Application of lIVERFASt Biomarkers to Evaluate Longitudinal Hepatic Fibrosis and Inflammation after HCV cure

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BACKGROUND / INTRODUCTION

- Hepatitis C virus (HCV) infection is a common cause of both liver cirrhosis and hepatocellular carcinoma
- Successful Direct antiviral agents (DAA) therapy is associated with >95% sustained virological response
- Although the goal of HCV treatment is to achieve SVR, patients with advanced fibrosis and cirrhosis still have a high risk of developing HCC
- It is important to identify patients who are at risk for liver disease complications after achieving SVR

AIMS

- To evaluate the prognostic values of LIVERFASt as a noninvasive biomarker in evaluating changes in fibrosis and inflammation post-DAA therapy
- To identify risks associated with HCC and liver disease progression after HCV cure post-DAA

METHODS

- Retrospective cohort study in a single tertiary liver center
- Patients achieved DAA-induced HCV cure with follow-up >1 year who had pretreatment and follow-up sera in the biorepository were included
- Medical record review was performed to record HCC, hepatic decompensations, and comorbid conditions
- APRI and FIB-4 scores were calculated and correlated with the LIVERFASt Fibrosis scores at baseline.
- LIVERFASt™ is a blood-based diagnostic test that combines 10 biomarkers and algorithm technology to determine the fibrosis, inflammatory activity, and steatosis of the liver.

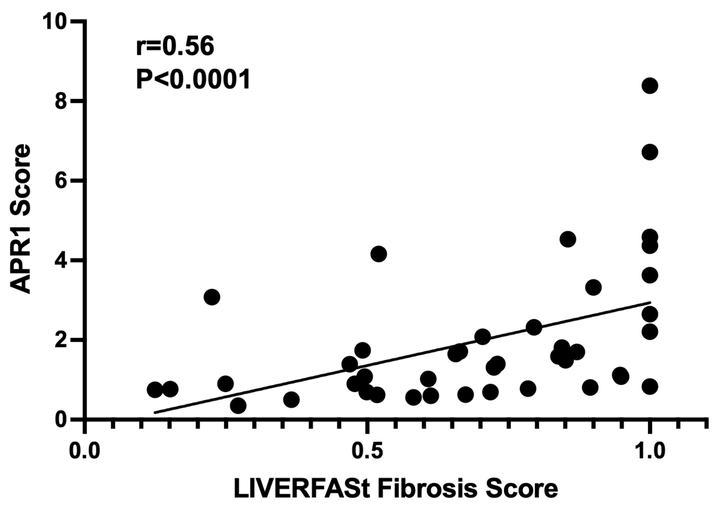
Required Biomarkers of LIVERFASt

LIVERFASt			
Biomarkers in SI units	**Fibrosis test**	**Activity test**	**Steatosis test**
		Quantitative scores (0-1)	
Age, yrs	x	x	x
Gender	x	x	x
BMI, kg/m²			x
Alpha2-macroglobulin, g/l	x	x	x
Apolipoprotein A1, g/l	x	x	x
Haptoglobin, g/l	x	x	x
Total bilirubin	x	x	x
Gamma glutamyl transpeptidases (GGT), IU/l	x	x	x
Alanine aminotransferases (ALT), IU/L		x	x
Triglycerides, mmol/L			x
Fasting glucose, mmol/L			x
Total cholesterol, mmol/L			x
Aspartate aminotransferases (AST), IU/l			x

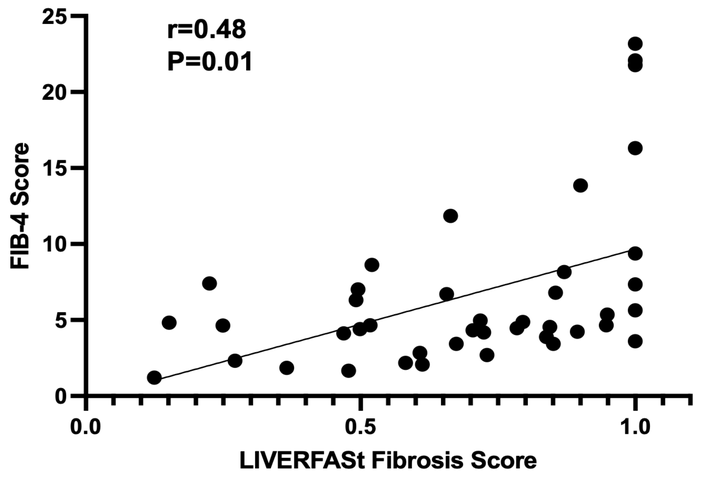
RESULTS

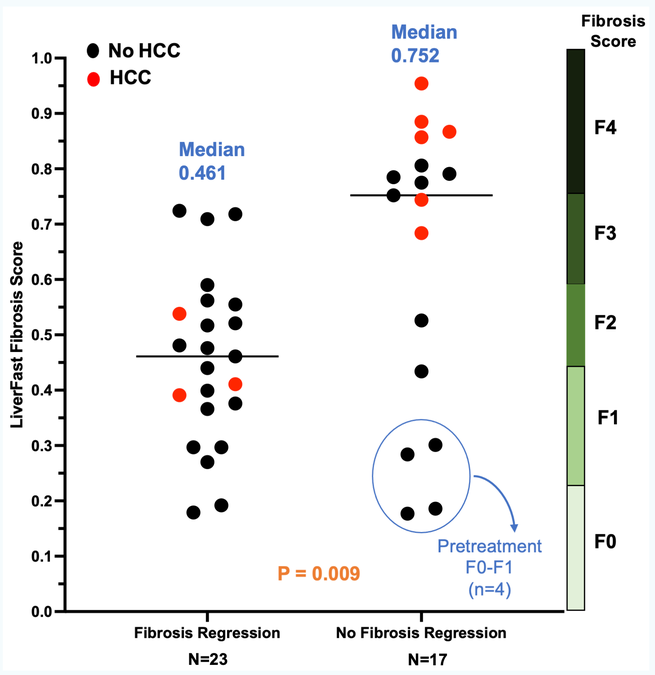
- A total of 40 patients with a post-DAA follow-up period of 37 (17- 62) months were included in the analysis
- **Gender:** Male (62%); Female (38%)
- **Race:** White (65%), African American (22.5%), Asians (7.5%), Hispanic (2.5%), unknown (2.5%)
- **Age:** 58 (33-78) years
- **HCV Genotype:** **1a** 20 (50%), **1b** 10 (25%)
- **Pretreatment Stage 3-4 fibrosis:** 34 (85%)

Correlation of pretreatment APR1 and LIVERFASt



Correlation of pretreatment FIB-4 and LIVERFASt





Hepatic fibrosis changes post-DAA

- At follow-up: 23 (58%) had ≥ 1 stage fibrosis regression
- 3 (7.5%) had progression of fibrosis
- 14 (35%) had no changes; 4 had F0-F1 at baseline

HCC post-DAA

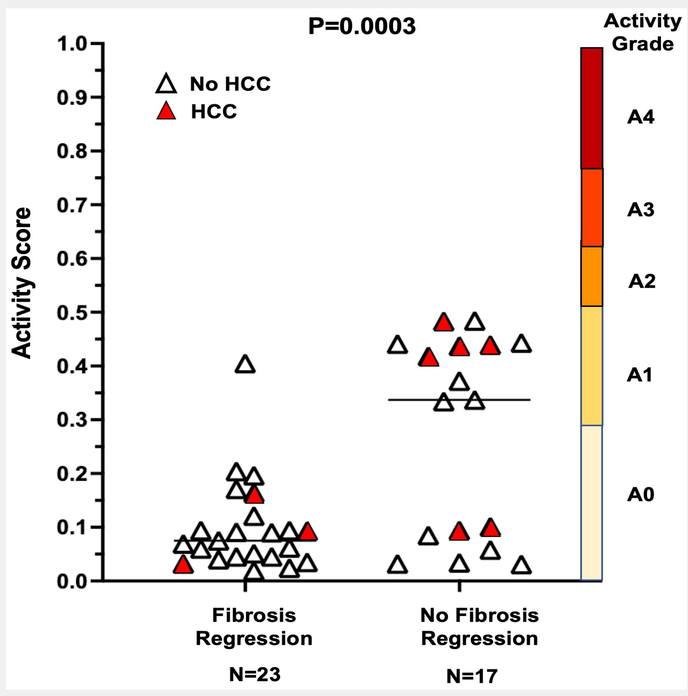
- 9 developed HCC between 2.1 and 5.8 years after HCV cure, and 8 had advanced fibrosis prior to DAA.
- 5 (56%) had unchanged F3-4 stage
- 1 (11%) progressed from F2 to F4 fibrosis and had active inflammation
- 3 (33%) had fibrosis regression. All had a history of hepatic decompensation prior to DAA

Hepatic fibrosis changes post-DAA

- At baseline, 16(70%) and 8(47%) patients with and without subsequent fibrosis regression had inflammation Activity score ≥1 grade, respectively (p=0.15)
- At follow-up:
  - 22 (96%) with fibrosis regression had grade 0 Activity
  - 10 (59%) with no fibrosis regression had grade ≥1 activity

Active Inflammation post-DDA

- HCC: 4 (44%) had Activity score ≥ 1
- No HCC:
  - 6 (55%) without fibrosis regression had Activity score ≥ 1
  - 2 had active alcohol use; one progressed to F4
  - 1 ANA(+) autoimmune hepatitis
  - 2 had portal hypertension, and one also had BMI>30
  - 1 No obvious comorbid condition



CONCLUSIONS

- LIVERFASt has prognostic values by monitoring changes in hepatic fibrosis and inflammation after HCV cure
- Patients with advanced fibrosis and hepatic decompensation remain at high risk for HCC after HCV cure and require ongoing HCC Surveillance
- Patients with persistent hepatic inflammation despite SVR are at risk for liver disease progression and complications
- Other causes of liver disease must be evaluated for patients with hepatic inflammation or progressive fibrosis after HCV cure