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Magnetic Resonance Elastography-Based Prediction Model for Hepatic Decompensation in NAFLD; a Multi-Center Cohort Study

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Abstract

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AUTHOR CONTRIBUTIONS

Study concept and design: BKK, VA, RL; data acquisition: VA, AM, TN, NT, NI, AN, RI, MG, DK, AE, MN, AA, RL; data analysis: VA, BKK, JB; drafting of the manuscript: BKK, VA; critical revision and approval of the final manuscript: all authors.

Potential conflict of interests:

Namiki Izumi is on the speakers' bureau for Gilead and AbbVie.

Rohit Loomba consults for Aardvark Therapeutics, Altimmune, Anylam/Regeneron, Amgen, Arrowhead Pharmaceuticals, AstraZeneca, Bristol-Myer Squibb, CohBar, Eli Lilly, Galmed, Gilead, Glympse bio, Hightide, Inipharma, Intercept, Inventiva, Ionis, Janssen Inc., Madrigal, Metacrine, Inc., NGM Biopharmaceuticals, Novartis, Novo Nordisk, Merck, Pfizer, Sagimet, Theratechnologies, 89 bio, Terns Pharmaceuticals and Viking Therapeutics. His institutions received research grants from Arrowhead Pharmaceuticals, Astrazeneca, Boehringer-Ingelheim, Bristol-Myers Squibb, Eli Lilly, Galectin Therapeutics, Galmed Pharmaceuticals, Gilead, Intercept, Hanmi, Intercept, Inventiva, Ionis, Janssen, Madrigal Pharmaceuticals, Merck, NGM Biopharmaceuticals, Novo Nordisk, Merck, Pfizer, Sonic Incytes and Terns Pharmaceuticals. He is the co-founder of LipoNexus Inc.

Mazen Noureddin consults for, advises, and received grants from BMS, Gilead, GSK, Madrigal, NovoNordisk, Terns, and Takeda. He consult for and advises Altimmune, Boehringer Ingelheim, Cytodyn, 89Bio, Echosens, Merck, OWL, Perspecturm, Pfizer, Roche, and Siemens. He owns stock in and received grants from Viking. He received grants from Allergan, Akero, Galectin, Genfit, Conatus, Corcept, Enanta, Novartis, Shire, and Zydus. He owns stock in Anaetos, Rivus, CIMA, and Chronwell.

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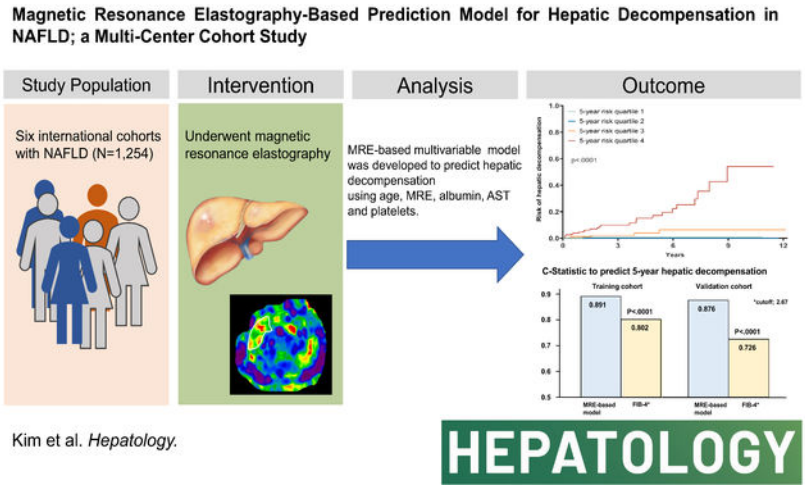
The remaining authors have nothing to report.

Background and Aims: Magnetic resonance elastography (MRE) is an accurate, continuous biomarker of liver fibrosis, however, the optimal combination with clinical factors to predict the risk of incident hepatic decompensation is unknown. Therefore, we aimed to develop and validate an MRE-based prediction model for hepatic decompensation for patients with non-alcoholic fatty liver disease (NAFLD).

Approach & Results: This international multi-center cohort study included participants with NAFLD undergoing MRE from six hospitals. A total of 1,254 participants were randomly assigned as training (n=627) and validation (n=627) cohorts. The primary endpoint was hepatic decompensation, defined as the first occurrence of variceal hemorrhage, ascites, or hepatic encephalopathy. Covariates associated with hepatic decompensation on Cox-regression were combined with MRE to construct a risk prediction model in the training cohort then tested in the validation cohort. The median (IQR) age and MRE values were 61 (18) years and 3.5 (2.5) kPa in the training cohort and 60 (20) years and 3.4 (2.5) kPa in the validation cohort. The MRE-based multivariable model included age, MRE, albumin, AST and platelets had excellent discrimination for the 3- and 5-year risk of hepatic decompensation, c-statistic 0.912 and 0.891 respectively, in the training cohort. The diagnostic accuracy remained consistent in the validation cohort with a c-statistic of 0.871 and 0.876 for hepatic decompensation at 3- and 5-years respectively and was superior to FIB-4 in both cohorts (P<.05).

Conclusions: An MRE-based prediction model allows for accurate prediction of hepatic decompensation and assists in the risk stratification of patients with NAFLD.

Graphical Abstract



Keywords

non-alcoholic fatty liver disease; hepatic decompensation; ascites; varices; non-invasive; prediction

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) affects over 25% of the general population worldwide (1–3) and its prevalence has been increasing as the number of patients with obesity and metabolic syndrome continues to rise (4–8). Patients with NAFLD, particularly the subset with non-alcoholic steatohepatitis (NASH) can develop cirrhosis, hepatocellular carcinoma (HCC), and may have an increased risk for extra-hepatic malignancy and cardiovascular disease (9–15).

Fibrosis stage is the strongest predictor of future outcomes among patients with NAFLD (16), however, histologic staging among the entire affected population is impractical, due to its invasive nature, risk of complications, sampling error, and inter- and intra-observer variability (17). Among non-invasive surrogate markers, magnetic resonance elastography (MRE) has excellent diagnostic accuracy for fibrosis, including at earlier fibrosis stages (18–24). Recent longitudinal studies have demonstrated that higher liver stiffness on MRE is associated with liver-related outcomes including hepatic decompensation and mortality (25–29). Other clinical and demographic data may complement MRE and the combination may provide increased clinical utility in predicting the risk of liver-related events, however, the optimal combination is unknown.

Therefore, using an international multi-center multi-ethnic cohort, we aimed to develop and validate an MRE-based prediction model to provide accurate prognostic information regarding liver-related outcomes among patients with NAFLD.

MATERIALS AND METHODS

This is a retrospective cohort study with data from six centers from the United States, Europe and Asia; the University of California San Diego, Mayo Clinic Rochester, Cedars Sinai, Musashino Red Cross Hospital, Yokohama City University, and Ankara University School of Medicine with cohort development as previously described (25).

Key inclusion criteria were adults age ≥ 18 years with NAFLD and liver stiffness (LS) measurement by MRE who were assessed for hepatic decompensation, HCC, and death. NAFLD was defined as hepatic steatosis on imaging or a historical liver biopsy in the absence of significant alcohol consumption. Secondary causes of hepatic steatosis and other chronic underlying liver disease include viral hepatitis, consistent with the American Association for the Study of Liver Diseases NAFLD Practice Guidance as previously published (30).

Key exclusion criteria were a previous history of hepatic decompensation or HCC before enrollment or within 3 months of enrollment, follow-up duration of < 3 months, and incomplete critical laboratory data (Figure 1). The study was approved by the Institutional Review Board at each site.

Magnetic Resonance Elastography

Liver stiffness assessment was performed using 2-dimensional MRE. The stiffness values of the hepatic parenchyma were measured by drawing regions of interest (ROI) within the

region of highest confidence on confidence maps avoiding the liver capsule, major vessels, gall bladder, and fissures. When reporting estimates of liver fibrosis, mean stiffness in kilopascals was calculated by averaging the values from the ROIs for each patient.

Covariates

Covariates selected *a priori* to be evaluated in a combined model included age, sex, body mass index (BMI), a diagnosis of hypertension (HTN), a diagnosis of type 2 diabetes mellitus (DM), albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and platelet count. Each variable was available for the entire dataset per inclusion/exclusion criteria.

Outcome Measures and Follow up

The primary outcome measure was hepatic decompensation, defined as a composite endpoint including ascites, hepatic encephalopathy, or variceal hemorrhage at 3- and 5-years. ***Secondary outcomes*** include incident HCC defined by histology or Liver Reporting and Data Systems (LI-RADS) for definite HCC, i.e. LI-RADS 5, and all-cause mortality at 3- and 5-years.

Patient Follow-up

Follow-up time started at the time of the MRE. Participants were followed until the development of hepatic decompensation, HCC, death, or the last clinical encounter. Follow-up assessment was performed by a retrospective chart review.

Statistical Analysis

Patient characteristics, including demographic, laboratory, imaging, and outcome data are reported as median (interquartile range [IQR]) for continuous variables and N (%) for categorical variables. For the primary outcome, the cohort was randomly split in a 1:1 ratio into training and validation cohorts.

The distribution of liver stiffness on MRE and other non-normally distributed covariates were log or exponentially transformed, if appropriate, given that incorrectly specified functional forms can appear as violations of the proportional hazards assumption (31). Univariable Cox proportional hazards regression was used to identify factors associated with the primary and secondary outcomes. A multivariable Cox proportional hazards model including all identified factors from the univariable model was applied in the training cohort and the final model was identified using backward stepwise removal of variables with $P \geq .10$. The diagnostic accuracy of the model was evaluated in the training and validation cohorts. The diagnostic accuracy of the models was compared to FIB-4 using the method by DeLong (32).

All statistical analyses were performed using R version 4.0.5 or SAS, version 9.2 (SAS Institute), and a two-tailed P value less than 0.05 was considered statistically significant.

RESULTS

Patient Selection and Characteristics of Study Population

The study population included 1,254 participants (Figure 1). Participants in the training cohort (n=627) had a median (IQR) age of 61.0 (18.0) years and a BMI of 29.1 (8.1) kg/m². The validation cohort had a median (IQR) age of 60.0 (20.0) years and a BMI of 28.8 (9.2) kg/m². Median (IQR) liver stiffness on MRE for training and validation cohorts was 3.5 (2.5) and 3.4 (2.5) kPa, respectively (Table 1). The median (IQR) follow-up time in the training and validation cohorts was 3.0 (4.0) years and 2.8 (4.0) years, respectively.

Predictors of Hepatic Decompensation

Among 1,254 patients, 68 (5.4%) met the composite primary outcome of hepatic decompensation including varices needing treatment, ascites, or hepatic encephalopathy. Ten patients who developed variceal hemorrhage (0.8%), 60 who developed ascites (4.8%), and 35 who developed hepatic encephalopathy (2.8%) (Table 1).

In univariable analysis in the training cohort, age, DM, ln (MRE), square (albumin), ln (AST), and platelet count were significantly associated with hepatic decompensation (Table 2). In multivariable-adjusted models, age [adjusted HR (aHR)= 1.02 (95% CI: 1.00–1.05, p=.0848)], ln (MRE) [aHR= 2.58 (95% CI: 1.12–5.96, P=.0262)], square (albumin) [aHR= 0.89 (95% CI: 0.81–0.97, P=.0068)], ln (AST) [aHR= 2.08 (95% CI: 1.17–3.72, P=.0132)], and platelets [aHR= 0.98 (95% CI: 0.98–0.99, P<.0001)] met the statistical threshold for inclusion in the multivariable model (p<.10) (Table 2). The final multivariable model was equal to 0.024 × Age + 0.949 × ln(MRE) − 0.122 × square (albumin) + 0.734 × ln(AST) − 0.016 × platelets. The equation parameters and risk calculation information are shown in Supplemental Table 1. The equation derived in the validation cohort was evaluated in quartiles and stratified the risk of hepatic decompensation in the validation cohort (p<.0001) (Figure 2).

Diagnostic performance of MRE-based multivariable model for hepatic decompensation at 3- and 5-years

The diagnostic accuracy of the MRE-based multivariable model using age, MRE, albumin, AST, and platelets for hepatic decompensation at 3-years was c= 0.912 in the training cohort, which was statistically significantly better than the c-statistic of the FIB-4, c= 0.821 (P< .0001) (Table 3). The results remained consistent in the validation cohort for the 3-year risk of hepatic decompensation with the MRE-based multivariable model, c= 0.871, which was superior to FIB-4 c= 0.750 (P=.003).

Likewise, the diagnostic accuracy of such an MRE-based multivariable model for hepatic decompensation at 5-years was c= 0.891 in the training cohort, which was statistically significantly better than the c-statistic of the FIB-4, c= 0.802 (P< .0001) (Table 3). The results remained consistent in the validation cohort for the 5-year risk of hepatic decompensation with the MRE-based multivariable model, c= 0.876, which was superior to FIB-4 c= 0.726 (P=.0001).

Diagnostic performance of MRE-based multivariable model for HCC at 3- and 5-years

Among the study population (N=1,254), 16 patients (1.3%) developed incident HCC. A univariable Cox proportional hazards regression model demonstrated age, BMI, DM, ln (MRE), square (albumin), ln (ALT), and platelets as significant predictors of HCC (Supplemental Table 2). In a multivariable model, BMI [aHR=0.91 (95% CI: 0.83–0.99; P=.0345)], DM [aHR=6.73 (95% CI: 1.70–26.66); P=0.067], ln (MRE) [aHR=3.90 (95% CI: 1.06–14.42; P=.0412)], and platelets [aHR=0.98 (95% CI: 0.97–0.99, P=.0003)] remained associated with incident HCC. The MRE-based multivariable model using BMI, DM, MRE, and platelets demonstrated high diagnostic accuracy for HCC at 3- and 5-years, c= 0.876 and 0.911 respectively (Supplemental Table 3). The MRE-based multivariable model was superior to FIB-4 at 3- and 5-years (P=.0059 and P<.0001).

Diagnostic performance of MRE-based multivariable model for all-cause mortality at 3- and 5-years

Among the study population (N=1,254), 90 participants died (6.9%) over the study period and 24 died after having hepatic decompensation or HCC. A univariable Cox proportional hazards regression model demonstrated age, ln (MRE), square (albumin), ln (ALT), and platelets were associated with death (Supplemental Table 4). In a multivariable model, age [aHR=1.03 (95% CI: 1.01–1.05, p=.0029)], ln (MRE) [aHR=1.55 (95% CI: 0.98–2.44, p=.0637), albumin [aHR=0.83 (95% CI: 0.79–0.88, p<.0001)], and ln (ALT) [aHR=0.72 (95% CI: 0.52–0.99, p=.0487)] remained associated with death. The MRE-based multivariable model using age, MRE, albumin, and ALT demonstrated good diagnostic accuracy for death at 3- and 5-years, c= 0.806 and 0.760 respectively (Supplemental Table 5). The MRE-based multivariable models were superior to FIB-4 at 3- and 5-years (P<.0001 and P=.0003).

Sensitivity analyses of the MRE-based multivariable model for hepatic decompensation

Among the entire cohort, the diagnostic accuracies of the MRE-based multivariable model for hepatic decompensation at 3- and 5-years were c=0.883 and 0.880, respectively, both of which were statistically significantly better than those of MRE alone, c= 0.823 (p=.0314) and 0.817 (P=.001), respectively (Supplementary Table 6).

In addition, among patients without compensated advanced chronic liver disease (cACLD, defined as MRE < 3.63 kPa; n=683), six had hepatic decompensation and an MRE-based multivariable model risk score greater than the median value (=.0013474) was associated with a higher risk of 5-year hepatic decompensation (P=0.0208), compared to those with a score less than the median value (Supplemental Figure 1). The diagnostic accuracy of the MRE-based multivariable model among patients who did not have cACLD for the 3- and 5-year risk of hepatic decompensation was c=0.778 and c=0.804 respectively (Supplemental Table 7).

Among patients with cACLD (defined as MRE ≥ 3.63 kPa; n=571), 62 had hepatic decompensation and an MRE-based multivariable model risk score greater than the median value (=.0013474) was associated with a higher risk of 5-year hepatic decompensation (P<.0001), compared to those with a score less than the median value (Supplementary

Figure 1). The MRE-based multivariable model had significantly higher diagnostic accuracy than a MELD score of 15 for the 3- and 5-year risk of hepatic decompensation (both P<.0001). The MRE-based multivariable model had numerically higher c-statistics compared to MELD as a continuous measure to predict 3- (0.996 vs. 0.788, respectively) and 5-year (0.826 vs. 0.520, respectively) risk of hepatic decompensation, however, this difference was below the threshold for significant significance (Supplementary Table 7).

DISCUSSION

In this multi-center, international study of adults with NAFLD, we found that the MRE-based multivariable model with age, MRE, albumin, AST, and platelets best predicted the risk of hepatic decompensation in training and validation cohorts. The diagnostic accuracy of the MRE-based multivariable model for the 3- and 5-year risk of decompensation remained between 0.88–0.91 in training and validation cohorts and was superior to FIB-4. The combination of clinical parameters widely available in routine practice with MRE may offer more refined risk prediction for patients with NAFLD. Applying the MRE-based multivariable model as an online calculator (NAFLDMREcalculator.com) can quickly yield the 3- and 5-year risk of hepatic decompensation, guiding clinical management as well as patient counseling. Existing clinical tools primarily dichotomize risk, whereas the MRE-based multivariable model provides granular information to the patient regarding prognosis and risk of key clinical outcomes. As treatment strategies emerge, accurate prognostication will help determine the individuals at greatest need of treatment.

In Context with Published Literature

Fibrosis stage on liver biopsy has been adopted as a surrogate marker for future liver-related outcomes in clinical trials based on longitudinal studies demonstrating its association with liver-related outcomes and death. (10, 16) Recently, studies have demonstrated the direct association of non-invasive tests (NITs) such as FIB-4 index (33, 34), liver stiffness on vibration-controlled transient elastography (35), and MRE (25, 27, 36, 37) on liver-related events. The combination of NITs may offer enhanced risk prediction for liver-related events and to date, this has been evaluated with the MEFIB index, combining MRE and FIB-4, which had a high negative predictive value (25). Boursier et al.(38) reported on the sequential combination of FIB-4 and VCTE and demonstrated a strong association with liver-related events. Here, we evaluated a candidate set of variables and then formed a multivariable model for hepatic decompensation that retained excellent diagnostic accuracy in a multi-ethnic validation cohort. Using the MRE-based multivariable model, the estimated 3- and 5-year risk of hepatic decompensation can be provided in clinical care, presenting a more granular understanding of a patient's risk. This approach resembles risk stratification in cardiovascular disease through Framingham (39) and ASCVD (40) risk scores and if validated, may inform the need for treatment in patients with NAFLD. Importantly, the score differentiated the risk of hepatic decompensation in patients with and without cACLD, despite the low risk (1%) for decompensation in the subset of patients without cACLD.

Importantly, the MRE-based multivariable models for HCC and all-cause mortality also demonstrated good diagnostic accuracy and outperformed FIB-4. As the utilization of liver

biopsy in NAFLD decreases, the ability to predict HCC risk and determine the need for screening without overt evidence of cirrhosis remains an unmet need. In our study, T2DM was associated with hepatic decompensation and HCC on univariable analysis but did not remain a significant predictor of hepatic decompensation in multivariable models. In our cohort, there T2DM was collinear with age and MRE, which resulted in T2DM not remaining in the multivariable model for hepatic decompensation, although it remained strongly associated with HCC in multivariable models.

Strengths and Limitations

This study has several notable strengths. First, our international multi-center, multi-ethnic cohort included a large sample size of > 1,200 patients who underwent baseline MRE and laboratory tests, making this one of the largest studies of NAFLD-related outcomes. Furthermore, the high number of incident hepatic decompensation events (n=68, 5.4%) allowed for adequate power to assess multivariable models in a training and validation cohort.

However, we also acknowledge several limitations. First, MRE was only assessed at a single time point in this study. This score was developed to assess prognosis at a single time point and future studies will be required to assess the dynamics of changes in this score over time and its impact on a patient's risk of hepatic decompensation. To date, there are limited data on the association between change in MRE and change in liver histology in cohorts of 50–100 patients (23, 41). A recent study evaluated the impact of change in MRE on liver-related outcomes and demonstrated that progression in liver stiffness on MRE in 29 patients with compensated cirrhosis was associated with hepatic decompensation or death (42). Future studies may evaluate if serial MRE measurements over time can refine the prediction of future liver-related events, although the clinical value of accurate risk prediction with a single MRE value remains significant. Second, primarily because MRE has become available in the clinical practice more recently compared to other NITs, e.g. VCTE or other blood-based markers, our study has a relatively short median follow-up duration. Thus, future, multicenter, prospective studies with long-term follow-up are recommended to validate the prognostic role of this MRE-based multivariable model. Vibration-controlled transient elastography (VCTE) data was not available, precluding the head-to-head comparison between VCTE-based vs. MRE-based multivariable models. However, MRE is the most accurate non-invasive biomarker of fibrosis and the MRE-based multivariable model outperformed MRE alone. Last, since all patients in the present study belonged to retrospective cohorts at academic medical centers, a subset of clinical events may not have been captured. Nevertheless, our outcome assessment, performed by hepatologists, will have high specificity and the decreased sensitivity would result in a more conservative estimate regarding the clinical utility of the MRE-based multivariable model. Future prospective studies evaluating this MRE-based multivariable model with systematic assessment of hepatic decompensation are recommended.

Implications for future research and clinical practice

Future studies will need to include head-to-head comparisons with other non-invasive tests, including VCTE, to compare performance and identify the optimal context of use.

However, for patients with MRE assessment, the MRE-based multivariable model using age, MRE, albumin, AST, and platelets has excellent diagnostic accuracy to predict hepatic decompensation in adult patients with NAFLD and may be used to predict the 3- and 5-year risk of hepatic decompensation to counsel patients and inform treatment decisions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

MRE	Magnetic resonance elastography
IPDMA	individual participant data pooled meta-analysis
NAFLD	nonalcoholic fatty liver disease
LS	liver stiffness
BMI	body mass index
AASLD	American Association for the Study of Liver Diseases
LI-RADS	Liver Reporting and Data Systems
LSM	liver stiffness measurement, SD: standard deviation, IQR: interquartile range
MELD	model for end-stage liver disease
HCC	hepatocellular carcinoma

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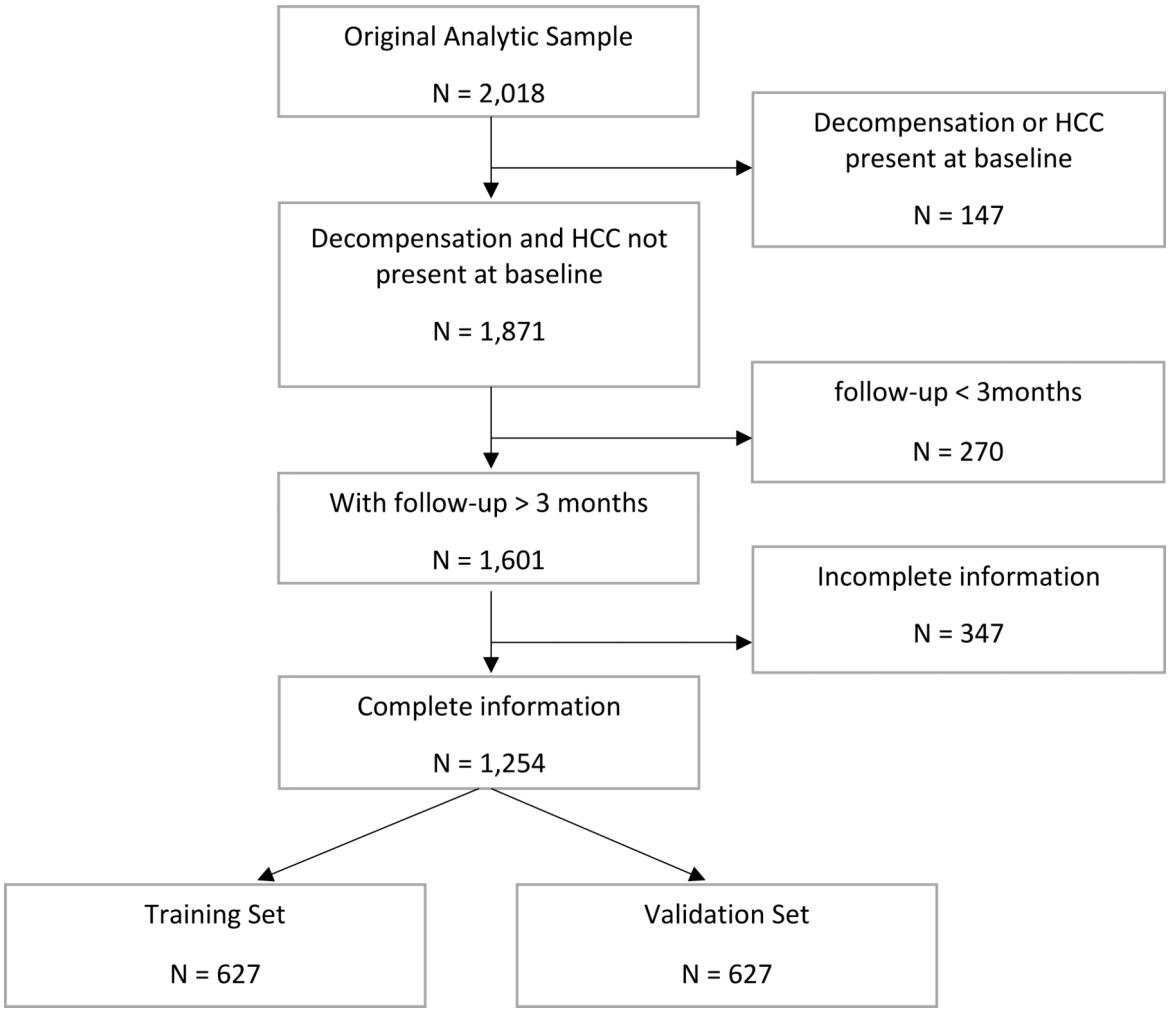

Figure 1:
Study Cohort Derivation Diagram

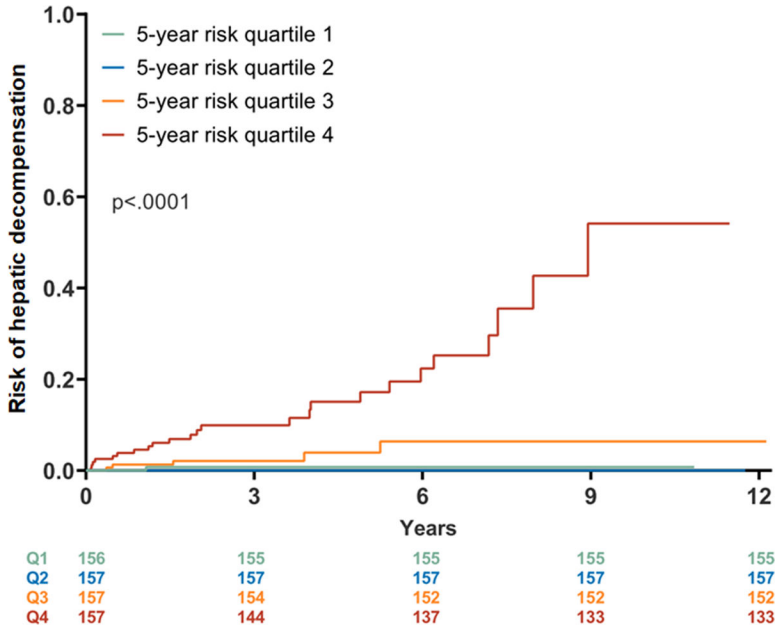

Figure 2:

Cumulative Incidence of Hepatic Decompensation by Quartiles of Risk on the MRE-Based Multivariable Model

Table 1.

Characteristics of the study population in the training and validation cohorts

	Training cohort (N=627)	Validation cohort (N=627)
Age (yrs), median (IQR)	61.0 (18.0)	60.0 (20.0)
Male, N (%)	289 (46%)	310 (49%)
BMI (kg/m^2), median (IQR)	29.1 (8.1)	28.8 (9.2)
HTN, N (%)	198 (32%)	191 (30%)
Diabetes, N (%)	230 (37%)	219 (35%)
MRE (kPa), median (IQR)	3.5 (2.5)	3.4 (2.5)
Albumin (g/dL), median (IQR)	4.3 (0.5)	4.3 (0.6)
ALT (U/mL), median (IQR)	46.0 (41.0)	47.0 (50.0)
AST (U/ml), median (IQR)	40.0 (32.0)	42.0 (32.0)
Total Bilirubin (mg/dL), median (IQR)	0.6 (0.5)	0.6 (0.5)
Platelet count (*10^3/uL), median (IQR)	195.0 (106.0)	202.0 (110.0)
Follow up time (yrs), median (IQR)	3.0 (4.0)	2.8 (4.0)
Follow up time (yrs), min-max	0.3 – 12.1	0.3–12.1
Variceal hemorrhage, N (%)	5 (1%)	5 (1%)
Ascites, N (%)	33 (5%)	27 (4%)
Hepatic encephalopathy, N (%)	21 (3%)	14 (2%)
Composite Primary Outcome, N (%)	38 (6%)	30 (5%)
HCC, N (%)	9 (1%)	7 (1%)
Death, N (%)	50 (8%)	34 (5%)

Abbreviations: IQR, interquartile range; BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; MRE, magnetic resonance elastography; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HCC, hepatocellular carcinoma

Table 2.

Univariable and multivariable Cox proportional hazards regression analysis for hepatic decompensation in the training cohort (N=627)

	Univariable Models		Final Model	
	Crude HR (95% CI)	**P-value**	**Adjusted HR (95% CI)**	**P-value**
Age (per 1 year increase)	1.05 (1.02, 1.08)	.0007	1.02 (1.00, 1.05)	.0848
Sex				
Male	Ref			
Female	1.01 (0.53, 1.90)	.9875		
BMI (per 1 kg/m^2)	1.04 (0.99, 1.08)	.1069		
HTN				
No	Ref			
Yes	1.26 (0.66, 2.40)	.4842		
DM				
No	Ref			
Yes	3.18 (1.61, 6.31)	.0009		
ln (MRE [kPa]), per 1 log-unit increase	10.14 (4.91, 20.95)	<.0001	2.58 (1.12, 5.96)	.0262
square (albumin [g/dL]), per 1-unit increase	0.80 (0.74, 0.86)	<.0001	0.89 (0.81, 0.97)	.0068
ln (ALT [U/mL]), per 1 log–unit increase	0.88 (0.54, 1.44)	.6160		
ln (AST [U/mL]), per 1 log–unit increase	2.22 (1.31, 3.76)	.0030	2.08 (1.17, 3.72)	.0132
Platelet count (*10^3/uL), per 1- unit increase	0.98 (0.97, 0.98)	<.0001	0.98 (0.98, 0.99)	<.0001

Multivariable model included all significant (p<.10) variables from univariable models. Non-significant (p>.10) terms were dropped stepwise from final model. Log transformation using natural log.

Abbreviations: HR, hazard ratio; CI, confidence interval; BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; MRE, magnetic resonance elastography; ALT; alanine aminotransferase; AST, aspartate aminotransferase

Table 3.

Diagnostic performance of the MRE-based multivariable model using age, MRE, albumin, AST, and platelets for 3- and 5-year risk of hepatic decompensation in training (N=627) and validation (N=627) cohorts

	Concordance Index (Uno's C-Statistic)			
	Training cohort (N=627)		Validation cohort (N=627)	
	Estimate (SE)	Difference between reduced and Full models, p-value	Estimate (SE)	Difference between reduced and Full models, p-value
3-year				
Full model	.9117 (.0245)		.8707 (.0337)	
FIB-4*	.8210 (.0250)	<.0001	.7502 (.0452)	.0003
5-year				
Full model	.8914 (.0258)		.8758 (.0303)	
FIB-4*	.8022 (.0303)	<.0001	.7255 (.0525)	.0001

* FIB-4 cut-point of 2.67 used to define high-risk

Abbreviations: MRE, magnetic resonance elastography; AST, aspartate aminotransferase; SE, standard error