

Fibrosis/Cirrhosis Evaluation in Hepatitis C

Chuong Tran, MD

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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 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

- Initially developed for HCV patients
- Uses age, GGT, cholesterol, and platelet count
- Not widely used

Scoring systems: many others

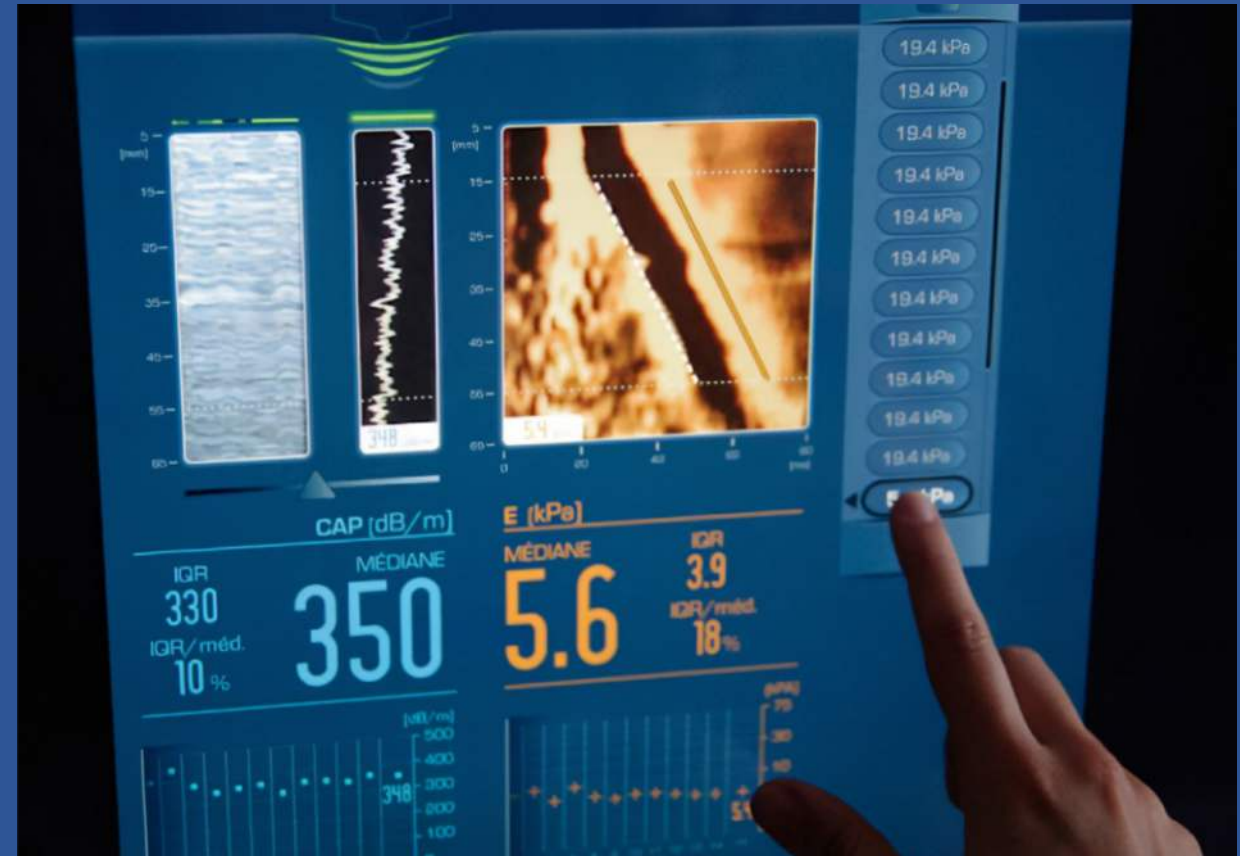
- AST/ALT ratio
- AST-Platelet index (API)
- AST-platelet-GGT-AFP index (APGA)
- Goteborg University Cirrhosis Index (GUCl)
- Cirrhosis Discriminate Score (CDS)
- The Lok Score

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

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

What happens after HCV treatment?

- HCV cure with DAA has been shown to reduce degree of fibrosis
- It seems controversial whether HCV cure also reduce steatosis
- Many recent studies explored the effectiveness of using different modes of fibrosis evaluation (serum markers, scoring systems, imaging)
- Currently there is no consensus guideline on this topic
- If patient had advanced fibrosis (F3) or cirrhosis prior to HCV treatment, they should continue to be followed by hepatology
- If patient had no significant fibrosis prior to HCV treatment, continue follow up is controversial

Mahalo!

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