Noninvasive Diagnosis and Staging of Liver Disease

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Outline

• Brief overview of the anatomy of liver
• Liver-related lab tests
• Chronic liver disease progression
• Estimation of liver fibrosis
• Non-invasive means of liver fibrosis evaluation
• Summary
Liver

Liver-related Labs

- Aspartate Aminotransferase (AST)
- Alanine Aminotransferase (ALT)
- Alkaline Phosphatase
- Gamma Glutamyl Transpeptidase (GGT)
- Bilirubin
- Albumin
- Prothrombin time (PT/INR)
- Platelet count
Causes of Chronic Liver Disease

- Chronic Viral Hepatitis (B,C)
- Alcoholic Liver Disease
- Nonalcoholic Fatty Liver Disease
- Autoimmune Liver Diseases (Autoimmune Hepatitis, Primary Biliary Cholangitis, Primary Sclerosing Cholangitis)
- Inherited Metabolic Defects (Hemochromatosis, Wilson Disease, Alpha-1-antitrypsin deficiency, etc.)
- Other
Progression of Chronic Liver Disease

Staging of Liver Fibrosis

Faria S, Ganesan K, et al. MR imaging of liver fibrosis: current state of art; 2009; Oct; 29(6); 1615-35
Liver Biopsy

- Percutaneous
- Transjugular
- Laparoscopic
- EUS-guided

http://www.mayoclinic.org/tests-procedures/liver-biopsy/multimedia/liver-biopsy/img-20007146
Liver Biopsy

**Benefits**
- Diagnosis
- Staging

**Risks**
- Pain
- Bleeding
- Infection, perforation, etc.

**Pitfalls:**
1. Sampling error
2. Subjective bias
3. Impracticability in obtaining serial biopsies
Noninvasive Assessment of Liver Fibrosis

Serologic tools:
- AST/ALT ratio
- AST to Platelet ratio index (APRI)
- FIB-4
- Forns index
- FibroSure
- FibroScore
- FibroSpect
- FibroMeter
- ELF score

Imaging tools:
- Traditional modalities (Ultrasound, CT, MRI)
- Newer techniques (Transient Elastography, Acoustic Radiation Force Impulse Imaging & Magnetic Resonance Elastography)
APRI

\[ \text{APRI} = \frac{\text{AST Level}}{\text{Platelet Count} \times 10^9/L} \times 100 \]

AST (Upper Limit of Normal)

Higher APRI score predictive of advanced fibrosis
APRI<1 = no/mild fibrosis; APRI>2=cirrhosis
Serologic Tools for Fibrosis Assessment

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

APRI<1 = no/mild fibrosis; APRI>2=cirrhosis


\[
\text{FibroIndex} = 1.738 - 0.064 \times \text{platelet count (10}^3/\text{mm}^3)
\]
\[
+ 0.05 \times \text{AST (IU/L)}
\]
\[
+ 0.463 \times \text{gamma globulin (g/dL)}
\]

Koda M et al. Fibroindex, a practical index for predicting significant fibrosis in pts with chronic hep C. *Hepatology*; 2007; 45; 297-306
Cross-sectional Imaging

Ultrasound: heterogeneous texture

CT: nodular liver contour

Cross-sectional Imaging

CT: Caudate lobe hypertrophy

MRI: Dilated portal vein

Cross-sectional Imaging

Pitfalls:

• Lack of objectivity
• Inability to diagnose lesser degrees of fibrosis
• Even cirrhosis can be missed when gross changes in liver are not evident on imaging
• Subtle signs of cirrhosis have low inter-reader agreement
Transient Elastography

Results in KPa
Range: 2.5-75 KPa

Transient Elastography

Transient Elastography

Pitfalls:

• Failure to obtain a valid result (obesity, narrow intercostal spaces, etc.)

• Can be spuriously high during a hepatitis flare

• On the contrary, Transient Elastography can also help diagnose cirrhosis in patients under-staged by biopsy

Magnetic Resonance Elastography (MRE)

- 3-dimensional imaging
- Potential to assess the stiffness of entire liver
- High technical success in obese & NASH patients as well
- Results range from 0.5 to 10 KPa

- Not available widely
- Expensive
- Requires trained radiologists
Magnetic Resonance Elastography (MRE)

MRE: focal increased stiffness

MRI T2W: corresponding confluent fibrosis

Summary

• Chronic liver disease from varied causes can lead to liver fibrosis
• Liver biopsy is considered the gold standard for fibrosis assessment
• Noninvasive tools have been proven to be reliable in differentiating between advanced and non-advanced fibrosis
• APRI is a simple index based on routine lab tests that can accurately diagnose cirrhosis and advanced fibrosis
• Elastography of the liver provides objective estimates of liver fibrosis using either ultrasound or MR techniques