

# Hepatic Fibrosis Staging and Non-Invasive Tests

Fredric Gordon, MD, FAASLD, FAST, AGAF  
Chief, Abdominal Transplant Medicine  
Medical Director of Liver Transplantation  
Tufts Medical Center  
Professor of Medicine  
Tufts Medical School  
Boston, MA



## Objectives

- Staging liver disease with non-invasive testing (NITs)
- Determining when to refer if patient has advanced liver disease
- Identifying patients that qualify for HCC screening

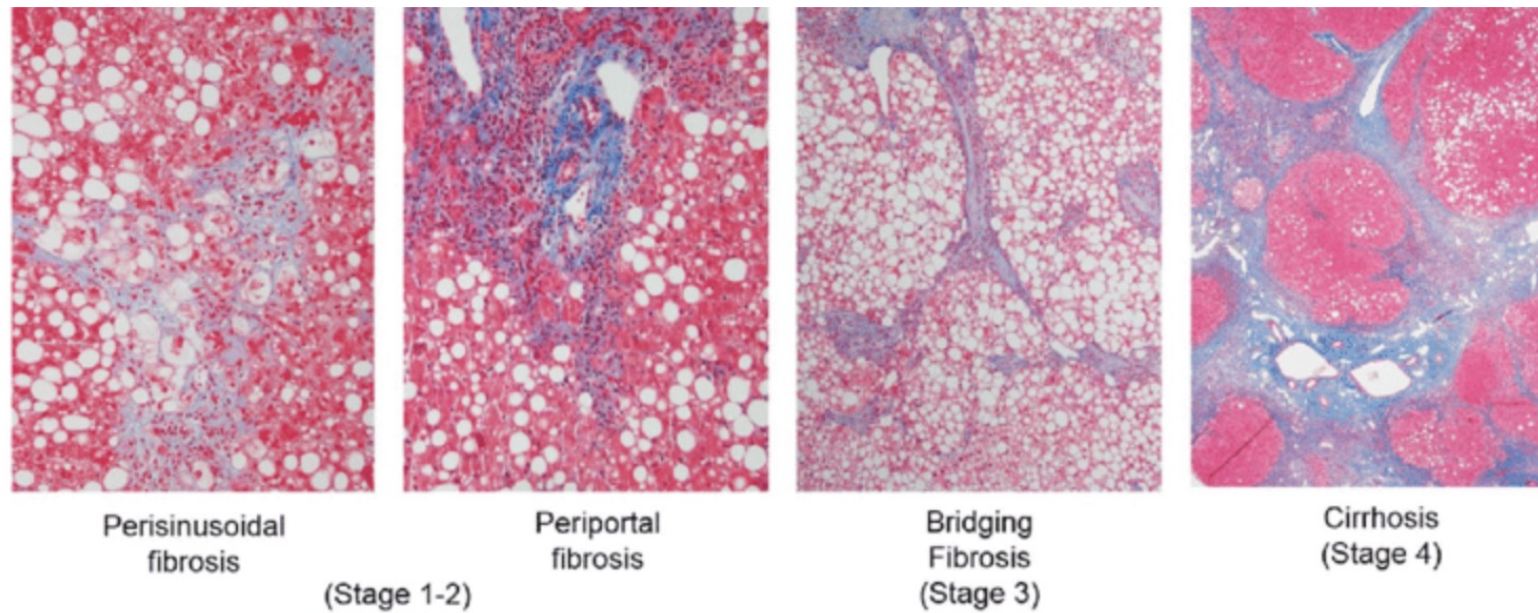
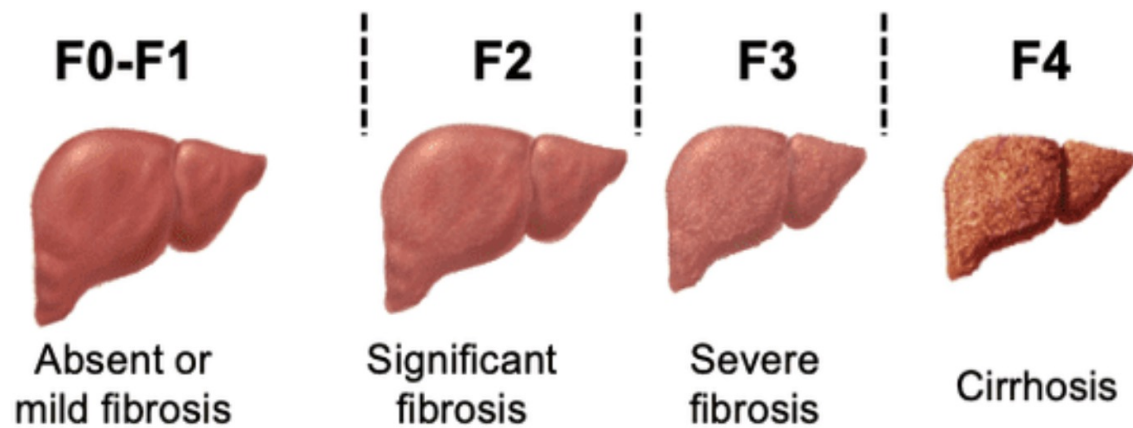


# Liver Histology Nomenclature

- Grade
  - Degree of **inflammation**
  - Often reflected by the liver enzymes (AST, ALT)
  - 0-4 (0-3 in MASH)
- Stage
  - Dynamic
  - Degree of fibrosis (scarring)
    - Stage 0 – no
    - Stage 1 – minimal
    - Stage 2 – mild
    - Stage 3 – moderate
    - Stage 4 – severe (= cirrhosis)



# Stage





## Non-Invasive Tests (NITs)

- Liver Biopsy – now historical
  - NOT non-invasive
  - Complication rate 6-7%
    - 0.5% major
- NITs – Readily available tests to assess the degree of hepatic fibrosis
  - Demographics
  - Blood
  - Radiology



## Cheap and Easy

$$\text{APRI} = \frac{\frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelet Count (10}^9\text{/L)}} \times 100$$

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}}$$

NAFLD fibrosis score

$$\begin{aligned} & -1.675 + 0.037 \times \text{age (years)} + 0.094 \times \text{BMI} + \\ & 1.13 \times \text{impaired fasting glucose/diabetes} \\ & (\text{yes} = 1, \text{no} = 0) + 0.99 \times \text{AST/ALT ratio} - 0.013 \\ & \times \text{platelet (}\times 10^9\text{/l)} - 0.66 \times \text{albumin (g/dL)} \end{aligned}$$



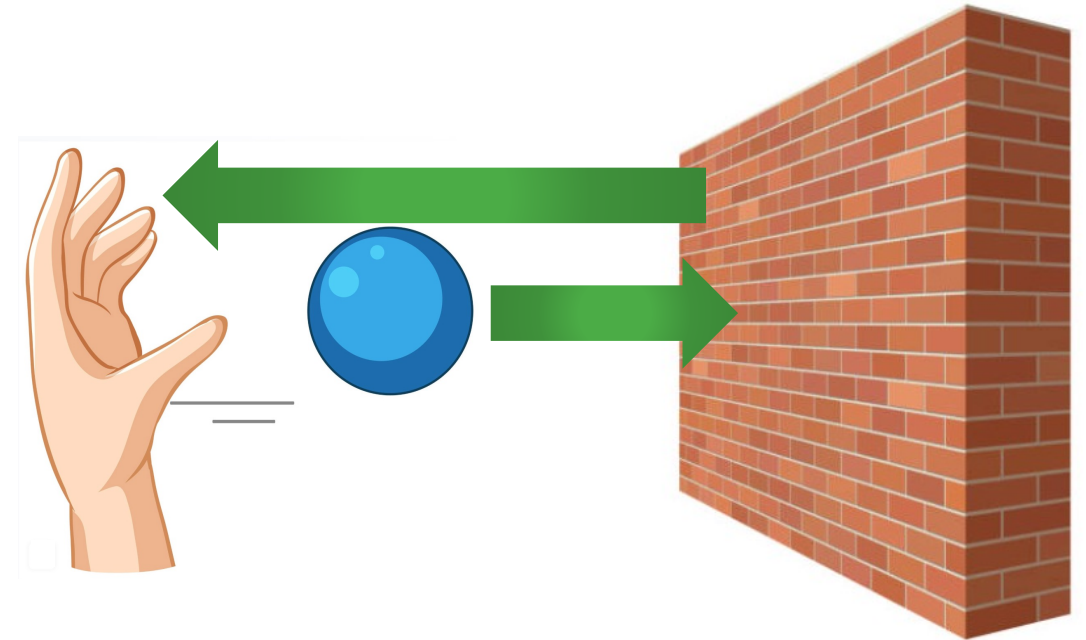
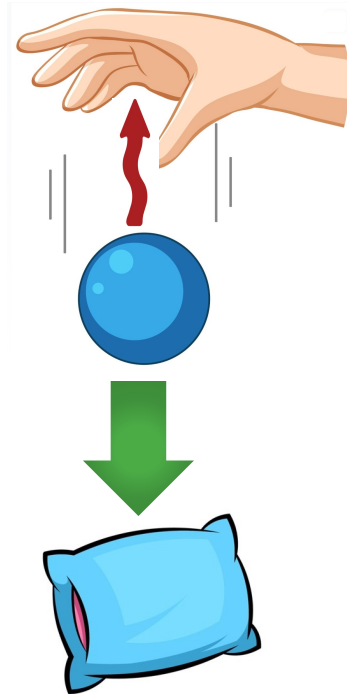
## More Expensive, Longer Turnaround

- Proprietary blood tests
  - FibroSure
  - FibroTest
  - Enhanced Liver Fibrosis (ELF) Score



## Expensive, Special Equipment

- Transient Elastography (FibroScan)
- Shear Wave Elastography (2D-SWE, ARFI)
- MR Elastography







## Elastography False Positives

- Right heart failure/pulmonary hypertension
- Severe hepatic inflammation
- Obesity
- Ascites
- Fluid overload
- Recent fatty meal
- Pregnancy
- Technical
- High IQR



## Non-Invasive Tests for Advanced Fibrosis ( $\geq F3$ )

Test	Sensitivity	Specificity	NPV	PPV	Notes
APRI	~65–70%	~70–75%	~70–80%	~55–65%	Best at ruling out cirrhosis rather than F3
FIB-4	~70–80%	~70–80%	~80–90%	~60–70%	Low cutoff = strong rule-out; high cutoff = moderate rule-in
NAFLD Fibrosis Score	~70%	~75–80%	~80–90%	~60–70%	High rate of indeterminate results
FibroTest (FibroSure)	~75–80%	~75–85%	~80–85%	~70–75%	Better for viral hepatitis than NAFLD
ELF	~80–90%	~80–90%	~85–95%	~70–85%	Validated in NAFLD and viral hepatitis
Transient Elastography (FibroScan)	~85–90%	~85–90%	~85–95%	~75–85%	Accuracy improves for cirrhosis; limited in obesity/ascites
Shear Wave Elastography (ARFI, 2D-SWE)	~80–90%	~80–85%	~85–90%	~70–80%	Comparable to FibroScan; integrated into ultrasound
MR Elastography	~90–95%	~90–95%	~90–98%	~85–95%	Highest accuracy; limited availability, costly



## Role for Liver Biopsy

- Discordant, irreconcilable information
  - Examples:
    - FIB-4 very high (advanced scarring), FibroScan F1, platelets 110K
    - FIB-4 low (low stage), spleen 16 cm, varices, FibroScan F2
    - MR elastography low (low stage), ascites, platelets 85K, large spleen, normal echocardiogram
- Suspect a secondary liver disease
- No NITs are available or possible



## When to Refer to GI/Hepatology

- Assistance in diagnosis or staging needed
- Advanced fibrosis (stage 3 or 4) if:
  - Decompensating event
    - Variceal bleeding
    - Ascites
    - Encephalopathy
    - Jaundice
  - Pre-operative clearance
  - MELD 3.0 score
    - $\geq 12$  with liver symptoms
    - $\geq 15$
- Uncomfortable with management



## When to Refer to GI/Hepatology

- Communicate with your local GI/hepatology and/or transplant program
  - “Rules” are transplant program specific
    - Age
    - Weight
    - Preferred MELD 3.0 score for referral
    - Alcohol
    - Live donor



## Identifying Patients for HCC Screening

- All patients with cirrhosis (F4) except those with poor life expectancy
  - Including those with cured HCV, even if remodeled to a lower stage
- Some patients categorized as F3
  - But have evidence of portal hypertension
    - Splenomegaly
    - Thrombocytopenia
    - Ascites
    - Varices
  - Hepatitis C
  - MASH, especially if diabetic



## Identifying Patients for HCC Screening

- Non-cirrhotic chronic hepatitis B:
  - Asian men  $\geq 40$  years of age
  - Asian women  $\geq 50$  years of age
  - African men and women  $\geq 20$  years of age
  - Family history of HCC
  - High HBV DNA (typically  $\geq 1$  million international units/mL)
  - Co-infection with hepatitis D, HIV, or HCV



## Appropriate Monitoring in Cirrhosis

- Lab testing every 3-6 months
  - Hepatic function panel
  - INR
  - BMP
  - CBC
  - AFP
- Imaging of the abdomen every 6 months
  - Guidelines recommend ultrasound
  - Many hepatologists prefer Doppler US alternating with triphasic MRI
- Assessment for portal hypertension every 1-3 years
  - Non-invasive assessment
    - Fibroscan  $<20$  kPa AND platelets  $\geq 150$  = no clinically significant portal hypertension
  - EGD





## Summary

- Discussed grading and staging of liver disease
- Use NITs to stage your patients
  - Repeat as needed, with clinical or laboratory changes, or every 1-3 years
- Refer when signs or symptoms of liver failure or when help is needed
- Communicate with your local programs
- Monitor your advanced fibrosis (and some chronic hepatitis B) patients for clinically significant portal hypertension, decompensation, and the development of hepatocellular carcinoma

# Thank You

