

Supplementary Appendix

Supplement to: Kim, BK, Bergstrom J, Loomba R et al. **Magnetic Resonance Elastography-Based Prediction Model for Hepatic Decompensation in NAFLD; a Multi-Center Cohort Study**

Supplemental Table 1. Equation parameters for estimation of 3-Year and 5-Year risk of hepatic decompensation in the training cohort (N=627)

S ₀ (t) at 3 years	S ₀ (t) at 5 years	Mean Score	Individual Score
.9681	.9490	0.059	= 0.024 x Age + 0.949 x ln(MRE) – 0.122 x square(albumin) + 0.734 x ln(AST) – 0.016 x Platelets

Final risk estimation is calculated as: $1 - S_0(t)^{e^{(Individual\ Score - Mean\ Score)}}$

Analysis Variable : Risk_5yr						
N Obs	N	Minimum	25th Pctl	Median	75th Pctl	Maximum
627	627	3.2010848E-6	0.000370560	0.0013474	0.0059716	0.2086715

Sensitivity and specificity for median cutpoint of risk score

Median cutpoint (.0013474) specificity=.54, sensitivity=.97

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Numbers lost if cut to follow-up < 6-months

N=57 (out of 1,254) have follow-up < 6-months (N=30 in training/N=27 in validation)

Supplemental Table 2. Univariable and multivariable Cox proportional hazards regression analysis for HCC among the entire cohort (N=1254)

	Univariable Models		Final Model	
	Crude HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
Age	<u>1.07 (1.02, 1.12)</u>	<u>.0048</u>		
Sex				
Male	Ref			
Female	<u>0.41 (0.14, 1.19)</u>	<u>.1016</u>		
BMI	<u>0.92 (0.84, 1.00)</u>	<u>.0608</u>	<u>0.91 (0.83, 0.99)</u>	<u>.0345</u>
HTN				
No	Ref			
Yes	<u>0.85 (0.30, 2.47)</u>	<u>.7706</u>		
DM				
No	Ref		Ref	
Yes	<u>6.93 (1.97, 24.32)</u>	<u>.0025</u>	<u>6.73 (1.70, 26.66)</u>	<u>.0067</u>
<u>ln (MRE [kPa]), per 1 log-unit increase</u>	<u>14.64 (4.95, 43.34)</u>	<u><.0001</u>	<u>3.90 (1.06, 14.42)</u>	<u>.0412</u>
<u>Square (albumin [g/dL]), per 1-unit increase</u>	<u>0.84 (0.75, 0.94)</u>	<u>.0026</u>		
<u>ln (ALT [U/mL]), per 1 log-unit increase</u>	<u>0.51 (0.24, 1.09)</u>	<u>.0808</u>		
<u>ln (AST [U/mL]), per 1 log-unit increase</u>	<u>1.38 (0.58, 3.24)</u>	<u>.4650</u>		
<u>Platelet count (*10³/uL), per 1-unit increase</u>	<u>0.98 (0.97, 0.99)</u>	<u><.0001</u>	<u>0.98 (0.97, 0.99)</u>	<u>.0003</u>

Multivariable model included all significant (p<.10) variables from univariable models. Non-significant (p≥.10) terms were dropped stepwise from final model.

Abbreviations: HCC, hepatocellular carcinoma; 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

Supplemental Table 3. Diagnostic performance of the MRE-based multi-variable model using BMI, DM, MRE, and platelets vs FIB-4 for 3- and 5-year risk of HCC

Concordance Index (Uno's C-Statistic)		
Full Set (N=1254)		
	Estimate (SE)	Difference between reduced and Full models, p-value
3-year		
Full model	<u>.8762</u> (<u>.0520</u>)	
FIB-4*	<u>.7937</u> (<u>.0493</u>)	p= <u>.0059</u>
5-year		
Full model	<u>.9111</u> (<u>.0344</u>)	
FIB-4*	<u>.8236</u> (<u>.0416</u>)	p< <u>.0001</u>

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

Abbreviations: MRE, magnetic resonance elastography; BMI, body mass index; DM, diabetes mellitus; HCC, hepatocellular carcinoma; SE, standard error

Supplemental Table 4. Univariable and multivariable Cox proportional hazards regression analysis for all-cause mortality (N=1,254)

	Univariable Models		Final Model	
	Crude HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
Age	<u>1.05 (1.03, 1.07)</u>	<u><.0001</u>	<u>1.03 (1.01, 1.05)</u>	<u>.0029</u>
Sex				
Male	Ref			
Female	<u>0.95 (0.62, 1.46)</u>	<u>0.8268</u>		
BMI	<u>0.98 (0.95, 1.01)</u>	<u>0.1802</u>		
HTN				
No	Ref			
Yes	<u>0.83 (0.53, 1.32)</u>	<u>.4404</u>		
DM				
No	Ref			
Yes	<u>1.02 (0.66, 1.58)</u>	<u>.9246</u>		
<u>ln (MRE [kPa]), per 1 log-unit increase</u>	<u>3.05 (1.98, 4.72)</u>	<u><.0001</u>	<u>1.55 (0.98, 2.49)</u>	<u>.0637</u>
<u>Square (albumin [g/dL]), per 1-unit increase</u>	<u>0.81 (0.77, 0.85)</u>	<u><.0001</u>	<u>0.83 (0.79, 0.88)</u>	<u><.0001</u>
<u>ln (ALT [U/mL]), per 1 log-unit increase</u>	<u>0.53 (0.38, 0.74)</u>	<u>.0002</u>	<u>0.72 (0.52, 0.99)</u>	<u>.0487</u>
<u>ln (AST [U/mL]), per 1 log-unit increase</u>	<u>1.26 (0.87, 1.84)</u>	<u>.2243</u>		
<u>Platelet count (*10³/uL), per 1-unit increase</u>	<u>0.99 (0.99, 0.99)</u>	<u><.0001</u>		

Multivariable model included all significant (p<.10) variables from univariable models. Non-significant (p≥.10) terms were dropped stepwise from final model.

Supplemental Table 5. Diagnostic performance of multivariable MRE-based model using age, MRE, albumin and ALT for 3- and 5-year risk of all-cause mortality

Concordance Index (Uno's C-Statistic)		
Full Set (N= <u>1,254</u>)		
	Estimate (SE)	Difference between reduced and Full models, p-value
3-year		
Full model	<u>.8060 (.0314)</u>	
FIB-4*	<u>.6192 (.0389)</u>	<u>p<.0001</u>
5-year		
Full model	<u>.7593 (.0329)</u>	
FIB-4*	<u>.6380 (.0285)</u>	<u>p=.0003</u>

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

Abbreviations: MRE, magnetic resonance elastography; SE, standard error

Supplemental Table 6. Sensitivity analyses: diagnostic performance of multivariable MRE-based multivariable model for 3- and 5-year risk of hepatic decompensation vs MRE alone among the entire population

Concordance Index (Uno's C-Statistic)		
Entire population (N=1254)		
	Estimate (SE)	Difference between reduced and Full models, p-value
3-year		
Full model	.8825 (.0211)	
MRE	.8227 (.0274)	.0314
MRE*	.7384 (.0196)	<.0001
5-year		
Full model	.8797 (.0183)	
MRE	.8170 (.0236)	.0010
MRE*	.7310 (.0191)	<.0001

*MRE cut-point of 3.63 used to define high-risk

Abbreviations: MRE, magnetic resonance elastography; SE, standard error

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I think that analysis using MRE cutoff of 3.63 might be removed. What do you think?

Supplemental Table 7. Sensitivity analyses: diagnostic performance of multivariable MRE-based model using age, MRE, albumin, AST and platelets for 3- and 5-year risk of hepatic decompensation among patients with or without cACLD

Concordance Index (Uno's C-Statistic)				
	Patients without cACLD (MRE < 3.63 kPa)		Patients with cACLD (MRE ≥ 3.63 kPa)	
	Estimate (SE)	Difference between reduced and Full models, p-value	Estimate (SE)	Difference between reduced and Full models, p-value
3-year				
Full model	.7783 (.0524)		.9959 (.1030)	
MELD	.7045 (.0499)	.0941	.7884 (.3160)	.4813
5-year				
Full model	.8039 (.0396)		.8257 (.0956)	
MELD	.6928 (.0438)	.0128	.5195 (.1403)	.0751

Abbreviations: MRE, magnetic resonance elastography; AST, aspartate aminotransferase; cACLD, compensated advanced chronic liver disease; SE, standard error; MELD, model for end-stage liver disease

TOTAL N=1,254	MRE ≥ 3.63 kPa (N=571)	MRE < 3.63 kPa (N=683)
Composite Primary Outcome, N (%)	62 (11%)	6 (1%)
TOTAL N=1,041 (with MELD info)	MRE ≥ 3.63 kPa (N=512)	MRE < 3.63 kPa (N=529)
Composite Primary Outcome, N (%)	55 (11%)	4 (1%)

