

# Fibrosis/Cirrhosis Evaluation in Hepatitis B

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# 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, including HBV
- 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

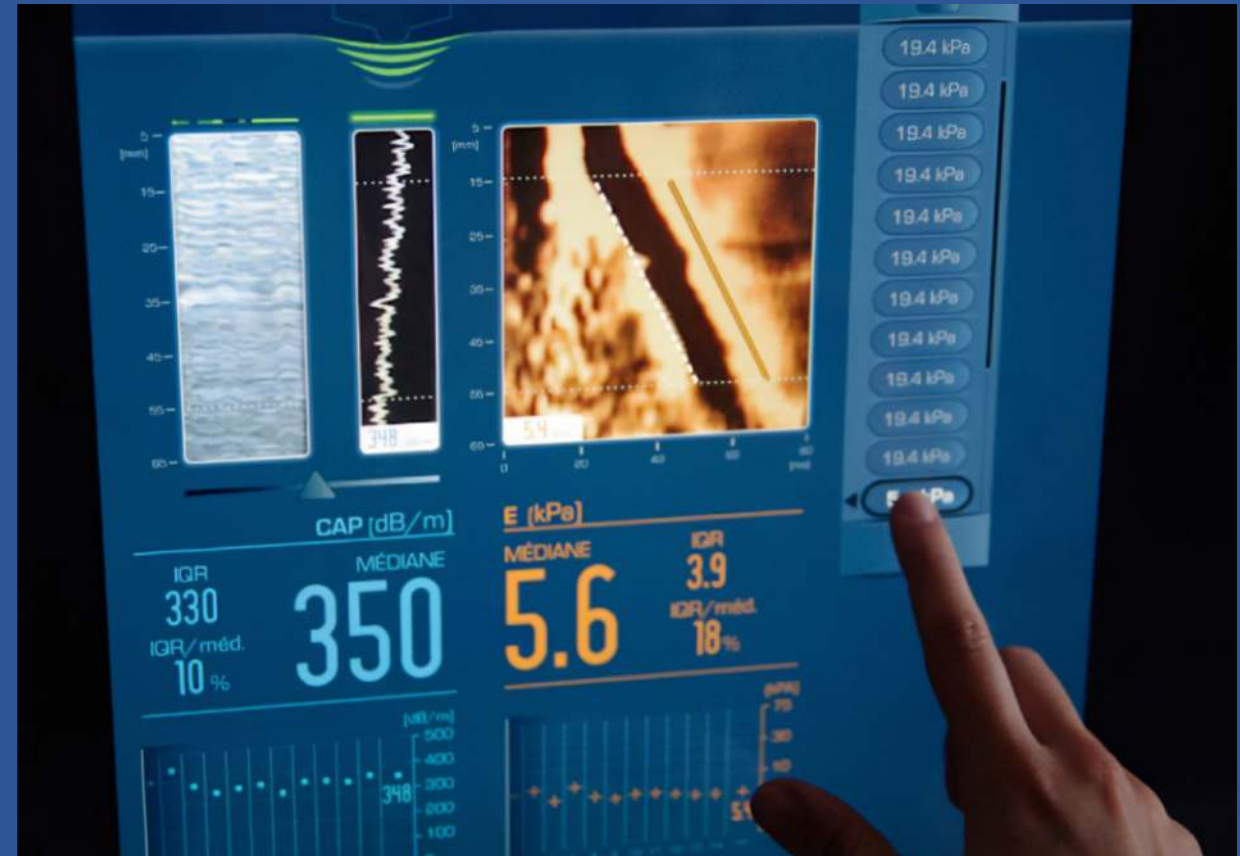
- AST/ALT ratio
- AST-Platelet index (API)
- AST-platelet-GGT-AFP index (APGA)
- Goteborg University Cirrhosis Index (GUCI)
- Cirrhosis Discriminate Score (CDS)
- The Lok Score

# Direct serum markers of fibrosis

- Fibrometer: age, platelets, hyaluronic acid, AST, prothrombin index, urea, and  $\alpha$ 2-macroglobulin
- Hepascore: age, gender, hyaluronic acid, bilirubin, gamma-glutamyl-transpeptidase ( $\gamma$ GT), and  $\alpha$ 2-macroglobulin
- Enhanced Liver Fibrosis (ELF) index: hyaluronic acid, TIMP-1 and PIIINP
- Fibrotest/Fibrosure:  $\alpha$ -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

# 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:

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