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An LSM Based Strategy is Comparable to HVPG Measurement to Predict Further Events in Patients with Cirrhosis with Variceal Bleeding as Their Index Decompensation

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Background and aims: **Limited data exist on strategies other than hepatic venous pressure gradient (HVPG) estimation to predict future events in patients with cirrhosis presenting with variceal bleed (VB) but are otherwise compensated. We assessed whether liver stiffness measurement (LSM) during VB episode could accurately predict this risk.** ***Methods:*** **Consecutive patients with cirrhosis with VB as their index decompensation event underwent HVPG and LSM estimation during the VB episode in this prospective study. New onset further decompensation events (ascites, VB, encephalopathy) was assessed over follow-up. The performance characteristics of postbleed LSM were compared with model for end stage liver disease (MELD) score and HVPG to predict future decompensation and were cross-validated.** ***Results:*** **Mean age of the cohort (n = 68) was 44.2 years and alcohol-related liver disease (55.9%) was the most common etiology. Over a median follow-up of 14 (9–18) months, 18(26.4%) patients developed further decompensation with ascites being the most common event. Patients with further decompensation had a higher median postbleed LSM [60.5 kPa (53–70) vs. 25 kPa (18–34), $P < 0.001$], HVPG [19 mm Hg vs. 16 mmHg, $P = 0.005$], and MELD score [12.5 (11–14.7) vs. 10 (8–12) $P < 0.001$]. The area under receiver-operator characteristics curve for postbleed LSM [0.928 (95%CI: 0.868–0.988)] was higher than both HVPG [0.733(0.601–0.865), $P = 0.003$] and MELD score [0.776(0.664–0.889), $P = 0.019$] to predict further decompensation. Optimism-corrected c-statistic using MELD and postbleed LSM was similar to a combination of HVPG, MELD, and postbleed LSM.** ***Conclusion:*** **Postbleed LSM is comparable to HVPG estimation in predicting further decompensation events in patients with otherwise compensated cirrhosis presenting with VB. (J Clin Exp Hepatol xxxx;xxx:xxx)**

Variceal bleeding (VB) is the most common decompensating event after ascites in the natural history of patients with advanced compensated cirrhosis.[1] Patients presenting with isolated VB in the absence of other decompensation have an excellent 6-week outcomes.[2] A more important question in this group of patients is their risk of future decompensation such as development of ascites, rebleeding, and/or encephalopathy as stated by Baveno consensus.[3] Further development of ascites is the most relevant event in these patients that determines the overall outcome.[4] In the absence of hepatic venous pressure gradient (HVPG) estimation, it is difficult to predict outcomes in this otherwise low risk cohort. The traditional liver disease severity scores may be insensitive and absence of other decompensation at this stage makes future risk stratification of portal hypertension a challenge and an unmet need in these patients.[2,3]

Noninvasive tools such as liver stiffness measurement (LSM) are emerging as an alternative to HVPG in the management of patients with advanced compensated cirrhosis. There are data to support their use as an alternative to HVPG measurement in different scenario to guide clinical decisions.[5,6] Evidence pertaining to the utility of LSM is restricted to patients with compensated cirrhosis. Most patients with decompensated cirrhosis may not benefit from LSM estimation as they have already decompensated and may have spuriously elevated reading due to ascites. However, index VB episode with no previous decompensation represents a unique situation where LSM could be accurate and may still be relevant for predicting future events. We have shown previously that measurement of LSM during VB episode can accurately predict long-term risk of

Keywords: variceal bleed, cirrhosis, postbleed LSM, HVPG, portal hypertension, nomogram

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Abbreviations: AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; CI: Confidence Interval; CTP: Child-Turcotte-Pugh; HCC: Hepatocellular cancer; HE: Hepatic encephalopathy; HR: Hazard ratio; HVPG: hepatic venous pressure gradient; LSM: liver stiffness measurement; MELD: Model for end stage liver disease; PVT: Portal vein thrombosis; VB: variceal bleeding

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rebleeding and is comparable to HVPG measurement.[7] It remains to be seen if postbleed LSM can substitute HVPG measurement to predict new onset further decompensation such as further rebleeding, new onset ascites or new onset encephalopathy in this otherwise low-risk cohort.

The present prospective study assessed the LSM during the VB episode. We compared its prognostic significance with that of HVPG estimation to predict new onset further decompensation in patients with otherwise compensated cirrhosis presenting with VB as their index event.

PATIENTS AND METHODS

Study Design and Population

Consecutive patients with cirrhosis and VB as the first and only decompensation event being followed up at All India Institute of Medical Sciences, New Delhi (India) between 2020 and 2022 were considered for inclusion in this present prospective study. Patients with any previous decompensation such as presence of clinical ascites/overt HE, diagnosis of hepatocellular cancer at the time of presentation, presence of occlusive main portal vein thrombosis (PVT) or Budd Chiari syndrome on imaging at presentation, possible clinical diagnosis of alcoholic hepatitis (with bilirubin more than 5 mg/dl), previous diagnosis of extrahepatic portal vein obstruction, or noncirrhotic portal hypertension based on imaging/biopsy/portal pressure estimation were excluded from the present study. All details of patients were included after anonymizing their personal details to avoid their identification, and all additional procedures performed in this study were in in accordance with the 1975 Helsinki declaration and its later amendments or comparable ethical standards. Ethical clearance for this study was obtained from the institutional ethics committee.

Management Protocol

Patients presenting with VB were managed according to standard protocol at our center which incorporates the Baveno-VI consensus recommendations.[3,7] This included resuscitation, antibiotics, vasoactive medication, and transfusion according to recommendations. Endoscopic band ligation was performed for control of bleed. After 24 h of band ligation, vasoactive medication was stopped, and patients were started on carvedilol 6.25 mg per day, which was gradually increased to 12.5 mg per day in the absence of adverse events. Long-acting formulation of carvedilol was not used. Surveillance endoscopy was performed every 3 weeks till obliteration of varices.

Liver Stiffness Measurement

LSM was done within 24 h of presentation. Assessment of LSM was performed on a FibroScan 1 touch 502 (Echosens, Paris, France) after overnight fasting on the right lobe of the liver. Measurements were done using M probe as per manufacturer's recommendations, except in those with abdomen obesity, where XL probe was used.[8] Ten acquisitions were performed on each patient on each day, and the ratio of interquartile range (IQR) to the median (M) of readings (IQR/M) < 0.3 was taken as marker of valid measurement. If invalid, repeat measurements were taken.

Hepatic Venous Pressure Gradient (HVPG) Estimation

Measurement was done using standard technique involving right internal jugular vein catheterization and introduction of balloon wedge pressure catheter in the right hepatic vein under fluoroscopic control. HVPG was determined by subtracting the free hepatic venous pressure (FHVP) from the wedged pressure (WHVP) estimated after balloon inflation (HVPG = WHVP – FHVP). All measurements were performed in triplicate in each patient and were repeated if the difference between the three readings was more than 1 mmHg.

HVPG measurement was done after band ligation either on day of procedure or on the subsequent day. Under local anesthesia, a central lumen venous catheter (7F; Arrow; Arrow Medical, Athens, TX) was placed in the right internal jugular vein under ultrasound guidance by Seldinger technique. HVPG was measured through a balloon wedge pressure catheter (Arrow, Arrow Medical) introduced in the right hepatic vein under fluoroscopic control. The zero-reference point was set at the mid-axillary point, and the free hepatic venous pressure was measured by keeping the catheter into the lumen of the hepatic vein. The balloon of the catheter was then inflated to wedge the lumen of hepatic vein, and this was confirmed by absence of reflux into IVC after injection of 2 ml intravenous contrast and appearance of a sinusoidogram. The pressure tracing at this juncture showed absence of wave forms and the pressure was labeled as WHVP. All measurements were performed in triplicate in each study. If the difference between the three readings was more than 1 mmHg, all the readings were discarded and fresh measurements were done. The HVPG was determined by subtracting the free hepatic venous pressure (FHVP) from the wedged pressure (WHVP) (HVPG = WHVP – FHVP). The normal value of the HVPG in our hemodynamic laboratory is below 5 mm Hg (1–4 mmHg).

Data Collection

Demographic, clinical, and relevant laboratory parameters were collected at baseline. The baseline liver disease specific scores such Child-Turcotte-Pugh (CTP) and model for end stage liver disease (MELD) scores were calculated. Endoscopic details such as type of VB (esophageal or gastric) were recorded. The details of relevant outcomes such as

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development of new decompensation (ascites, variceal rebleeding, and HE), survival, liver transplant, or insertion of transjugular intrahepatic portosystemic shunt (TIPS) insertion were assessed over follow-up. Data were prospectively collected in predesigned questionnaires over follow-up from outpatient clinic visits. In case of events needing hospitalization, details were retrieved from medical records to confirm their exact nature. Events occurring outside hospital were recorded on subsequent patient visits and were also verified telephonically in patients who could not follow-up physically. Treatment-related records such as etiology specific treatment for viral cirrhosis, prophylaxis for rebleeding such as serial variceal obliteration and use of nonselective beta blockers, evaluation of ongoing risk factors such as active alcohol consumption and management of other complications were also noted. Acute VB was defined as per Baveno-VI recommendations.[9] Hepatic encephalopathy was defined according to standard criteria.[10] Development of acute on chronic liver failure (ACLF) was defined as per EASL definition.[11]

OUTCOMES

The main outcome of the study was to assess the cumulative incidence of new onset further decompensation (ascites/encephalopathy/rebleeding) over follow-up after the index VB episode. We restricted our outcome to the above-mentioned decompensating events and did not include ACLF and hepatorenal syndrome as these are usually late events in the natural history of cirrhosis and occur as a consequence of, or involve some combination of the aforementioned decompensating events.

Statistical Analysis

Baseline characteristics of included patients stratified based on incident decompensations were recorded as number (%) or based on the normality of distribution, as mean ± SD/median (interquartile range) as appropriate. These characteristics were then compared using chi-square test/Fischer exact test for categorical variables and Student's *t*-test/analysis of variance (ANOVA) for continuous variables with a normal distribution. Continuous variables with nonnormal distribution were compared using independent samples Kruskal–Wallis test. For all statistical tests, a *P*-value <0.05 was considered statistically significant.

Receiver-operator characteristics (ROC) curves were generated for comparison of predictive value of HVPG, postbleed LSM, and MELD score for further decompensation events, and areas under respective ROC curves were compared using Delong test. In addition, multivariate logistic regression and Cox-proportional hazards analysis were conducted combining postbleed LSM and MELD score with and without HVPG to improve predictive accuracy. First, a logistic regression model was constructed for prediction of those in whom acute decompensations were noted. In view of small sample size, an optimism-corrected c-statistic was estimated using 1000-fold bootstrapping validation, which has previously been shown to be a better validation tool in comparison to sample splitting, cross-validation without replication, and leave-1-out cross-validation, which produce relatively biased estimates.[12] Finally, a diagnostic nomogram was generated for the models for visual representation of contribution of individual elements and to demonstrate the degree of confidence with which acute decompensations could be predicted.

All data were entered using Microsoft Excel 2011 and was analyzed using Rstudio Version 1.4.1106. In addition to the base packages in R, tidyverse, rms, tableone, OptimalCutpoints, readxl, and plotROC packages were used.

RESULTS

Baseline Characteristics

Over the duration of the study (July 2020–May 2022), out of 395 patients presenting with VB at our center, 109 patients with previously compensated cirrhosis presented with VB who were eligible for the study after satisfying the exclusion criteria. A total of 107 patients underwent LSM assessment, while 68 patients underwent all investigations, including HVPG and were included in the study (Figure 1) (Table 1). All patients were Child-Turcotte-Pugh class A at the time of recruitment (median CTP score 6 (IQR 6-6). Most patients were middle-aged males (mean age 44.2 years, 13.2% females) and had nonviral etiologies of cirrhosis, with alcohol being the most common etiology (55.9%) followed by NASH (17.6%), HBV (8.8%), and HCV (2.9%).

OUTCOMES

Over a median duration of 14 (10–18) months, 18 (26.4%) patients had further decompensation events. Five patients (7.3%) developed more than one decompensation event and one (1.5%) succumbed. Two patients required TIPS placement for refractory ascites. None of the patients underwent liver transplant. Ascites was the most common new decompensation event (n = 18; 26.4%), followed by rebleed (n = 4; 5.8%) and HE (n = 2, 2.9%).

Patients who developed further decompensation event after index VB episode (n = 18) were older (mean age 49.33 (SD 10.01) years vs. 42.44 (11.40) years for no decompensations; P = 0.027) and more obese (mean BMI 28.90 (6.08) vs. 21.62 (2.03); P = 0.039). They also had higher serum bilirubin (median 2.40 mg/dl [IQR: 1.85–2.90] vs. 1.20 mg/dl [0.80, 2.00]; P = 0.001), higher INR (mean

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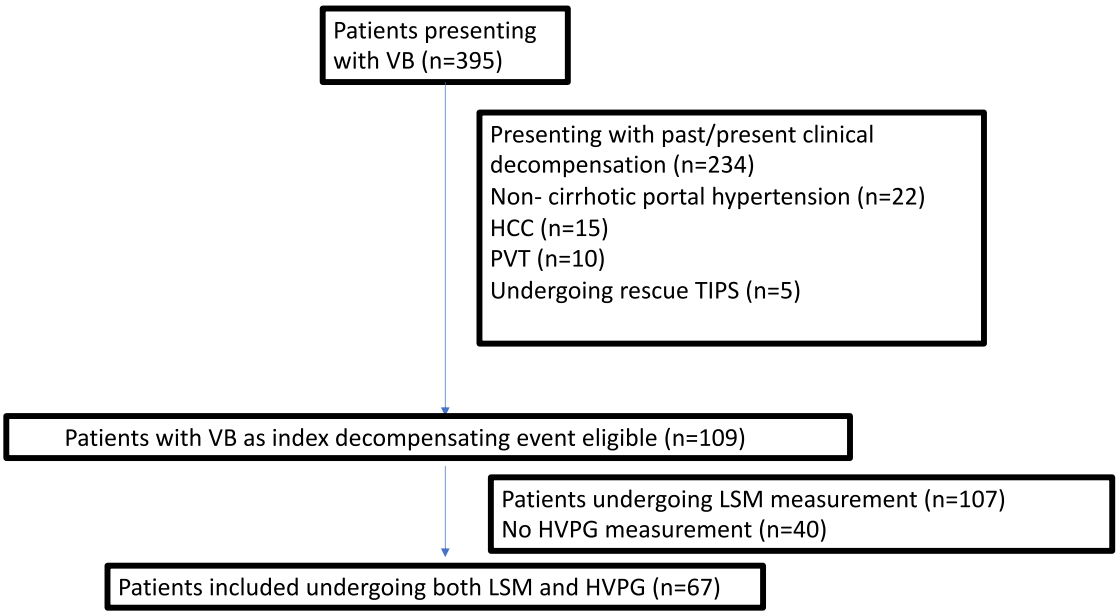

Figure 1 Consort diagram showing recruitment of patients for the present study.

1.38 (0.21) vs. 1.24 (0.15); P = 0.005) and consequently a higher MELD score (median MELD 12.50 [11.00, 14.75] vs. 10.00 [8.00, 12.00]; P < 0.001) at presentation. Rest of baseline laboratory parameters were similar in both groups of patients. The mean HVPG was significantly higher in those with further decompensation [19.1 (3.3) mmHg vs. 16 (4.09) mmHg, P = 0.005]. Patients with further decompensation also had a significantly higher postbleed LSM [60.5 (53.5–70.9) kPa vs. 25 (18–34.2) kPa, P < 0.001] than those without further decompensation.

Risk Stratification Using Postbleed LSM and HVPG

Postbleed LSM had a good predictive value for predicting further decompensation events, with area under ROC curve of 0.928 (95% CI 0.868–0.988), which was significantly better than both HVPG (AUROC 0.733 (0.601, 0.865); P = 0.003) and MELD score (AUROC 0.776 (0.664, 0.889); P = 0.019) (Figure 2). Postbleed LSM higher than 38 kPa had a sensitivity of 88.8% and specificity of 84% for predicting further decompensation over follow-up. Cox-proportional hazards model combining postbleed LSM, HVPG, and MELD identified postbleed LSM (hazard ratio: 1.057 (95%CI: 1.041–1.073); P < 0.001 and MELD (HR: 1.218 (95% CI: 1.122–1.321); P = 0.016) as the only statistically significant predictive factors for further decompensations (Supplementary Table 1). Validation statistics also suggested that a model using a combination of LSM and MELD could achieve an optimism-corrected c-statistic of 0.931, which was only marginally lower than a model combining HVPG, LSM, and MELD, which generated an optimism-corrected c-statistic of 0.937. Nomograms for both models are provided in Figure 3, which could be used to determine the risk of further decompensations with or without HVPG, respectively.

DISCUSSION

HVPG estimation is useful for estimating the risk of further decompensation and survival in patients with otherwise compensated cirrhosis who present with VB.[13,14] Our proof-of-concept study shows that LSM after VB (postbleed LSM) predicts this risk of decompensation better than HVPG. Postbleed LSM of 38 kPa or more could accurately stratify the cohort according to their risk of further decompensation with 88.4% sensitivity and 84% specificity. Model combining MELD score and postbleed LSM provided similar information to a model incorporating all three variables (MELD, postbleed LSM, and HVPG).

One of the important unanswered questions in the natural history of cirrhosis is the risk of future events when patients present with VB as their index and only decompensating event. While extensive data are present on those presenting with ascites, our understanding of the natural course of this group is limited. The pioneer natural history study by D'Amico *et al.* showed that around 37% of patients (n = 75) decompensate with ascites over 20 years.[1] The predominant inclusion of viral cirrhosis, retrospective nature, and heterogeneity in the management practice over years remains major limitation of that study.

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Table 1 Baseline Characteristics and Outcomes in Patients Presenting With VB Stratified by Presence or Absence of Future Decompensation.

	Overall (n = 68)	New decompensation events (n = 18)	No new decompensation events (n = 50)	*P* value
Demographic details				
Age	44.26 (11.39)	49.33 (10.01)	42.44 (11.40)	0.027
Sex (Females %)	9 (13.2)	1 (5.6)	8 (16.0)	0.474
Weight (kg)	63.98 (11.89)	70.20 (11.62)	61.76 (11.31)	0.017
Height (cm)	163.33 (6.50)	163.25 (3.95)	163.40 (8.53)	0.975
BMI	24.86 (5.53)	28.90 (6.08)	21.62 (2.03)	0.039
Etiology (%)				0.099
• NASH	12 (17.6)	2 (11.1)	10 (20.0)	
• Alcohol	38 (55.9)	11 (61.1)	27 (54.0)	
• Hepatitis B	6 (8.8)	2 (11.1)	4 (8.0)	
• Hepatitis C	2 (2.9)	2 (11.1)	0 (0.0)	
• Others	10 (14.7)	1 (5.6)	9 (18.0)	
Laboratory parameters				
Hemoglobin (g/dl)	9.32 (2.15)	9.19 (2.61)	9.37 (1.99)	0.774
Total Leukocyte count (1000/mm^3) (median [IQR])	7700.00 [4550.00, 8725.00]	7770.00 [4925.00, 8000.00]	7250.00 [4600.00, 8975.00]	0.972
Platelet count (1000/mm^3) (median [IQR])	75.00 [55.75, 113.25]	77.00 [63.75, 115.25]	74.00 [55.00, 110.00]	0.713
Blood urea (mg/dl) (median [IQR])	40.00 [29.67, 65.00]	43.00 [29.23, 60.47]	39.35 [31.50, 66.00]	0.631
Creatinine (mg/dl)	0.82 (0.19)	0.85 (0.21)	0.81 (0.19)	0.415
Serum sodium (meq/dl)	139.00 [136.75, 142.00]	141.50 [136.50, 144.00]	139.00 [137.00, 140.00]	0.152
Total serum Bilirubin (mg/dl) (median [IQR])	1.65 [0.81, 2.50]	2.40 [1.85, 2.90]	1.20 [0.80, 2.00]	0.001
Direct Bilirubin (mg/dl) (median [IQR])	1.00 [0.55, 1.25]	1.20 [1.05, 1.90]	0.70 [0.45, 0.85]	0.005
AST(U/L) (median [IQR])	56.00 [36.00, 86.25]	56.00 [40.50, 88.25]	55.50 [34.50, 85.50]	0.491
ALT(U/L) (median [IQR])	44.50 [27.50, 63.75]	49.00 [31.50, 66.50]	42.00 [27.00, 63.00]	0.394
ALP(U/L) (median [IQR])	235.00 [160.50, 280.00]	198.00 [136.25, 280.00]	240.00 [181.50, 280.00]	0.332
Total Protein (g/dl)	6.20 (0.86)	6.49 (0.72)	6.04 (0.91)	0.277
Albumin(g/dl)	3.46 (0.45)	3.38 (0.37)	3.48 (0.48)	0.398
Prothrombin time	15.59 (1.77)	16.34 (1.84)	15.18 (1.66)	0.167
International Normalized Ratio (INR)	1.28 (0.18)	1.38 (0.21)	1.24 (0.15)	0.005
Lactate (median [IQR])	2.05 [1.50, 3.00]	3.00 [1.65, 4.20]	2.00 [1.50, 2.40]	0.249
C-reactive protein (CRP) (median [IQR])	1.35 [0.27, 2.00]	2.00 [1.55, 4.95]	0.60 [0.20, 1.80]	0.032
MELD (median [IQR])	11.00 [8.00, 13.00]	12.50 [11.00, 14.75]	10.00 [8.00, 12.00]	<0.001
CTP score (median [IQR])	6.00 [6.00, 6.00]	6.00 [6.00, 6.00]	6.00 [5.00, 6.00]	0.012
Clinical presentation and management				
Shock (%)	1 (1.5)	0 (0)	1 (2.0)	1
Transfusion requirement (%)	4 (5.8)	1 (5.6)	3 (15.0)	1
LSM (median [IQR])	28.00 [21.00, 53.90]	60.50 [53.90, 70.50]	25.00 [18.50, 34.25]	<0.001

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Table 1 (*Continued*)

	Overall (n = 68)	New decompensation events (n = 18)	No new decompensation events (n = 50)	*P* value
CAP	217.47 (43.95)	211.33 (41.08)	220.31 (46.56)	0.691
HVPG	16.84 (4.11)	19.11 (3.31)	16.02 (4.09)	0.005
Active bleeding in UGIE (%)	6 (8.8)	3 (16.7)	3 (6.0)	0.377
Outcomes				
Incident decompensations				
• Ascites (%)	18 (26.4)	18 (100.0)	0 (0)	<0.001
• Rebleed (%)	4 (5.8)	4 (22.2)	0 (0)	0.004
• HE(%)	2 (2.9)	2 (11.1)	0 (0)	0.114
Incident infections (%)	2 (2.9)	2 (11.1)	0 (0)	0.114
TIPS insertion	2 (2.9)	2 (11.1)	0 (0)	
Deaths	1 (1.5)	1 (5.6)	0 (0.0)	0.013

Note. All quantitative data is presented as mean (SD) and all qualitative data is presented as n(%) unless otherwise specified. List of abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; ALP, alkaline phosphatase; CAP, controlled attenuation parameter; CTP, Child-Turcotte-Pugh; HE, hepatic encephalopathy; HVPG, hepatic venous pressure gradient; IQR, interquartile range; LSM, liver stiffness measurement; MELD, model for end stage liver disease; NASH, nonalcoholic steatohepatitis; TIPS, transjugular intrahepatic portosystemic shunt.

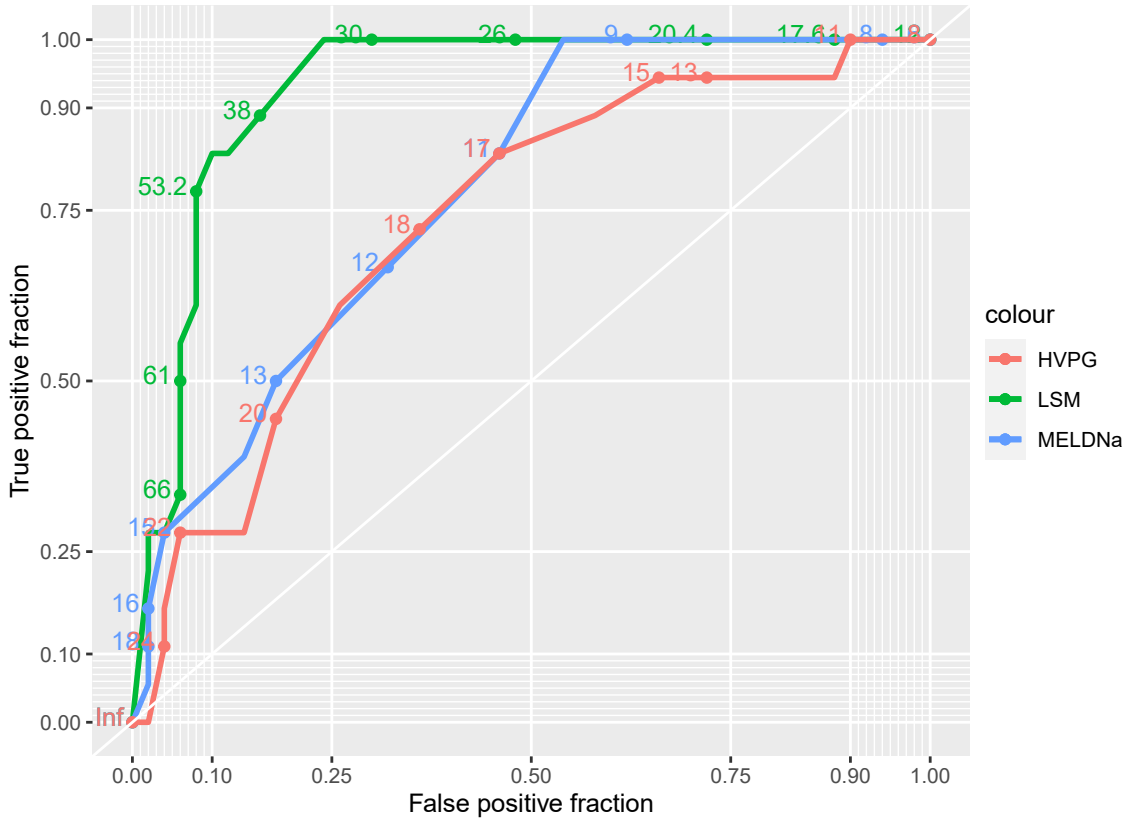

Figure 2 Receiver-operator characteristics curve representing the performance characteristics of different predictive tools for future hepatic decompensation events. Hepatic venous pressure gradient (HVPG) is presented in red, while liver stiffness measurement ad MELD score are presented in green and blue, respectively.

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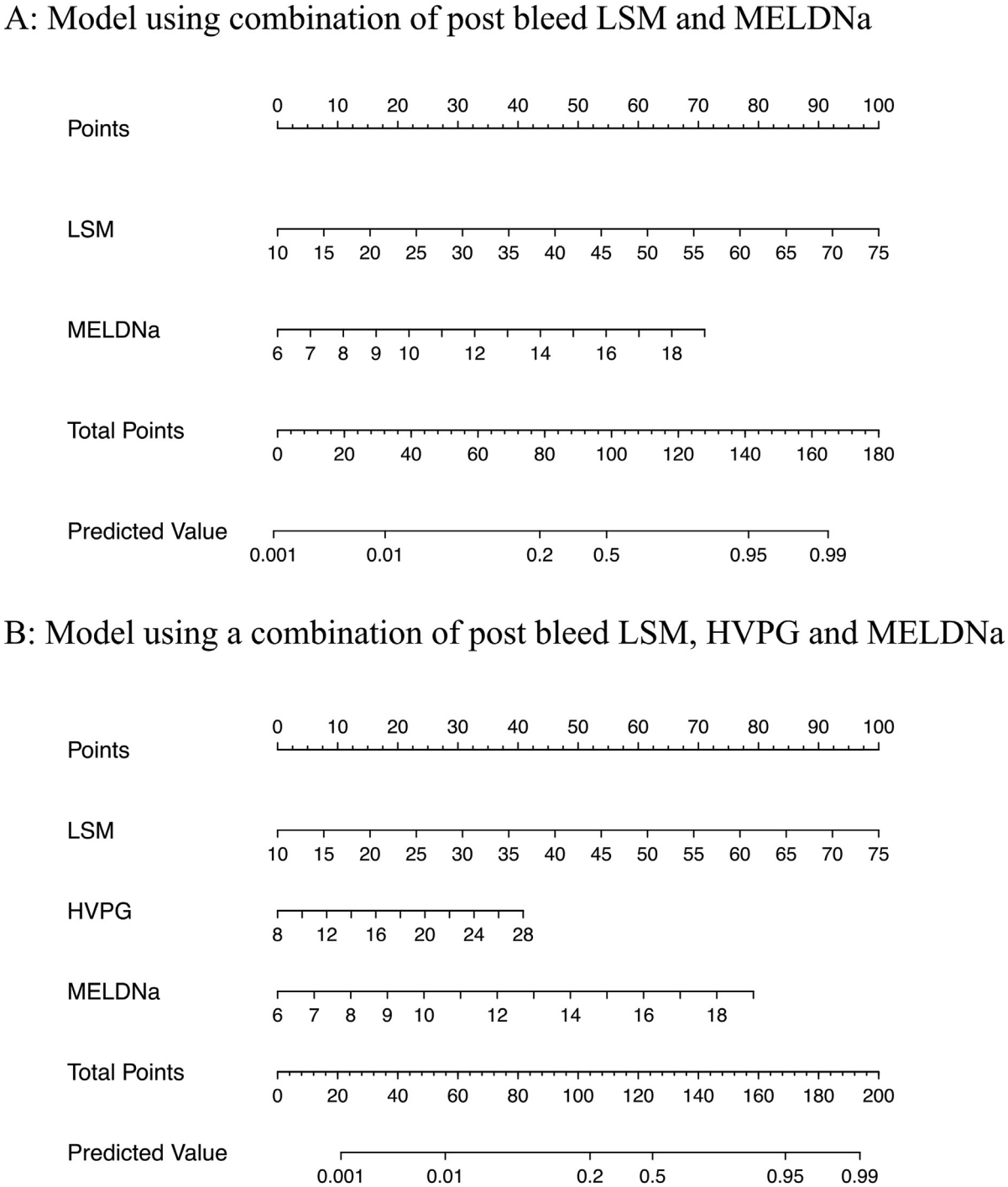

Figure 3 Proposed nomograms for estimating the risk of hepatic decompensation using combinations of different predictive tools. A represents a model combining LSM and MELD score while, B represents a model combining LSM, HVPG and MELD score. Risk of decompensation can be estimated by estimating points for each of individual predictors on top scale (labeled Points) and adding them. The total score can be converted to decompensation risk (labeled Predicted Value) from the bottom scale (labeled Total Points). LSM, liver stiffness measurement; HVPG, hepatic venous pressure gradient; MELD-Na, model for end-stage liver disease score.

Our study was prospective, had patients predominantly with nonviral cirrhosis, and received uniform management of portal hypertension. In addition, we used carvedilol as the agent for secondary prophylaxis. While short-term outcomes are excellent, more than 25% patients decompensated after the index VB event over next 1 year in our study. Ascites was the most frequent further decompensating event followed by rebleeding and encephalopathy. Risk

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factors for decompensation include a higher MELD score, higher BMI, an elevated HVPG, and a higher postbleed LSM.

Noninvasive methods such as LSM are emerging as an effective alternative to HVPG measurement in predict the risks of future events in compensated cirrhosis. However, in patients with decompensated cirrhosis, their utility is uncertain given risk of inaccurate estimation with ascites and presence of more reliable signs of liver dysfunction at this stage which predicts future events. As mentioned earlier, compensated cirrhosis with VB as the only decompensation is a unique stage in this regard where LSM estimation may still be relevant. Our data show that LSM measured at this stage predicts the risk of further decompensation more accurately than even HVPG estimation. Postbleed LSM is therefore a potential noninvasive and pragmatic tool to stratify this cohort. It is easy to measure unlike HVPG, whose estimation is resource intensive and can be routinely practiced in only limited centers around the world.

Combination of postbleed LSM with MELD score may further enhance our predictive accuracy for further decompensations, as the nomograms demonstrate. In essence, using a combination of only those two parameters, the risk of future decompensations could be predicted with sufficient accuracy with estimates ranging from 0.1% to 99%. While the risk estimates need to be validated in larger prospective cohorts, these results highlight the value of postbleed LSM in this setting. Further, addition of HVPG to the model had limited impact on its accuracy, indicating that HVPG may offer little additional information over and above postbleed LSM and MELD score.

The strength of the study includes its prospective design, consecutive recruitment, and the use of uniform management strategy for treatment of patients. Although the sample size is limited with limited duration of follow-up, this is a proof-of concept assessing the validity of assessment of postbleed LSM in this group of patients. Our data show that decompensation remains frequent despite use of carvedilol, a more potent portal pressure lowering agent. The limited duration deters us from making conclusion on survival outcomes. We limited the analysis to only those undergoing both LSM and HVPG estimation. This led to exclusion of 37% of eligible patients, and this is another major limitation of our study. However, our findings were robust, and to ensure uniformity, we restricted analysis to those with all available parameters. Other limitations include lack of mechanistic insights on the determinants of postbleed LSM, the timing of measurement, its reliability and insufficient information on potential impact of different treatment regimens including endoscopic interventions used in VB episode and vascular flow changes in VB on this measurement. Lack of validation in different population also remains a potential limitation of our study.

Overall, our findings are a proof-of-concept that postbleed LSM is a potentially useful noninvasive tool to stratify patients presenting at this stage to predict future decompensation events. Long-term outcomes of the stratified cohorts and mechanistic insights of this need to be better defined and validated in future studies.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

SA: Statistical analysis; writing of original draft; critical revision.

SS: Study concept, study implementation; writing of original draft and critical revision.

AS: Study concept; study overview; critical revision.

CONFLICTS OF INTEREST

All authors have none to declare.

FINANCIAL DISCLOSURE

None.

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SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jceh.2023.04.008.

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