MR Elastography Based Fibrosis Correlates with Clinical Liver Events in Patients with Nonalcoholic Fatty Liver Disease (NAFLD): A Multi-center Study

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1 INTRODUCTION

- Liver fibrosis assessed by liver biopsy has been shown to predict liver outcomes in patients with nonalcoholic fatty liver disease (NAFLD) and remains the gold standard in phase 3 trials.
- MR elastography (MRE) has been shown to be highly correlated with liver biopsy in assessing liver fibrosis and is currently used in phase 2 trials.
- Data to assess the correlation between MRE and clinical liver events are lacking.

2 AIM

- To investigate the association between MRE and clinical liver events/death in NAFLD patients
- To identify the cut-offs to predict clinical liver events in a large cohort of NAFLD patients from both Cedars-Sinai and the Texas Liver Institute

3 METHOD

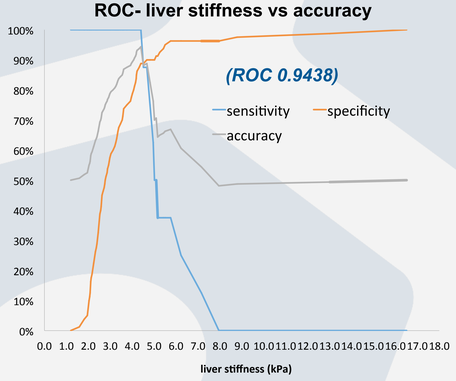
- A multi-center study of NAFLD patients from Texas and California who underwent MRE were recruited from May 2016 to June 2018.
- Clinical liver events included: decompensation events such as ascites, hepatic encephalopathy (HE), esophageal variceal bleeding (EVB), liver transplant and death.
- We categorized the cohort into 3 groups: 1) non-cirrhosis group, 2) cirrhosis without decompensation group and 3) cirrhosis with decompensation group.
- Fishers exact test - compare categorical variables
- ROC was used for MRE liver stiffness to determine the best cut-offs
- Logistic regression model was used to predict decompensation.

4 RESULTS

Table 1. Patients' Characteristics

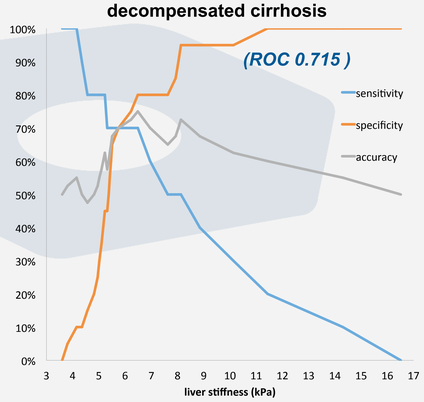
Variable	N = 245
Gender (Female)	131.0 (53.5%)
Age	56.0 (46-65)
Ethnicity	
Non-Hispanic	164.0 (66.9%)
Hispanic	75.0 (30.6%)
Decline/Missing	6.0 (2.5%)
Race	
White	208.0 (84.9%)
Black	8.0 (3.3%)
Asian	12.0 (4.9%)
Other	16.0 (6.5%)
Declined/Unknown	1.0 (0.4%)
DM2	114.0 (47.0%)
HTN	118.0 (48.0%)
Hyperlipidemia	143.0 (59.8%)
Cirrhosis	30.0 (12.3%)
BMI Median (IQR) kg/m^2	32.0 (28.1-35.7)
HbA1C Median (IQR) %	6.0 (5.6-6.9)
ALT Median (IQR) U/L	43.0 (26.0-67.0)
AST Median (IQR) U/L	32.0 (23.0-49.0)
Alk.Phos Median (IQR) U/L	78.0 (62.0-98.0)
Albumin Median (IQR) g/dl	4.4 (4.2-4.6)
Bilirubin Median (IQR) mg/dl	0.6 (0.4-0.7)
Platelets (PLT) Median (IQR) (1000/mm3)	229.5 (184.8-283.0)

Figure 1. MRE Threshold for No Cirrhosis vs. Cirrhosis



Liver stiffness	Sensitivity	Specificity	Accuracy
4.395(kPa)	100%	88%	94.4%

Figure 2. MRE Threshold for Decompensated vs Compensated Cirrhosis



Liver stiffness (kPa)	Sensitivity	Specificity	Accuracy
6.48	70.0%	80.0%	75.0%

Table 3. Associations between different clinical liver events and MRE liver stiffness

Clinical Liver Events	Median (kPa)	p value
Ascites-Yes	**7.40** (4.85-10.15)	**<0.001**
Ascites-No	2.50 (2.10-3.28)	
Hepatic encephalopathy (HE)-Yes	**9.50** (8.20-10.76)	**<0.001**
Hepatic encephalopathy (HE)-No	2.50 (2.10-3.28)	
Esophageal variceal bleed (EVB)-Yes	**10.15** (9.28-11.12)	**0.017**
Esophageal variceal bleed (EVB)-No	2.50 (2.11-3.33)	
Deceased- Yes	**10.15** (9.18011.12)	**0.016**
Deceased- No	2.50 (2.10-3.31)	

Table 2. Clinical parameters in the 3 groups

Variable	Non cirrhosis	Compensated cirrhosis	Decompensated cirrhosis	p value
Gender (female)%	89.31%	6.11%	4.58%	0.426
DM2 %	43.93%	70.00%	60.00%	0.087
Hyperlipidemia %	89.51%	6.29%	4.20%	0.688
Liver stiffness (kPa)	2.43 (2.10-3.00)	5.37 (4.98-6.11)	7.80 (5.60-10.44)	**<0.001**
Age	56.00 (45.60-6.5.00)	58.00 (52.00-62.00)	65.50 (53.00-71.50)	0.249
BMI (IQR) kg/m2	31.90 (28.00-35.50)	35.18 (32.00-40.50)	29.89 (28.20-34.40)	0.018
TG (mg/dl)	142.50 (113.50-229.50)	67.00 (142.00-201.50)	113.00 (106.00-201.50)	0.584
HDL (mg/dl)	45.00 (38.00-53.00)	38.00 (31.50-48.00)	58.00 (56.00-62.00)	**0.027**
TC (mg/dl)	182.00 (153.00-211.00)	165.00 (145.50-200.00)	207.00 (137.00-231.50)	0.411
HDL (mg/dl)	45.00 (38.00-53.00)	38.00 (31.50-48.00)	58.00 (56.00-62.00)	**0.027**
LDL (mg/dl)	102.00 (77.00-129.00)	103.00 (84.50-139.50)	122.00 (91.00-125.50)	0.858
ALT (U/L)	43.00 (25.00-65.30)	42.00 (29.50-68.00)	43.00 (34.50-127.50)	0.656
AST (U/L)	31.00 (23.00-45.50)	34.00 (28.80-54.50)	66.5 (41.30-116.80)	**0.006**
Alk Phos (U/L)	77.50 (62.00-96.80)	71.50 (60.80-91.80)	128.50 (95.30-163.20)	**0.006**
Albumin (g/dl)	4.50 (4.30-4.60)	4.40 (4.10-4.50)	4.10 (3.80-4.20)	**0.004**
T bili (mg/dl)	0.50 (0.40-0.70)	0.65 (0.50-1.10)	0.65 (0.45--1.10)	**0.050**
Platelets (IQR) (1000/mm3)	240.50 (195.50-288.20)	146.00 (126.50-185.50)	154.50 (99.80-215.50)	**<0.001**
HbA1C (IQR) %	5.90 (5.60-6.80)	6.40 (5.90-7.00)	6.30 (6.20-7.40)	0.388

Table 4. Logistic model for Cirrhosis with Decompensation

Predictor	OR	lower	upper	p value
Liver Stiffness(kPa)	3.09	1.84	5.20	<0.001

5 CONCLUSIONS

- This novel study demonstrated that in NAFLD patients higher liver stiffness as measured by MRE cut off ≥ 6.48 kPa was associated with overall decompensation and mortality in a large multicenter cohort.
- Our study identified different MRE cut-offs associated with individual clinical liver events.
- These MRE cut-offs could allow physicians to identify NAFLD patients at higher risk of liver related complications and eventually death.
- Further long-term prospective studies are warranted to confirm our results

6 REFERENCES

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7 CONTACT

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