

Fibrosis/Cirrhosis Evaluation in Hepatitis C

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Why is fibrosis evaluation important in HCV?

- Advanced fibrosis/cirrhosis leads to development of hepatocellular carcinoma
- Delay in fibrosis staging reduce the likelihood of achieving HCV treatment and cure
- AASLD 2023 guidelines for HCV recommended fibrosis evaluation in all patients with HCV infection

Assessment of fibrosis/cirrhosis

- Physical exam
- Laboratory data
- Imaging studies
- Scoring systems using laboratory data
- Direct serum markers of fibrosis
- Imaging-based techniques
- Liver biopsy

Liver biopsy

- Gold standard
- Assess both inflammatory activity and fibrosis stage
- Many disadvantages:
 - Invasive, risk of complications
 - Patient acceptance
 - High cost
 - Availability: need for specialists (radiology, hepatology, pathology)
 - Sampling variability
- For all above reasons, not routinely recommended, UNLESS non-invasive tests indeterminate

Physical exam

- Typical evidence of chronic liver disease
 - Sarcopenia
 - Spider angiomata
 - Palmar erythema
 - Jaundice, scleral icterus
 - Ascites, edema
 - Caput medusae
 - Asterixis, encephalopathy, ankle clonus
- Positive exam findings typically suggest decompensated disease

Laboratory data

- Reduce liver synthetic function:
 - Coagulopathy (increased INR)
 - Low albumin
- Evidence of portal hypertension:
 - Low platelet
 - Sometimes anemia and leukopenia
- Increased RDW
- Liver enzymes could be normal
 - In cirrhosis, ALT can be much lower compared to AST

Scoring systems: FIB-4

- FIB-4 initially developed for HCV/HIV co-infected patients
 - Has been validated in other liver diseases since then
- Formula uses age, AST, ALT, and platelets
- Cutoff of 1.45 can be used to rule out advanced fibrosis
 - Negative predictive value 86%, sensitivity 71%, specificity 73%
- FIB-4 not reliable to evaluate regression of fibrosis following antiviral therapy

Scoring systems: APRI

- AST to platelet ratio index (APRI)
- APRI score >2 rules in cirrhosis
- APRI score <1 rules out cirrhosis
- Readily available lab values, simple and easy to use
- Some studies showed APRI and FIB-4 performed similarly
- Other studies showed APRI had lower performances than FIB-4 and transient elastography
- A cost-effectiveness meta-analysis showed that both APRI and FIB-4 were not as cost effective as transient elastography

Scoring systems: Forns index

- Also initially developed for HCV patients
- Modestly useful in HBV patients
- Uses age, GGT, cholesterol, and platelet count
- Not widely used

Scoring systems: many others

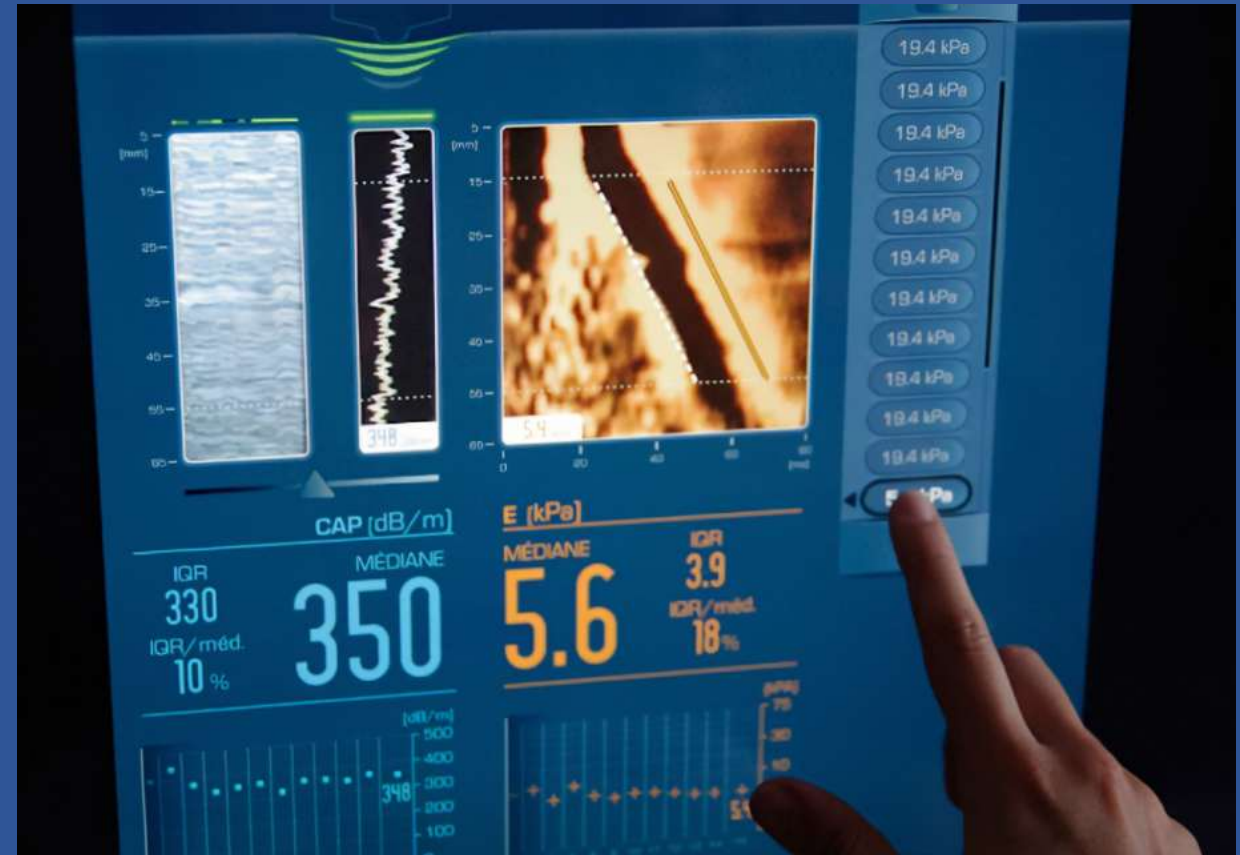
- AST/ALT ratio
- AST-Platelet index (API)
- AST-platelet-GGT-AFP index (APGA)
- Goteborg University Cirrhosis Index (GUCI)
- Cirrhosis Discriminate Score (CDS)
- The Lok Score

Direct serum markers of fibrosis

- Fibrometer: age, platelets, hyaluronic acid, AST, prothrombin index, urea, and α 2-macroglobulin
- Hepascore: age, gender, hyaluronic acid, bilirubin, gamma-glutamyl-transpeptidase (γ GT), and α 2-macroglobulin
- Enhanced Liver Fibrosis (ELF) index: hyaluronic acid, TIMP-1 and PIIINP
- Fibrotest/Fibrosure: α -2-macroglobulin, apolipoprotein A1, haptoglobin, L-glutamyl transpeptidase, and bilirubin
- Limitations: cost and availability

Transient elastography - Fibroscan

- Stiffness (given in kilo Pascals)
 - Stiffness predicts degree of fibrosis
- CAP – Controlled Attenuation Parameter
 - Predicts degree of steatosis



Transient elastography - Fibroscan

Fibrosis Stage	Sensitivity	Specificity	AUROC
F2	0.81	0.82	0.88
F3	0.82	0.87	0.91
F4	0.86	0.87	0.93

AUROC: area under receiver operator curve

- Limitations:
 - Availability (dedicated machine, operator training)
 - Cost
- Many factors that may produce inaccurate results:
 - Obesity
 - NASH
 - Alcohol use
 - Nonfasting state (stomach/intestinal contents can affect reading)
 - Abnormal liver tests (ALT>100, elevated alkaline phosphatase)
 - Iron overload

Fibroscan results may be falsely negative immediately after HCV treatment

Acoustic radiation force impulse elastography

- ARFI elastography – uses radiation-forced impulses to measure liver stiffness while using B-mode ultrasonography
- Comparable to transient elastography
- May have a tendency to over-estimate fibrosis in patients with F0-2, and patients with high BMI

Shear wave elastography (SWE)

- One study showed SWE had a highest AUROC when compared to scoring systems and to transient elastography across all fibrosis stages
- Had higher successful acquisition rate compared to transient elastography
- Like other imaging techniques, limitations include availability, expertise, and cost

MR Elastography (MRE)

- Much higher technical success rate compared to transient elastography
- Also much higher rate of reproducibility
- Depending on the cutoff values used, MRE can achieve AUROC up to 0.99
- Again, cost and availability

Summary

- Many non-invasive techniques to assess fibrosis/cirrhosis
 - This makes the role of liver biopsy less and less prominent
- Many of these tests have been validated, so it comes down to what's available in deciding which test to use
- At this time, the most diagnostically accurate strategy is using a combination of these tests to evaluate for fibrosis/cirrhosis
 - Use what's available to your patients, and know that all of these tests have limitations

Mahalo!

- References:

- Debika Bhattacharya, Andrew Aronsohn, Jennifer Price, Vincent Lo Re, the American Association for the Study of Liver Diseases–Infectious Diseases Society of America HCV Guidance Panel , Hepatitis C Guidance 2023 Update: American Association for the Study of Liver Diseases– Infectious Diseases Society of America Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection, *Clinical Infectious Diseases*, 2023
- Jones AT, Moreno-Walton L, Sossamon SD, Tahmeena F, Tran T, Briones C, Stevens R, Isaacson K, He H, Rhodes S, Percak J, Kissinger PJ. Delays in fibrosis staging reduce the likelihood of achieving hepatitis C treatment and cure. *Infect Dis (Lond)*. 2023 May;55(5):309-315.
- Parikh P, Ryan JD, Tsochatzis EA. Fibrosis assessment in patients with chronic hepatitis B virus (HBV) infection. *Annals of Translational Medicine* 2017; 5(3): 40.
- Ozyalvacli G, Kucukbayrak A, Kurt M, et al. Non-invasive fibrosis tests are correlated with necroinflammatory activity of liver in patients with chronic hepatitis B. *Clin Ter* 2014;165:e199-204.
- Lee JM, Seo YS, Kim TH, et al. The LAW index as an accurate indicator of the initiation of antiviral treatment in patients with chronic hepatitis B. *J Gastroenterol Hepatol* 2017;32:208-14.
- Liang XE, Zhong C, Huang L, et al. Stepwise Application of Transient Elastography and Routine Biomarkers Optimizes Hepatitis B Cirrhosis Detection. *J Gastroenterol Hepatol* 2016. [Epub ahead of print].