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Gastroenterology & Hepatology
Advanced Practice Providers

2020 Third Annual National Conference

November 19-21, 2020

Red Rock Hotel – Las Vegas, NV

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Use of Noninvasive Markers for Fibrosis and Steatohepatitis

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Disclosures

Lisa Richards, FNP-BC

Speakers Bureau: Intercept Pharmaceutical, Clinical Area- NAFLD.

Ngoc Duong, PA-C

No financial relationships to disclose.

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Use of Noninvasive Markers for Fibrosis and Steatohepatitis

Ngoc Duong, MPAS, PA-C
Michael E. Debakey Veteran Affairs

Non-Invasive Markers of Fibrosis

- Serum Calculators
- Radiologic Tests

To Detect:

  - Significant Fibrosis: F2-F4
  - Advanced Fibrosis: F3-F4
  - Cirrhosis: F4

Serum Calculators for Fibrosis

Test Name	Components	Interpretation
FIB4	Age, AST, ALT, Platelets	• Score <1.45: predictor of **absence** of significant fibrosis • Score >3.25: predictor of **presence** of significant fibrosis
APRI	AST, ALT, Platelets	<.5 or> 1.5**.** If your **score** is less than or equal to 0.5, your liver is either completely free of fibrosis or has a tiny bit of scarring. If you have an **APRI score** of 1.5 or greater, your liver has scarring and likely some cirrhosis.
NAFLD Fibrosis score	Age, BMI, AST, ALT, Platelets, Albumin, Diabetes	• Score < -1.455: predictor of **absence** of significant fibrosis • Score >0.675: predictor of **presence** of significant fibrosis
BARD	BMI, AST, ALT, Diabetes	• >2 – predictive of significant fibrosis

FIB-4

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

<1.45 excludes severe fibrosis (F3-F4) with high negative predictive value

>3.25 has high predictive value for significant fibrosis (F3-F4)

Vallet-Pichard A, et al. *Hepatology*. 2007;46:32-6.

Aspartate Aminotransferase-to-Platelet-Ratio Index

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

- Estimate for predicting severe fibrosis or cirrhosis
- Most laboratories use an AST upper limit of 40 IU/mL
- APRI<0.5 will rule out cirrhosis
- All non-invasive tests do not work as well with intermediate levels of fibrosis

Ding D, et al. *Int J Clin Exp Med*. 2015;8:20876-82.

NAFLD Fibrosis Score

NAFLD Score = -1.675 + 0.037 × Age (years) + 0.094 × BMI (kg/m2) + 1.13 × IFG/diabetes (yes = 1, no = 0) + 0.99 × AST/ALT ratio – 0.013 × Platelet (×109/L) – 0.66 × Albumin (g/dL)

< -1.455 lower threshold, absence significant fibrosis (F0-F2 fibrosis)

> 0.675, upper threshold for advanced fibrosis (F3-F4 fibrosis)

Angulo. *Hepatology.* 2007.

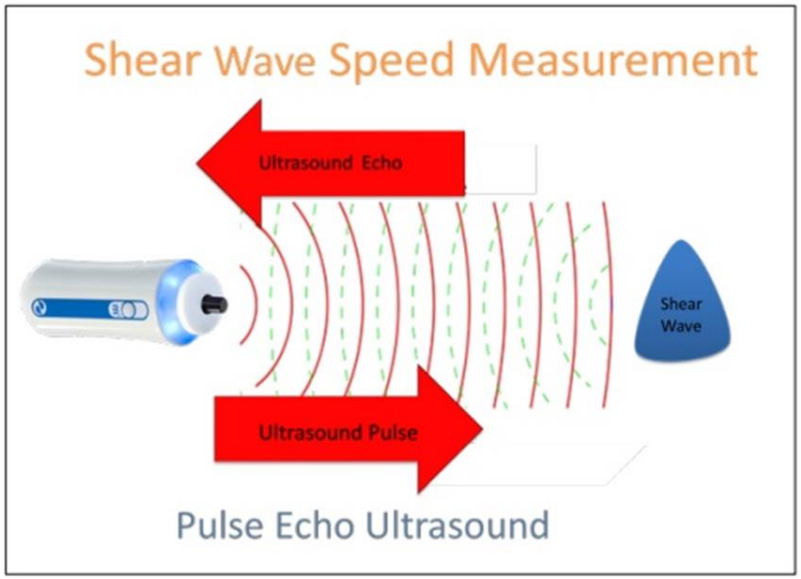
Fibrosis vs. Steatosis

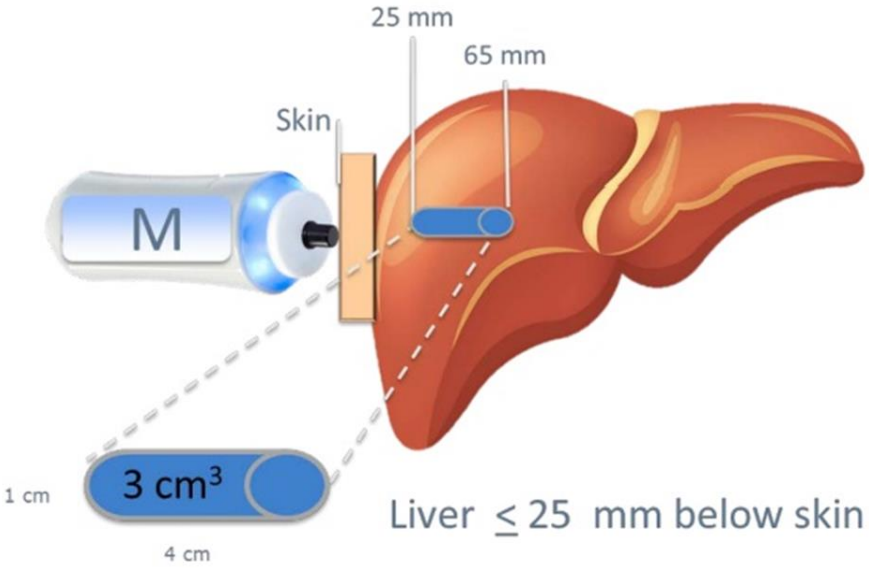
- Measurement of Fibrosis
  - Vibration controlled Transient Elastography (VTCE) –
    - Fibroscan
    - MR Elastography
- Measurement of Steatosis
  - Controlled Attenuation Parameter (CAP)
  - Proton Density Fat Fraction (PDFF)

Noninvasive Biomarkers

- Vibration Controlled Transient Elastography
- Magnetic Resonance Elastography

Fibroscan


Shear Wave Speed Measurement
Ultrasound Echo
Shear Wave
Ultrasound Pulse
Pulse Echo Ultrasound


25 mm
65 mm
Skin
M
1 cm
3 cm3
4 cm
Liver ≤ 25 mm below skin

Sample Report

Code 458887470

Birth date 1949-12-09

Gender Male

Admitting diagnosis ABNORMAL LFT

Referring physician DR.NATARAJAN

EXAMINATION

Date and time 2018-01-30 22:15:24

Operator NAOMI

Device Fibroscan 502TOUCH F60484

Probe XL 9 90488

Examination XL (Liver)

Number of valid measurements 15

Number of invalid measurements 0

Success rate 100%

V (m/s)	
Median	1,55
IQR*	0,13

E (kPa)	
Median	7,2
IQR*	1,3
IQR*/med	18 %

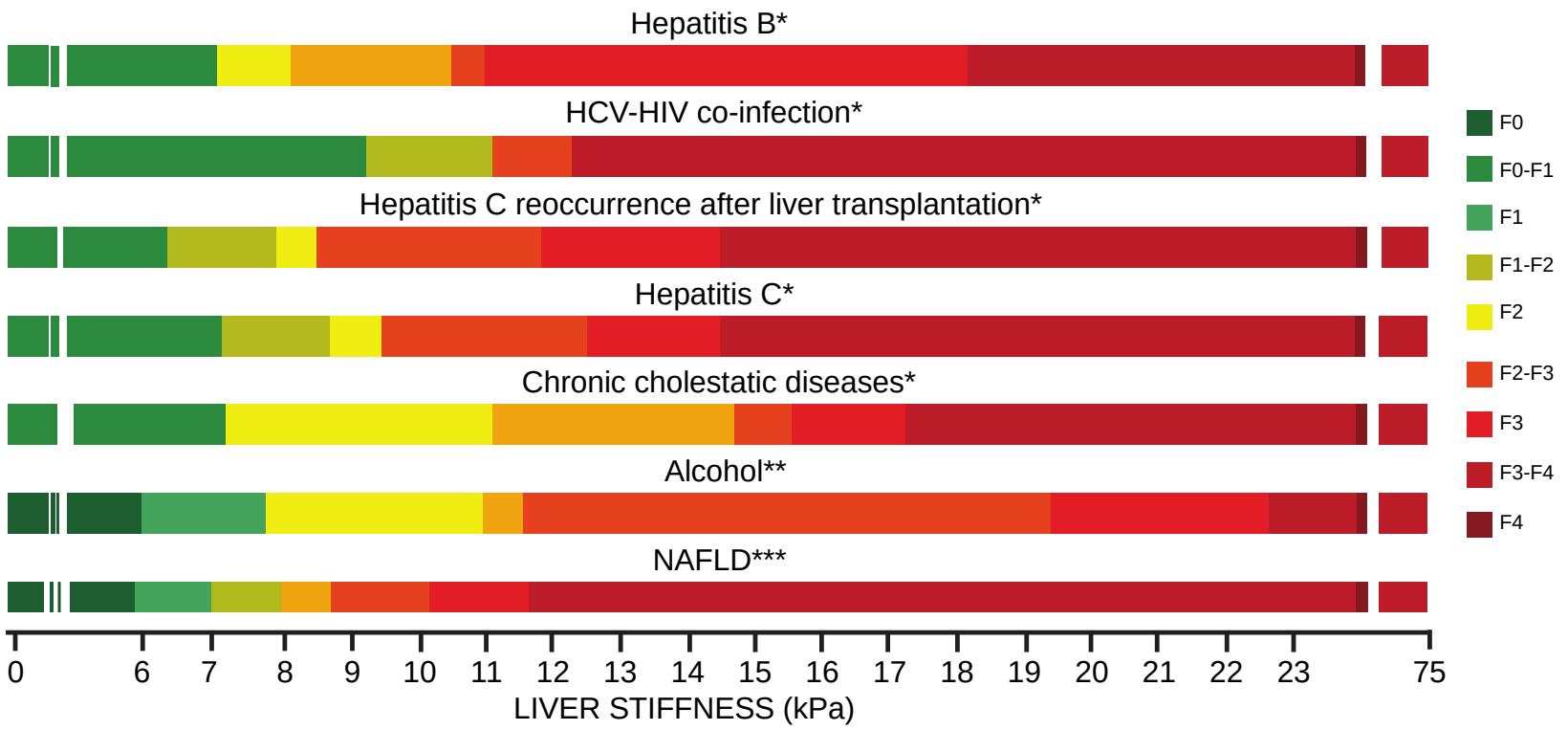
*IQR: interquartile range

Equivalent Liver stiffness is calculated using the formula $E = 3\rho Vs^2$ and assumes that liver tissue is isotropic, linear and purely elastic with a density (ρ) of 1000 kg/m3.

The values for shear wave speed and Young's modulus are relative indexes intended only for the purpose of comparison with other measurements performed using Fibroscan devices. Absolute values for these measurements may vary among measurement devices from different manufacturers.

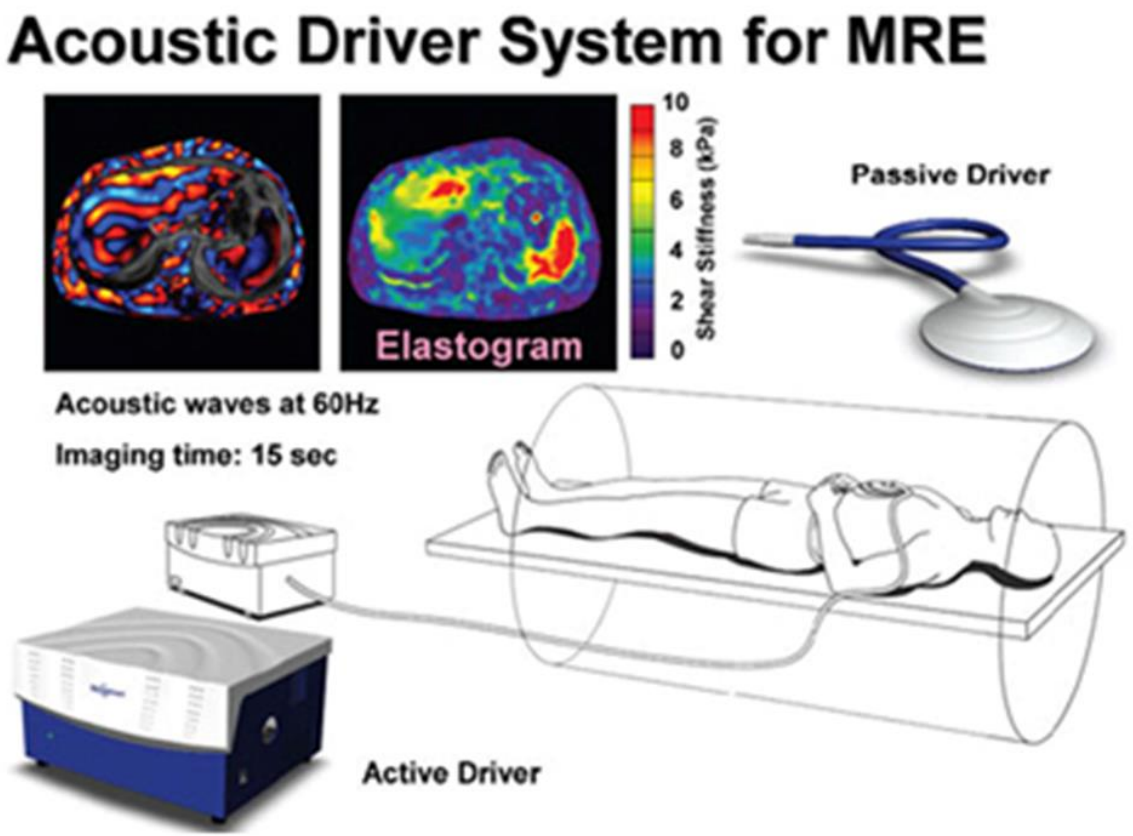
SWS median is defined as the value which converts to the stiffness median.

Interpretation



J Hepatol. 2009; 49:1062-68; *Aliment Pharmcol Ther*. 2008; 28:1188-98; *Hepatology*. 2010; 5:454-62.

MR Elastography



Factors Affecting Liver Stiffness

- Meals
- Subcutaneous Adiposity
- Hepatic Congestion/Ascites
- Inflammation
- Infiltrative Diseases
  - Amyloid
  - Malignancy

Performance

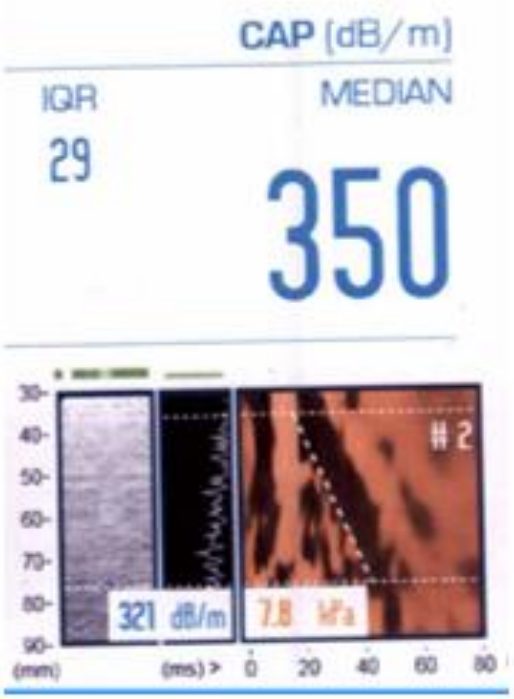
	Sensitivity	Specificity
Fibroscan	0.87	0.79
MRE	0.84	0.9

“In adults with NAFLD and a higher risk of cirrhosis, the AGA suggests using MRE, rather than VCTE, for detection of cirrhosis [High-risk populations are advanced age, obesity, particularly central adiposity, DM, ALT>2x ULN, estimated cirrhosis prevalence of 30%]

In adults with NAFLD and a lower risk of cirrhosis, the AGA makes no recommendation regarding the role of MRE or VCTE for detection of cirrhosis (usually primary care setting, prevalence cirrhosis <5%)”

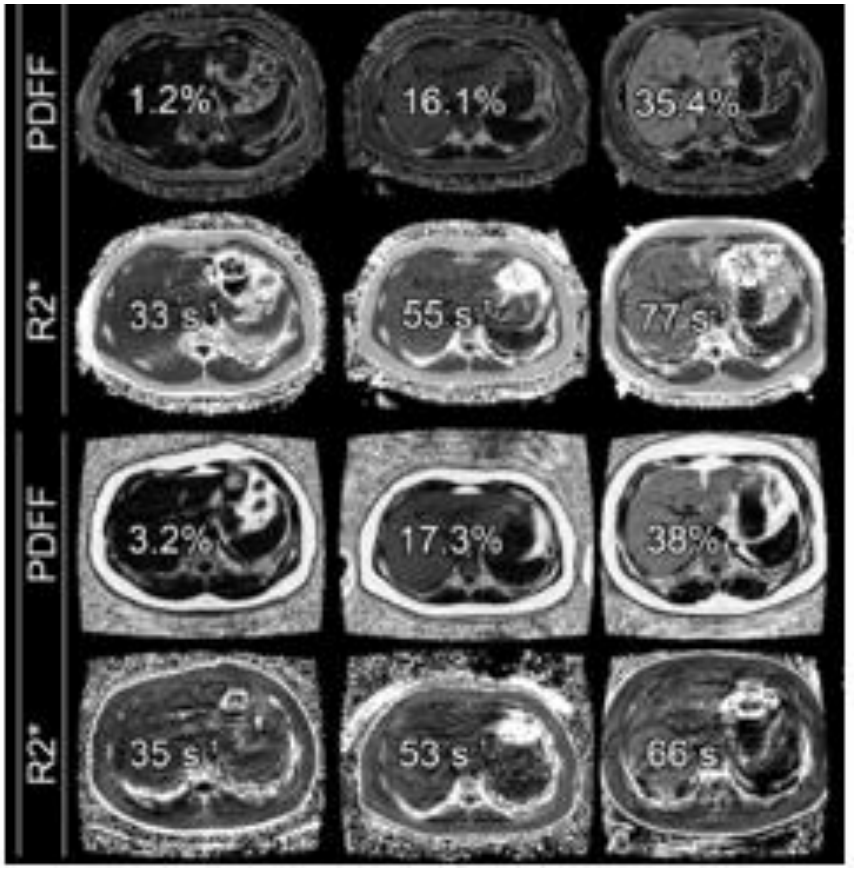
Controlled Attenuation Parameter (CAP)

Measures attenuation, or reduction in amplitude, of ultrasound waves travelling through a liver



Proton Density Fat Fraction (PDFF)

- Fraction of MRI-visible protons bound to fat, divided by all protons bound to fat and water in the liver
- Global assessment of steatosis



Take Home Points

- Non invasive measurements of fibrosis include serum calculators, Fibroscan, and MRI Elastography
- Non invasive measurements of steatosis include controlled attenuation parameter (CAP) and MRI-Proton Density Fat Fraction (PDFF)

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Thank You!

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Use of Noninvasive Markers for Fibrosis and Steatohepatitis

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UC San Diego Health System

Case Presentation

- 58 yo Hispanic male referred by PCP for evaluation of elevated liver enzymes and fatty liver seen on abdominal ultrasound
- PMH: Obese (BMI 33), HTN, T2DM and Dyslipidemia
- Medications: amlodipine, atorvastatin and metformin
- Social: exercises 2-3 times weekly at the gym. Drinks alcohol socially: AUDIT-C:3

Physical Exam

- Vital Signs Stable
- BMI 33
- Increased central obesity
- No focal liver signs
- Otherwise unremarkable

Rule Out Other Etiologies of Elevated Liver Enzymes

- Infectious
- Metabolic
- Autoimmune
- Biliary
- Drug/Toxin
- Vascular
- Idiopathic

Lab Results

- Results
  - AST: 55. ALT 80. Albumin: 4.1. Platelets: 190,000, INR 1.0. HCV & HBV: negative. ASMA, ANA normal. Remainder of labs unremarkable. Imaging: abdominal u/s: liver 18 cm with increased echogenicity
- Differential diagnosis:
  - Alcohol liver disease, NAFLD, Drug induced HS
- Is any further workup necessary?

Noninvasive Biomarkers

- Point of Care
  - VCTE
    - CAP: mostly utilized in research
- Clinical Calculators
  - FIB-4
  - APRI
  - NFS
- Imaging
  - MRI-PDFF
  - MRE

Loomba, R. et al. *Gastroenterology*. 2020.

Clinical Question

- Is there hepatic steatosis or liver fibrosis
- Significance of fibrosis
  - All cause mortality
  - Liver related mortality

Dulai et al. *Hepatology*. 2017

Clinical Case: Results

- Fib-4: 1.88
- APRI: 0.72
- VCTE: 7.3 kPa
- MRI-PDFF: 12 %
- MRE: 3.4 kPa

Clinical Diagnosis

- NAFLD:
  - Other etiologies ruled out
  - PDFF 12% consistent with hepatic steatosis
  - Noninvasive biomarkers suggestive of F2

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Thank You

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