H.3 Severity risk tools

Study	Aravinthan 2013[7]
Study type	Cohort study
Number of studies (number of participants	77 patients with biopsy-confirmed alcoholic liver disease cirrhosis
Countries and Settings	University Hospital, Southampton
Funding	Hepatology Endowment Fund and Addenbrooke's Charitable Fund
Duration of study	Median follow-up 57 months (1–120) after liver biopsy
Age, gender, ethnicity	Age: median 50 (26–80), gender: 56% men
Patient characteristics	All patients gave a history of sustained excessive alcohol consumption (men >30 g/d; women >20 g/d). All but one were consuming alcohol in excess at the time of liver biopsy (median 164 g/day (57–600). During follow-up, 61% of those who were

Study	Aravinthan 2013[7]
	consuming alcohol at the time of liver biopsy continued to consume alcohol. Other recognised causes of liver disease were excluded after appropriate investigations. All patients had routine haematology and biochemistry blood tests performed at the time of liver biopsy and were reviewed at least every 6 months until death, an adverse liver-related outcome or the censor point. Only those patients with complete follow-up data were included.
Severity risk tool (for example transient elastography, Child-Pugh, MELD)	MELD score
Outcome and timepoint	Adverse liver-related outcome (liver-related death, decompensation, variceal bleed, ALD and sepsis, liver transplantation, hepatocellular carcinoma)
During follow-up, 47% died of liver-related causes and two were considered for and underwent liver transplantation. A further 5 patients died of causes related to liver diseases. 26% experienced decompensation, 17% experienced variceal bleeding, 4% experienced sepsis, 0% developed hepatocellular carcinoma. Results : MELD score to predict adverse liver-related outcome AUC (95% CI): 0.59 (0.47–0.72) Optimal cut-off threshold for determining people who will/will not have the event (if calculated): Not reported General limitations according to PROBAST: Some components of the composite outcome do not match the protocol (sepsis, liver transplantation) therefore evidence is slightly indirect.	

Study	Ferlitsch 2012[36]
Study type	Prospective
Number of studies (number of participants	Patients referred to the hepatic haemodynamic lab and scheduled for baseline HPVG measurements were included. 286 patients with liver cirrhosis were included. Transient elastography measurements were performed on 145/189 patients who were compensated at baseline.
Countries and Settings	Department of Internal Medicine III, Division of Gastroenterology, Medical University of Vienna (Austria)
Funding	Skoda grant 2011 of the Austrian Society of Internal Medicine

Study	Ferlitsch 2012[36]
Duration of study	September 2006–December 2009
Age, gender, ethnicity	(For whole group, n=286) age: median 55, IQR 48–62; gender: 201 males, 65 females; ethnicity: not reported.
Patient characteristics	Liver cirrhosis was diagnosed histologically, clinically or by typical radiological findings. Aetiology of liver disease, age, HPVG, medical history including the presence of oesophageal varices, ascites, Child Pugh Score, haematological status, clinical chemistry and liver stiffness measured by transient elastography were recorded for each patient at the day of HPVG measurement. Exclusion: Presence of pre- and post-hepatic causes of portal hypertension. Severe cardiopulmonary or renal impairment, active infections, diabetes, anticoagulant therapy, antiplatelet drugs, current treatment with beta-blockers, statins or interferon. Patients with alcoholic liver disease needed to be abstinent from alcohol for at least 3 months.
Severity risk tool (for example transient elastography, Child-Pugh, MELD)	Measurement of liver stiffness was performed by transient elastography (transient elastography, Echosens) after an overnight fast. Results of liver stiffness were considered as adequate if the IQR was within the 30% interval of the median value and if the success rate was ≥70%. Results were recorded in kPa.
Outcome and timepoint	Patients were followed prospectively at least every 6 months at the outpatient clinic. All events, particularly decompensation by ascites, jaundice, grade 3/4 hepatic encephalopathy, variceal bleeding, death and liver transplantation were recorded. The national register of death was also screened.
Cumulative deaths at 12 months (total n=189): 16; 24 months: 32; 36 months: 41; 48 months: 45 Cumulative deaths or decompensation at 12 months (total n=189): 26; 24 months: 39; 36 months: 55; 48 months: 58 Results : Performance of transient elastography for predicting decompensation (in patients compensated at baseline only) AUC (95% CI): Optimal cut-off threshold for determining people who will/will not have the event (if calculated): Not reported Threshold: Not reported Sensitivity: 20.3 Specificity: 88.2 PPV: 56.8 NPV: 28.3 +ve/-ve likelihood ratios: 98.4/2.0	

Study	Ferlitsch 2012[36]
General limitations according to PROBAST: Transient elastography was unsuccessful in 41 of 128 compensated patients (mainly because of obesity) therefore ROC curves were calculated with the intention to diagnose (ITD) approach.	

Study	Finkenstedt 2012[44]
Study type	Prospective longitudinal study
Number of studies (number of participants	429 All adult patients with cirrhosis referred to the department August 2007–September 2009 plus analysis was carried out on frozen samples from a cohort of consecutive patients who were treated November 2005–January 2007.
Countries and Settings	Department of Gastroenterology and Hepatology at the University Hospital of Innsbruck, Austria
Funding	No commercial relationships
Duration of study	Median 1.3 years (IQR 0.6–3.5)
Age, gender, ethnicity	Age: mean 57.2 (SD: 12.0); gender: 136 female, 293 male; ethnicity: not reported.
Patient characteristics	Inclusion criteria: 18 years and above, diagnosed with cirrhosis (based on imaging studies, CT scan and/or ultrasound showing morphological signs compatible with end stage liver disease, oesophageal/cardiac varices or portal hypertensive gastropathy in the upper GI endoscopy and/or biochemical signs of cirrhosis). Exclusion criteria: missing laboratory parameters for calculation of MELD score, prior liver or kidney transplantation, renal replacement therapy prior to entry into the study, malignancies (including HCC) and loss to follow-up within 90 days. Patients lost to follow up after 90 days were censored with the last day they were known to be alive and patients who underwent liver transplantation were censored at that date.
Severity risk tool (for example transient elastography, Child-Pugh, MELD)	MELD was calculated according to the formula 0.957 * ln(creatinine) + 0.378 * ln(bilirubin) + 1.120 * ln(INR) + 0.643. The resulting score was multiplied by 10.
Outcome and timepoint	90-day mortality

Study	Finkenstedt 2012[44]
Results : During follow-up 50 patients (12%) underwent liver transplantation and 83 patients (19%) died. Main causes of death were multi-organ failure with or without sepsis (59%), variceal or non-variceal bleeding (19%) and hepatic decompensation (17%). Mean transplant-free survival was 1470 days with 3-month, 1-year and 3-year transplant-free survival rate of 92, 84 and 77% respectively. MELD AUC (95% CI): 0.9 (0.84–0.96) Optimal cut-off threshold for determining people who will/will not have the event (if calculated): Not reported Threshold: ≥16 Sensitivity: 85 Specificity: 83 Calibration: Calibration of MELD for 3-month mortality was poor for scores within the lower three quintiles but seemed to be fairly good in the fourth and fifth quintile of each score. The calibration of the scores for 1 year mortality was better but still remained imprecise within the lower quintiles. General limitations according to PROBAST: 90-day mortality slightly indirect outcome due to timing. At risk of bias due to optimal threshold calculated.	

Study	Kim 2012H[69]
Study type	Prospective, longitudinal study
Number of studies (number of participants	n=217 consecutive patients with HBV diagnosed with cirrhosis by liver biopsy and undergoing liver stiffness measurement on the same day. Recruitment from January 2005 to December 2007.
Countries and Settings	University Hospital, Seoul, Korea
Funding	Grant of the Korea Healthcare technology R&D Project, Ministry of Health and Welfare, Republic of Korea

Study	Kim 2012H[69]
Duration of study	Median 42.1 months (range 6.1–58.4 months). Followed up every 3 months.
Age, gender, ethnicity	Age, mean: 50.1 years; male/female: 141/76; mean liver stiffness measurement 16.2 (11.5) kPa; ethnicity: not reported. Fourty-two patients had already been under antiviral therapy before enrolment, 29 patients started at the time of enrolment and 36 after inclusion during the follow-up.
Patient characteristics	Inclusion: Diagnosed with cirrhosis by liver biopsy (F4 by METAVIR) and undergoing liver stiffness measurement on the same day. Indications for liver biopsy included assessment of severity of liver fibrosis and inflammation. All patients had well-preserved liver function (Child-Pugh A) and none of them had experienced prior decompensation. Exclusion: Any aetiologies for liver disease other than HBV, including liver cancer, co-infection with HCV, HDV, or HIV, other comorbidities (NASH, PSC, PBC), BMI >35, alcohol ingestion in excess of 40 g/day for <5 years, previous liver resection or transplantation, unreliable liver stiffness measurement with an IQR/M ratio >30% or a success rate <60%, or validated measurements <10, cardiac failure, liver biopsy unsuitable for staging (<15 mm).
Severity risk tool (for example transient elastography, Child-Pugh, MELD)	Transient elastography: Performed by a single experienced technician. Only examinations with an IQR/M ratio <30%, at least 10 valid measurements and a success rate of at least 60% were considered reliable. Operator blinded to patient's clinical and laboratory data.
Outcome and timepoint	Hepatic decompensation events (defined as the occurrence of any one of the following: ascites development, hepatic encephalopathy, variceal haemorrhage, deterioration of liver function to Child-Pugh class B or C).
26/217 (12%) had at least one hepatic decompensation event. Results : Transient elastography AUC (95% CI): 0.773 (0.686–0.860) Optimal cut-off threshold for determining people who will/will not have the event (if calculated): 18 kPa (Youden method) Threshold: Not reported Sensitivity: Not reported Specificity: Not reported PPV: Not reported NPV: Not reported +ve/-ve likelihood ratios: Not reported TP: Not reported	

Study	Kim 2012H[69]
FP: Not reported FN: Not reported TN: Not reported Other measures: Calibration: Not reported Score on Risk Tool: Risk of event: <13 kPa 0.93, 0.9, 2.31 and 4.02% at 1, 2, 3 and 4 years 13–18 kPa 5.88, 10.54, 132.74 and 23.10% at 1, 2, 3 and 4 years ≥18 kPa 13.38, 23.21, 30.5 and 55.32% at 1, 2, 3 and 4 years General limitations according to PROBAST: One component of the composite outcome does not match the protocol (deterioration of liver function to Child-Pugh class B or C) therefore evidence is slightly indirect.	

Study	Kim 2014D[70]
Study type	Prospective longitudinal study
Number of studies (number of participants	207 patients with chronic hepatitis B (CHB) who underwent transient elastography examinations and then started entecavir (0.5 mg/d) as the first-line antiviral agent within 2 weeks after transient elastography examination between June 2007 and May 2010 and completed two years of treatment at the hospital. A subgroup of 69 patients had cirrhosis.
Countries and Settings	Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
Funding	Grant of the Korea Healthcare Technology R&D Project, Ministry of Health and Welfare, Republic of Korea. The funders had no role in the study design, data and analysis, decision to publish or preparation of the manuscript.
Duration of study	2 years

Study	Kim 2014D[70]
Age, gender, ethnicity	For whole study population: age: 51 (20–72); gender: (61.1% male); ethnicity: not reported. Data not reported separately for cirrhotic subgroup.
Patient characteristics	Inclusions: CHB was defined as persistent presence of serum hepatitis B surface antigen for >6 months and HBV DNA positivity by PCR. Exclusions: Liver stiffness measurement failure (no valid shots, n=2), invalid liver stiffness measurement (n=5), HCC at enrolment or a history of HCC (n=8), Child-Pugh class B or C (n=6), evidence of hepatic decompensation (n=4), co-infection with hepatitis C, hepatitis D or HIV (n=2), right-sided heart failure (n=1), ascites or pregnancy (n=2), follow-up loss (n=15). Therefore 45 patients were excluded in total. A subgroup of 69 patients with cirrhosis were analysed separately. Cirrhosis was defined as: a platelet count <100,000/μL and ultrasonographic findings suggestive of cirrhosis including a blunted, nodular liver edge accompanied by splenomegaly >12 cm or oesophageal or gastric varices.
Severity risk tool (for example transient elastography, Child-Pugh, MELD)	Liver stiffness measurement was performed on the right lobe of the liver through the intercostal spaces in patients lying in the dorsal decubitus position with the right arm in maximal abduction. The operator located a liver portion that was at least 6 cm thick and free of large vascular structures and pressed the probe button to commence the measurement. One experienced technician (>20,000 examinations) who was blinded to patients' clinical data performed all liver stiffness measurements. The success rate was calculated by dividing the number of valid measurements by the total number of measurements. The IQR was defined as an index of intrinsic variability of liver stiffness measurement corresponding to the interval of liver stiffness measurement results containing 50% of the valid measurements between the 25th and 75th percentiles. When the liver stiffness measurement showed an IQR/M of >0.3, success rate of <60% or <10 valid measurements, it was regarded as invalid and excluded from the analysis.
Outcome and timepoint	All patients were screened ultrasonographically for HCC at their initial screening visit. Patients were followed up with α-fetoprotein and ultrasonography every 3 or 6 months. In addition to baseline liver stiffness measurements, follow-up values were measured during the course of ETV treatment (at 1 and 2 years). Furthermore, patients were monitored to detect clinical evidence of hepatic decompensation including variceal bleeding, ascites, hepatic encephalopathy, SBP and hepatorenal syndrome.
12 (17.4%) of the cirrhotic subgroup experienced development of liver-related events. Results: Liver stiffness to predict development of liver-related events within 2 years AUC (95% CI): 0.793 (0.62–0.852)	

Study	Kim 2014D[70]
Optimal cut-off threshold for determining people who will/will not have the event (if calculated): 19.0 kPa Threshold: 19.0 kPa (optimal) Sensitivity: 93.3 Specificity: 42.2 General limitations according to PROBAST: At risk of bias due to optimal threshold calculated.	

Study	Klibansky 2012[72]
Study type	Prospective, longitudinal study
Number of studies (number of participants	Final analysis n=667 consecutive recruitment (prior to this, 114 excluded due to no follow-up after transient elastography and 60 excluded because transient elastography was not performed successfully). Cirrhosis subgroup n=160. Recruitment between November 2004 and July 2007
Countries and Settings	Medical Centre, Israel
Funding	One author reports receiving consultant and grant research support from Echosens (producers of FibroScan), Quest and Prometheus.
Duration of study	Median 854 days after transient elastography. Followed up every 12 months and electronic medical records from these visits formed the database.
Age, gender, ethnicity	Whole population. Age: 51.0 (45–56); male/female: 415/262; ethnicity: White 514, Black 62, Asian 46, Hispanic 42, Native American 3; liver stiffness measurement 8.7 (5.9–17.9) kPa.
Patient characteristics	Inclusion: Patients with chronic liver disease of varying aetiology and liver fibrosis staging (study reports a subgroup of people with cirrhosis at baseline, proven by biopsy [15 mm in length with >5 portal tracts and performed within 3 years retrospectively or 6 months prospectively of transient elastography, or 10 mm in length if non-fragmented and deemed adequate] or clinical evidence [from imaging or evidence of portal hypertension or the presence of varices]). Exclusion: Patients who had previously experienced a clinical endpoint or had a Child-Pugh score >7 prior to or at the time of transient elastography were excluded.
Severity risk tool (for example	Transient elastography: At entry into the study. Transient elastography was considered successful only if a minimum of 8

Study	Klibansky 2012[72]
transient elastography, Child-Pugh, MELD)	acquisitions were obtained with >60% success rate.
Outcome and timepoint	Composite of individual predetermined clinical endpoints including death from any cause, first variceal bleed, new-onset ascites, new-onset encephalopathy, increase in Child-Pugh score by 2 or more, HCC or listing for liver transplant.
40/160 (25%) had an event in the cirrhosis subgroup during follow-up. Results: Transient elastography AUC (95% CI): 0.59 (0.50–0.69) Optimal cut-off threshold for determining people who will/will not have the event (if calculated): Not reported Threshold: 10.5 kPa Sensitivity: 0.975 Specificity: 0.1 PPV: 0.265 NPV: 0.923 +ve/-ve likelihood ratios: 1.08/0.25 Threshold: 8.0 kPa Sensitivity: 1.0 Specificity: 0.06 PPV: 0.26 NPV: 1.0 +ve/-ve likelihood ratios: 1.06/0 Threshold: 12.5 kPa Sensitivity: 0.93 Specificity: 0.16 PPV: 0.27 NPV: 0.86	

Study	Klibansky 2012[72]
+ve/-ve likelihood ratios: 1.1/0.47 Threshold: 15 kPa Sensitivity: 0.85 Specificity: 0.27 PPV: 0.28 NPV: 0.84 +ve/-ve likelihood ratios: 1.16/0.56 Threshold: 20 kPa Sensitivity: 0.8 Specificity: 0.39 PPV: 0.31 NPV: 0.86 +ve/-ve likelihood ratios: 1.32/0.51 Threshold: 30 kPa Sensitivity: 0.31 Specificity: 0.53 PPV: 0.66 NPV: 0.2 +ve/-ve likelihood ratios: 0.65/1.32 Threshold: 50 kPa Sensitivity: 0.05 Specificity: 0.93 PPV: 0.18 NPV: 0.75 +ve/-ve likelihood ratios: 0.67/1.03	

Study	Klibansky 2012[72]
	Threshold: 70 kPa Sensitivity: 0.03 Specificity: 0.98 PPV: 0.75 NPV: 0.25 +ve/-ve likelihood ratios: 1.0/1.0 Other measures: Calibration: not reported General limitations according to PROBAST: Two components of the composite outcome do not match the protocol (increase in Child-Pugh score by 2 or more, listing for liver transplantation) therefore evidence is slightly indirect.

Study	Perez-Latorre 2014[102]
Study type	Retrospective review
Number of studies (number of participants	All consecutive patients with HCV-related liver cirrhosis who underwent a liver workup comprising simultaneous assessment with transient elastography and determination of hepatic venous pressure gradient between January 2005 and December 2011. 60 patients with HCV-related liver cirrhosis, 36 of whom were co-infected with HIV.
Countries and Settings	Hospital Gregorio Maranon, Madrid
Funding	AIDS Research Network
Duration of study	Median follow-up 42 months
Age, gender, ethnicity	HCV/HIV (n=36): age 46 years (42–49); 75% male; ethnicity: not reported

Study	Perez-Latorre 2014[102]
	HCV (n=24): age 51 years (48–58); 67% male; ethnicity: not reported
Patient characteristics	HCV-related liver cirrhosis. The diagnosis of cirrhosis was confirmed by liver biopsy or by a liver stiffness measurement using transient elastography (≥14 kPa). Excluded: Patients with decompensated liver disease or a prior diagnosis of hepatocellular carcinoma.
Severity risk tool (for example transient elastography, Child-Pugh, MELD)	Transient elastography was performed using a transient elastography device (Echosens, Paris, France) after an overnight fast. A median value of 10 successful acquisitions was considered to be the representative measurement of liver stiffness. Ten acquisitions with a success rate ≥60% and an interquartile range to ratio <30% of the median value as representative measurements.
Outcome and timepoint	Liver decompensation (ascites, hepatic encephalopathy, variceal bleeding, jaundice) Hepatocellular carcinoma Liver-related events (decompensation or HCC, whichever occurred first) Note: Hepatic encephalopathy was diagnosed based on clinical findings; HIV-associated encephalopathy was excluded on the basis of clinical and laboratory parameters and neuroimaging. The source of gastrointestinal bleeding was confirmed by endoscopy where possible.
Results: Transient elastography, decompensation All patients: AUC (95% CI): 0.85 (0.69–1.0) Optimal cut-off threshold for determining people who will/will not have the event: Not reported Results: Transient elastography, liver-related event (decompensation or HCC, whichever occurred first) 12/60 (20%) had a liver-related event All patients: AUC: 0.85 (0.73–0.97) Optimal cut-off threshold for determining people who will/will not have the event: <25 kPa (absence of liver-related events) and ≥40 kPa (presence of liver-related events) Threshold: <25 kPa Sensitivity: 92 (72–100) Specificity: 65 (50–79) PPV: 39 (19–55) NPV: 0.97 (0.89–0.1)	

Study	Perez-Latorre 2014[102]
+ve/-ve likelihood ratios: 2.59 (1.7–3.93)/0.13 (0.02–0.8) TP: 11 FP: 17 FN: 1 TN: 31 Threshold: ≥40 kPa Sensitivity: 67 (36–98) Specificity: 90 (80–99) PPV: 0.62 (0.31–0.92) NPV: 91 (82–100) +ve/-ve likelihood ratios: 6.4 (2.55–16.08)/0.37 (0.17–0.8) TP: 8 FP: 5 FN: 4 TN: 43 Results: Transient elastography, hepatocellular carcinoma All patients: AUC: 0.77 (0.59–0.95) Optimal cut-off threshold for determining people who will/will not have the event: Not reported Other measures: Calibration: Not reported General limitations according to PROBAST: At risk of bias due to optimal threshold calculated.	

Study	Robic 2011[107]
Study type	Prospective longitudinal study
Number of studies (number of participants	n=150 patients with chronic liver disease: 8 refused follow-up, 24 followed up in other hospitals, 18 had exclusion reasons such as decompensation at inclusion, final analysis n=100 (subgroup analysis provided for n=65 with cirrhosis at baseline). Transient elastography failure in 4 patients due to obesity. Recruitment between 15 November 2005 and 15 October 2006.
Countries and Settings	France
Funding	Not reported. Nothing to disclose regarding funding or conflict of interests.
Duration of study	Patients were followed up for 2 years or until the first occurrence of a clinical decompensation, liver transplantation, or death. Mean follow up 491 days.
Age, gender, ethnicity	Whole populations: age (mean, SD): 56±13 (range 47–66), male/female: 59/41; ethnicity: not reported, liver stiffness measurement: 30.7±26.3 (30.8–75) kPa. Cirrhosis F4 n=65 (mean Child-Pugh 7.6 [5–11] and MELD 12.2 [5–15]). Oesophageal varices were grade 1 in 18 patients (27.7%), grade 2 in 25 patients (39%), and grade 3 in 4 patients (6%).
Patient characteristics	Inclusion: Compensated chronic liver disease Exclusion: At the time of inclusion, none of the patients had antiviral therapy or portal pressure modifying treatment.
Severity risk tool (for example transient elastography, Child-Pugh, MELD)	Transient elastography: Ten validated measures were performed for each patient. IQR was lower than 30% of the median value and success rate was at least 60%, according to the manufacturer's recommendations. The operator was not aware of HVPG values when conducting the analyses.
Outcome and timepoint	PHT-related complication (variceal bleeding and/or ascites) Clinical decompensation (defined as PHT-related bleeding, ascites, hepatorenal syndrome, hepatic encephalopathy, hepatocellular carcinoma, and/or sepsis) outcome also reported but not for subgroup with cirrhosis at baseline.
18/65 (27.7%) had a PHT-related complication Results: Transient elastography for predicting PHT-related complications AUC (95% CI): 0.734 (0.609–0.859) Optimal cut-off threshold for determining people who will/will not have the event: Not reported (used pre-published)	

Study	Robic 2011[107]
Threshold: 21.1 kPa (pre-published) Sensitivity: 100 Specificity: 41 PPV: 41 NPV: 100 +ve/-ve likelihood ratios: Not reported TP: Not reported FP: Not reported FN: Not reported TN: Not reported Other measures: Calibration: Not reported Score on Risk Tool: Risk of event: <21.1 kPa 47% ≥21.1 kPa 100% General limitations according to PROBAST: One component of the composite outcome does not match the protocol (sepsis) therefore evidence is slightly indirect.	

Study	Said 2004[115]
Study type	Retrospective cohort study
Number of studies (number of participants	1,611 consecutive patients from hepatology clinics and hepatology inpatient service Compensated patients=204
Countries and Settings	University of Wisconsin-Medison medical school university hospital, USA

Study	Said 2004[115]
Funding	Not reported
Duration of study	January 1994–December 2001 Median follow up was 24 months (1–72)
Age, gender, ethnicity	(Whole group) age: 50±12.5 (18–86); gender: 55% male; ethnicity: 88% Caucasian
Patient characteristics	Patient records were identified by discharge diagnosis codes. Patients with transient liver test abnormalities, acute liver diseases, hepatocellular carcinoma, cholangiocarcinoma and HIV and those who died of cardiac disease were excluded.
Severity risk tool (for example transient elastography, Child-Pugh, MELD)	MELD score was calculated at the initial visit using the formula: 3.8 lnBilirubin + 11.2 lnINR + 9.6 creatinine + 6.4
Outcome and timepoint	Survival was calculated from the date of first clinical contact. Mortality data were abstracted from hospital records and the national social security death index. Survival was censored at transplantation. ROC curves were plotted to measure the performance of MELD and Child-Pugh for predicting 1-year mortality.
Results: MELD score for predicting 1-year mortality AUC (95% CI): 0.75 (0.59–0.9) Results: Child-Pugh score for predicting 1-year mortality AUC (95% CI): 0.66 (0.50–0.82) General limitations according to PROBAST: None	

Study	Wang 2014B[158]
Study type	Prospective study
Number of studies (number of	271 consecutive patients were enrolled from January 2008 to October 2011. 51 were excluded (12 patients had failed liver

Study	Wang 2014B[158]
participants	stiffness measurements, 5 had unreliable liver stiffness measurements, 15 did not fulfil the inclusion criteria, 12 did not have follow-up liver stiffness measurements, 7 had hepatocellular carcinoma (HCC) development within 6 months after enrolment). 220 were included in the analysis.
Countries and Settings	Division of Hepato-Gastroenterology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Taiwan
Funding	A grant from Chang Gung Memorial Hospital
Duration of study	Median follow-up 36.9 months. All patients received baseline liver function reserve assessment, ultrasound to exclude the presence of ascites and HCC and esophagogastroduodenoscopy (EGD) to detect the presence of varices. Liver stiffness measurement was assessed at an interval of 6–12 months. Medical records were reviewed regularly. Patients were followed up with ultrasound surveillance for HCC at an interval of 3–6 months regularly. EGD was repeatedly performed at an interval of 1–3 years.
Age, gender, ethnicity	Age: 56.7±11.4; gender: 61.34% male,; ethnicity: not reported
Patient characteristics	Inclusion: Patients with hepatic cirrhosis in liver function reserve Child-Pugh classification A, without histories of decompensation or HCC. Hepatic cirrhosis was diagnosed with histological fibrosis stage 4 according to METAVIR, ultrasonography cirrhosis with splenomegaly and/or thrombocytopenia or ultrasonography cirrhosis based on an objective scoring system. Exclusion: Presence of ascites or HCC.
Severity risk tool (for example transient elastography, Child-Pugh, MELD)	Liver stiffness measurements were performed with an M-probe using the transient elastography (Echosens, Paris, France) in a fasting state by technicians with at least a 50-patient experience. The operator located a portion of the liver at least 60 mm thick and free of large vascular structures with assistance of ultrasound time-motion and A-mode images, and pressed the acquisition button to obtain a liver stiffness value. Liver stiffness was expressed as a median with an IQR in kPa. Liver stiffness measurement was deemed reliable only when 10 successful shots were performed, with greater than 60% success rate of measurements and the ratio of IQR to median less than 30% was obtained.
Outcome and timepoint	Hepatic decompensation was defined as variceal bleeding, ascites, spontaneous bacterial peritonitis or hepatic encephalopathy. Portal hypertension (PHT) progression included hepatic decompensation, varices development and varices growth. Clinical disease progression included PHT progression, HCC development and liver-related death.
CDP occurred in 49/220 (22.3%) patients, including HCC in 19 patients and PHT progression in 30 patients (of these 30, 9 had decompensation and 21 had varices growth).	

Study	Wang 2014B[158]
	Results: Baseline liver stiffness measurement (transient elastography) – prediction of CDP (49/220) AUC (95% CI): 0.668 (0.577–0.759) Optimal cut-off threshold for determining people who will/will not have the event (if calculated): 14 kPa Threshold: 14 kPa (optimal) Sensitivity: 57% (43–70) Specificity: 68% (61–75) Accuracy: 65% (59–72) PPV: 34 (24–44) NPV: 85 (78–90) +ve/-ve likelihood ratios: 1.78 (1.28–2.46)/0.63 (0.45–0.89) Results : Baseline liver stiffness measurement (transient elastography) – prediction of PHT (30/220) AUC (95% CI): 0.744 (0.65–0.838) Optimal cut-off threshold for determining people who will/will not have the event (if calculated): 17 kPa Threshold: 17 kPa (optimal) Sensitivity: 57% (39–73) Specificity: 78% (72–83) Accuracy: 75% (69–80) PPV: 29% (118–41) NPV: 92% (87–95) +ve/-ve likelihood ratios: 2.56 (1.7–3.87) /0.56 (0.37–0.84) Results: Baseline liver stiffness measurement (transient elastography) – prediction of decompensation AUC (95% CI): 0.929 (0.875–0.984) Optimal cut-off threshold for determining people who will/will not have the event (if calculated): 21.1 kPa Threshold: 21.1 kPa (optimal) Sensitivity: 78 (48–95) Specificity: 84 (79–89)

Study	Wang 2014B[158]
	Accuracy: 84 (79–89) PPV: 18 (8–31) NPV: 99 (97–100) +ve/-ve likelihood ratios: 4.97 (3.11–7.95)/0.26 (0.08–0.9) Results: Baseline liver stiffness measurement (transient elastography) – prediction of HCC AUC (95% CI): 0.504 (0.358–0.651) Optimal cut-off threshold for determining people who will/will not have the event (if calculated): 11.5 kPa Threshold: 11.5 kPa (optimal) Sensitivity: 53 (32–73) Specificity: 52 (45–59) Accuracy: 52 (46–59) PPV: 9 (5–16) NPV: 92 (86–96) +ve/-ve likelihood ratios: 1.1 (0.7–1.76) 0.91 (0.55–1.48) Results: Baseline liver stiffness measurement (transient elastography) – prediction of varices progression AUC (95% CI): 0.638 (0.525–0.75) Optimal cut-off threshold for determining people who will/will not have the event (if calculated): 12 kPa Threshold: 12 kPa Sensitivity: 62 (38–82) Specificity: 60 (53–67) Accuracy: 60 (54–67) PPV: 14 (8–23) NPV: 94 (88–97) +ve/-ve likelihood ratios: 1.56 (1.07–2.27)/0.63 (0.36–1.1) General limitations according to PROBAST: Four of the five outcomes contain a component which does not match the protocol (variceal development or growth).