseases, as long as liver function is preserved. DOACs should be used with caution in patients with impaired liver function (equivalent to Child-Pugh class B), as well as in patients with creatinine clearance below 30 mL/min. The use of DOACs in patients with severe liver dysfunction (equivalent to Child-Pugh C) is not recommended outside study protocols. (C.2) (New)

Anticoagulation and portal vein thrombosis (PVT) in cirrhosis

9.3 Screening for PVT is recommended in all patients who are potential liver transplant candidates, at the time of screening for hepatocellular carcinoma (D.2) (Changed)

9.4 Occurrence of PVT in the presence of HCC does not directly imply vascular malignant invasion, but further imaging is recommended (CT-scan and/or magnetic resonance imaging and/or contrast enhanced ultrasonography) (D.2) (Changed)

9.5 Anticoagulation is recommended in patients with cirrhosis and (i) recent (<6 months) completely or partially occlusive (>50%) thrombosis of the portal vein trunk with or without extension to the SMV, or (ii) symptomatic portal vein thrombosis, independently of the

extension, or (iii) portal vein thrombosis in potential candidates for liver transplantation, independently of the degree of occlusion and extension (C.2) (New)

9.6 In potential liver transplant candidates, the goal of anticoagulation is to prevent re-thrombosis or progression of thrombosis to facilitate adequate portal anastomosis in liver transplantation and reduce post-transplant morbidity and mortality (C.1) (Changed)

9.7 Anticoagulation should be considered in patients with cirrhosis and minimally occlusive (<50%) thrombosis of the portal vein trunk that (i) progresses on short-term follow-up (1-3 months) or (ii) compromises the superior mesenteric vein (C.2) (New)

9.8 Anticoagulation should be (i) maintained until portal vein recanalization or for a minimum of 6 months, (ii) continued after recanalization in patients awaiting liver transplantation, and (iii) considered to be continued after recanalization in all others, while balancing benefits in preventing recurrence and increasing survival and the risk of bleeding (C.1). (New)

9.9 Patients with low platelet count (e.g., <50 $x10^9$/L) are at higher risk of PVT, but also of bleeding complications on anticoagulation and require a case-by-case assessment (C.2). (Changed)

9.10 TIPS is recommended in patients with thrombosis of the portal vein trunk without recanalization on anticoagulation, especially in patients listed for liver transplantation (C.2) (New)

9.11 Anticoagulation is preferably initiated with LMWH and maintained with either LMWH, VKA or DOAC. Advantages of LMWH are that its use is based on solid data. VKA carry challenges with regard to INR monitoring in patients with cirrhosis. Advantages of DOACs are that they are easier to use but less data are available. (C.1). (Changed)

9.12 Currently available data suggest that there are no major safety concerns for DOACs in patients with Child-Pugh class A cirrhosis. Due to the possibility of accumulation, DOACs should be used with caution in Child-Pugh class B patients, as well as in patient with creatinine clearance below 30 mL/min. The use of DOACs in Child-Pugh class C patients is not recommended outside study protocols. (B.2) (New).

9.13 DOACs likely have different safety-efficacy profiles in patients with cirrhosis, although at the moment no recommendation can be made in favour of a specific DOAC in this setting (D.2) (New)

Porto-sinusoidal vascular disorder (PSVD)

9.14 Porto-sinusoidal vascular disorder (PSVD) is a broad clinico-pathological entity encompassing non-cirrhotic portal fibrosis, idiopathic portal hypertension or non-cirrhotic intrahepatic portal hypertension, and various overlapping histological patterns including

nodular regenerative hyperplasia, obliterative portal venopathy, hepatoportal sclerosis, incomplete septal cirrhosis. (B.1) (New)

9.15 Absence of portal hypertension does not rule-out PSVD. Presence of common causes of liver disease (e.g., viral hepatitis, excessive alcohol consumption, metabolic syndrome, etc.) does not rule-out PSVD, and both can coexist. Presence of portal vein thrombosis does not rule-out PSVD, and both can coexist. (B.1) (New)

9.16 PSVD should be considered in the following situations: (i) signs of portal hypertension contrasting with atypical features for cirrhosis (e.g., HVPG < 10 mm Hg; liver stiffness measurement < 10 kPa; smooth liver surface and no atrophy of segment IV; hepatic vein-to-vein communications; although none of these features is considered pathognomonic for PSVD); or (ii) liver blood test abnormalities or portal hypertension in a patient with a condition known to be associated with PSVD (Supplementary Table 1); or (iii) unexplained liver blood test abnormalities even without signs of portal hypertension. (B.1) (New)

Diagnosis of PSVD

9.17 Porto-sinusoidal vascular disorder can be observed in the absence of clinical, laboratory or imaging features of portal hypertension (B.1) (New)

9.18 A liver biopsy specimen of adequate size (> 20 mm) and of minimal fragmentation -or otherwise considered adequate for interpretation by an expert pathologist- is required for the diagnosis of PSVD (C.1) (New).

9.19 Diagnosis of PSVD requires the exclusion of cirrhosis and of other causes of portal hypertension (B.1), together with one of the following three criteria (C.2): (i) at least one feature specific for portal hypertension; or (ii) at least one histologic lesion specific for PSVD; or (iii) at least one feature not specific for portal hypertension together with at least one histologic lesion compatible although not specific for PSVD (Table 2). (New)

Table 2 Criteria in the definition of PSVD (adapted from ref.19)

	Feature of portal hypertension	**Histological lesions suggestive of PSVD assessed by an expert pathologist**
Specific	- Gastric, esophageal, or ectopic varices - Portal hypertensive bleeding - Porto-systemic collaterals at imaging	- Obliterative portal venopathy (thickening of vessel wall, occlusion of the lumen, vanishing of portal veins) - Nodular regenerative hyperplasia - Incomplete septal fibrosis (also called incomplete septal cirrhosis); this latter

		feature can only be assessed on liver explants and not on liver biopsies
Not specific	- Ascites - Platelet count < 150'000/mm^3 - Spleen size ≥ 13 cm in the largest axis	- Portal tract abnormalities (multiplication, dilatation of arteries, periportal vascular channels, aberrant vessels) - Architectural disturbance: irregular distribution of the portal tracts and central veins - Non-zonal sinusoidal dilatation - Mild perisinusoidal fibrosis

Management of PSVD

9.20 Once the diagnosis of PSVD is made, patients should be screened for associated immunological diseases, prothrombotic or genetic disorders and exposure to drugs/toxins (D.2) (New) (Supplementary Table 1).

9.21 Endoscopic screening for gastroesophageal varices is required at diagnosis of PSVD (C.1). (New)

9.22 The non-invasive Baveno VII criteria for screening of oesophageal varices used in patients with cirrhosis cannot be applied to patients with PSVD (B.1). (New)

9.23 During follow-up, the frequency of endoscopic screening for varices has not yet been defined. Management according to cirrhosis guidelines is recommended, expect for stopping rules (D.2) (New).

9.24 There is insufficient data on which therapy should be preferred for portal hypertension prophylaxis in PSVD. Management according to cirrhosis guidelines is recommended (D.2) (New)

9.25 A contrast enhanced CT-scan is suggested at diagnosis of PSVD in order to assess the anatomy/patency of the portal venous system and potential porto-systemic collaterals (D.2) (New).

9.26 Screening for portal vein thrombosis in patients with PSVD: there is no data on the best screening method and interval (D.2) (New). Doppler ultrasound every 6 months is suggested in patients with PSVD and features of portal hypertension (C.1) (New). In case of abdominal pain, Doppler ultrasound or cross-sectional imaging should be performed to rule-out splanchnic vein thrombosis. (B.1) (New)

9.27 No recommendation can be made for anticoagulation therapy to prevent the development of portal vein thrombosis in PSVD (D.2) (New)

9.28 In those patients developing PVT, anticoagulant therapy should be started according to recommendations for non-cirrhotic PVT (C.1) (New)

9.29 TIPS can be considered to treat severe complications of portal hypertension. Underlying/associated conditions, which negatively impact post-TIPS outcome, must be taken into account in making individual decision for TIPS insertion (C.2) (New)

9.30 Liver transplantation is an option in selected PSVD patients with severe or refractory complications of portal hypertension or with advanced liver dysfunction. Indication should be discussed in expert centers (D.2) (New)

Research Agenda

Anticoagulation in PVT in cirrhosis

- Assessment of the safety and efficacy of each single DOAC in patients with cirrhosis
- Identification of indicators associated with a favorable outcome in patients with cirrhosis and PVT treated with anticoagulants
- Stopping rules in long-term anticoagulant treatment in patients with cirrhosis and PVT
- Advantages and disadvantages of prophylactic vs. full dose anticoagulation in patients with cirrhosis and PVT
- Definition of response to treatment in patients with cirrhosis and PVT

PSVD:

- Natural history of PSVD without portal hypertension
- Improvement of non-invasive methods to screen for PSVD (e.g., cross sectional imaging, spleen stiffness measurement).
- Prophylaxis for PVT in patients with PSVD and signs of portal hypertension
- Incidence and predictors of development of PVT in patients with PSVD and efficacy of anticoagulation in this setting

Other issues

Besides the supporting data and consensus recommendations for the nine Baveno sessions, seven lectures were given at Baveno VII. The topics of these lectures were: ‘New concepts of risk stratification’, ‘Clinical stages and ordinal outcomes in portal hypertension’, ‘Lifestyle and genetic modifiers of liver disease progression’, Parenchymal extinction lesions (PELS) in progression. Can they regress?’, 'Fibrogenesis and regression of fibrosis’, 'Angiogenesis and progression of advanced chronic liver disease (ACLD)’, and 'Drugs to modify liver fibrosis progression and regression’. The nine Baveno sessions and the seven lectures will be summarized in the Baveno VII proceedings book

[17]. The Baveno VII consensus workshop was followed by a paediatric satellite meeting entitled 'Primary prophylaxis of variceal hemorrhage, complexities in the development of evidence-based approaches in paediatrics'.

Readers interested in examining the evolution of the recommendation on cirrhosis and portal hypertension can refer to the Baveno I-VI reports [2-4,7-10;12-14]

Use of the definitions and adherence to the recommendations in future studies is encouraged to provide further validation. The topics listed in the research agenda reflect the opinions of the experts about the areas where new information is most needed.

Baveno VII Faculty

The following were members of the Baveno VI Scientific Committee:
Roberto de Franchis [Milan, Italy (Honorary President)], Jaime Bosch [Bern, Switzerland (Chair)] Guadalupe Garcia-Tsao [West Haven, USA (Vice-Chair)], Thomas Reiberger [Vienna, Austria (Scientific Secretary)], Cristina Ripoll [Jena, Germany (Scientific Secretary)], Juan G Abraldes (Edmonton, Canada), Agustin Albillos (Madrid, Spain), Annalisa Berzigotti (Bern, Switzerland), Gennaro D'Amico (Palermo, Italy), Andrea De Gottardi (Lugano, Switzerland), Alessandra Dell'Era (Milan, Italy), Juan Carlos Garcia-Pagàn (Barcelona, Spain), Joan Genescà (Barcelona, Spain), Aleksander Krag (Odense, Denmark), Wim Laleman (Leuven, Belgium), Vincenzo La Mura (Milan, Italy), Dominique Thabut (Paris, France) Jonel Trebicka (Frankfurt, Germany), Emmanouil Tsochatzis (London, UK), Dominique Valla (Paris, France), Candid Villanueva (Barcelona Spain)

The following chaired sessions or lectures:
Agustin Albillos (Madrid, Spain), Annalisa Berzigotti (Bern, Switzerland), Jaime Bosch (Barcelona, Spain), Roberto de Franchis (Milan, Italy), Andrea De Gottardi (Lugano, Switzerland), Hector Ferral, (Evanston, USA),Juan Carlos Garcia-Pagàn (Barcelona, Spain), Guadalupe Garcia-Tsao (West Haven, USA), Joan Genescà (Barcelona, Spain), Virginia Hernandez-Gea (Barcelona, Spain), Wim Laleman (Leuven, Belgium), Mattias Mandorfer (Vienna, Austria), David Patch (London, UK), Pierre Emmanuel Rautou (Paris, France), Thomas Reiberger, (Vienna, Austria), Cristina Ripoll,(Jena, Germany), Shiv K Sarin (New Delhi, India), Dominique Thabut (Paris, France), Jonel Trebicka (Frankfurt, Germany) Emmanouil Tsochatzis (London, UK), Dominique Valla (Paris, France) .

The following participated in the presentations and the discussions as panellists in the consensus sessions:
Anna Baiges (Barcelona, Spain), Jasmohan Bajaj (Richmond, USA). Rafael Bañares (Madrid, Spain), Marta Barrufet (Barcelona, Spain),Lina Benajiba (Paris, France) Christophe Bureau (Toulouse, France), Vincenza Calvaruso (Palermo, Italy), Andres Cardenas (Barcelona, Spain), Alessandra Dell'Era (Milan, Italy), Angels Escorsell (Barcelona, Spain), Jonathan Fallowfield (Edinburgh, UK),Sven Francque (Antwerp, Belgium) Ron Gaba, (Chicago, USA), Susana Gomes Rodrigues (Bern, Switzerland), Guogong Han (Xi'an, China), Jidong Jia (Beijing, China), Jean Jacques Kiladjian (Paris, France),Aleksander Krag, (Odense, Denmark), Vincenzo La Mura (Milan, Italy), Sabela Lens, (Barcelona, Spain), Xuefeng Luo (Chengdu, China), Sarwa Darwish Murad (Rotterdam, The Netherlands),Valerie Paradis (Clichy, France), Salvatore Piano (Padua, Italy),Aurelie Plessier (Clichy, France),Massimo Primignani, Milan, Italy), Bogdan Procopet (Cluj-Napoca, Romania), Marika Rudler (Paris, France) ,Filippo Schepis, Modena, Italy), Marco Senzolo (Padua, Italy),Akash Shukla (Mumbai, India) Puneeta Tandon (Edmonton, Canada), Luis Tellez (Madrid, Spain) Maja Thiele (Odense, Denmark), Dhiraj Tripathi (Birmingham, UK), Laura Turco, (Bologna, Italy), Fanny Turon, (Barcelona, Spain) Candid Villanueva (Barcelona Spain). Hitoshi Yoshiji (Nara, Japan)

The following gave review lectures:
Juan G Abraldes (Edmonton, Canada), Annalisa Berzigotti (Bern, Switzerland), Gennaro D'Amico (Palermo, Italy), Jordi Gracia, (Barcelona, Spain), Massimo Pinzani, (London, UK), Vijay Shah (Rochester, USA), Ian Wanless (Halifax, Canada)

Conflict of interest

The participants of the Baveno-VII consensus conference declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

ACKNOWLEDGEMENTS

The Baveno VII Consensus workshop was endorsed and supported with unrestricted grants by the following: a) International Scientific Societies: EASL (European Association for the Study of the Liver), b) national scientific societies: AASLD (American Association for the Study of Liver Disease); AEEH (Spanish Association for the Study of the Liver), AFEF (French Association for the Study of the Liver), AIGO (Italian Association of Hospital Gastroenterologists and Endoscopists); AISF (Italian Association for the Study of the Liver); CIBERehd (Spanish network of biomedical investigation in liver and digestive diseases), ÖGGH (Austrian Society for Gastroenterology and Hepatology), SASL (Swiss Association for the Study of the Liver), SIGE (Italian Society of Gastroenterology), c) International Research Groups; Decision, Galaxy, Microb-Predict.

REFERENCES

1. Burroughs AK ed. Methodology and review of clinical trials in portal hypertension. Excerpta Medical Congress Service N° 763. Amsterdam, New York, Oxford, 1987
2. de Franchis R, Pascal JP, Ancona E, Burroughs AK, Henderson JM, Fleig W, Groszmann R, Bosch J, Sauerbruch T, Søderlund C, Lebrec D, Sørensen TIA, Pagliaro L. Definitions, methodology and therapeutic strategies in portal hypertension. A consensus development workshop. J Hepatol 1992;15: 256-261
3. de Franchis R Developing consensus in portal hypertension. J Hepatol 1996; 25:390-394
4. de Franchis R (editor). Portal Hypertension II. Proceedings of the second Baveno international consensus workshop on definitions, methodology and therapeutic strategies. Oxford, Blackwell Science, 1996
5. Spina GP, Arcidiacono R, Bosch J, Pagliaro L, Burroughs AK, Santambrogio R, Rossi A. Gastric endoscopic features in portal hypertension: final report of a consensus conference. J Hepatol 1994; 21:461-467
6. Grace ND, Groszmann RJ, Garcia-Tsao G, Burroughs AK, Pagliaro L, Makuch RW, Bosch J, Stiegmann GV, Henderson JM, de Franchis R, Wagner JL, Conn HO, Rodès J. Portal hypertension and variceal bleeding: an AASLD single topic symposium. Hepatology 1998; 28:868-880
7. de Franchis R. Updating consensus in portal hypertension: report of the Baveno III consensus workshop on definitions, methodology and therapeutic strategies in portal hypertension. J Hepatol 2000; 33:846-852
8. de Franchis R, Editor. Portal Hypertension III. Proceedings of the IIIrd Baveno International Consensus Workshop on Definitions, Methodology and Therapeutic Strategies. Blackwell Science, Oxford, UK, 2001

9. de Franchis R Evolving consensus in portal hypertension. Report of the Baveno IV consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol 2005; 43:167-176
10. de Franchis R Editor Portal Hypertension IV. Proceedings of the IVth Baveno international consensus workshop on methodology of diagnosis and treatment. Oxford, UK: Blackwell publishing; 2006
11. Garcia-Tsao G, Bosch J, Groszmann R. Portal hypertension and variceal bleeding, unresolved issues. Summary of an American Association for the study of liver disease and of the European Association for the Study of the Liver single-topic conference. Hepatology 2008; 47:1764-1772
12. de Franchis R on behalf of the Baveno V Faculty. Revising consensus in portal hypertension: Report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol 2010; 53:762-768
13. de Franchis R, Editor. Portal Hypertension V. Proceedings of the Vth Baveno international consensus workshop. Oxford, UK. Wiley-Blackwell, 2011
14. de Franchis R, on behalf of the Baveno VI Faculty. Expanding consensus in portal hypertension: report of the Baveno VI consensus workshop: stratifying risk and individualizing care for portal hypertension. J Hepatol 2015; 63:743-752
15. de Franchis R Editor. Portal Hypertension VI. Proceedings of the VIth Baveno consensus workshop: stratifying risk and individualizing care, New York, USA, Springer, 2016.
16. GRADE working group. Grading quality of evidence and strength of recommendations. BMJ 2004; 328:1490-1497
17. de Franchis R Editor. Portal Hypertension VII. Proceedings of the VIIth Baveno consensus workshop: Personalized care in portal hypertension, New York, USA, Springer, 2022.
18. Northup PG, Garcia-Pagan JC, Garcia-Tsao G, Intagliata NM, Superina RA, Roberts LN, et al. Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients with

Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases Hepatology 2021;73:366-413

19. De Gottardi A, Rautou PE, Schouten J, Rubbia-Brandt L, Leebeek F, Trebicka J,; VALDIG group. Porto-sinusoidal vascular disease: proposal and description of a novel entity. Lancet Gastroenterol Hepatol . 2019;4:399-411

ABREVIATIONS

ACLF = Acute on Chronic Liver Failure

AKI = Acute Kidney Injury

ALD = Alcoholic Liver Disease

AVB = Acute Variceal Bleeding

BATO = Balloon-occluded Antegrade Transvenous Obliteration

BCS = Budd-Chiari Syndrome

BRTO = Balloon-occluded Retrograde Transvenous Obliteration

BT = Balloon Tamponade

cACLD = Compensated Advanced Chronic Liver Disease

CLD = Chronic Liver Disease

CSPH = Clinically Significant Portal Hypertension

DOAC = Direct-Acting Oral Anti Coagulants

EHPVO = Extra Hepatic Portal Vein Obstruction

EUS = Endoscopic Ultrasound

EV = Esophageal Varices

EVL = Esophageal Variceal Ligation

FMT = Fecal Microbiota Transplantation

FHVP = Free Hepatic Venous Pressure

FXR = Farnesoid X Receptor

GAVE : Gastric Antral Vascular Ectasia

GEV = Gastro-Esophageal Varices

GOV1 = Gastro-Esophageal Varices, type 1

HBV = Hepatitis B Virus

HCC = Hepatocellular Carcinoma

HCV = Hepatitis C Virus

HDV = Hepatitis Delta Virus

HE = Hepatic Encephalopathy

HRS = Hepato Renal Syndrome

HV = Hepatic Vein

HVOTO = Hepatic Vein Outflow Tract Obstruction

HVPG = Hepatic Vein Pressure Gradient

ICU = Intensive Care Unit

IGV = Isolated Gastric Varices

INR = International Normalized Ratio

IVC = Inferior vena Cava

LSM = Liver Stiffness Measurement

MELD = Model for End-stage Liver Disease

MPN = Myelo Proliferative Neoplasm

MR = Magnetic Resonance

NAFLD: Non-Alcoholic Fatty Liver Disease

NASH = Non-Alcoholic Steato-Hepatitis

NIT = Non-Invasive Tests

NSBB = Nonselective Beta Blockers

PH = Portal hypertension

PHG = Portal Hypertensive Gastropathy

PHP = Portal Hypertensive Polyp

PPG = Portal Pressure Gradient

PRBC = Packed Red Blood Cells

PSVD = Porto-Sinusoidal Vascular Disorder

PTFE = Poly Tetra Fluoro Ethylene

pTIPS = pre-emptive TIPS

PVT = Portal Vein Thrombosis

SAAG = Serum-Ascites Albumin Gradient

SBP = Spontaneous Bacterial Peritonitis

SEMS = Self Expanding Metal Stent

SSM = Spleen Stiffness Measurement

SVR = Sustained Virological Response

SWE = Shear Wave Elastography

TE = Transient Elastography

TIPS: Transjugular Intrahepatic Porto-systemic Shunt

VNT = Varices Needing Treatment

WHVP = Wedged Hepatic Venous Pressure