

# NON-INVASIVE TESTING FOR FIBROSIS AND SEROLOGICAL MARKERS IN LIVER DISEASES

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# NON INVASIVE TESTS/NON INVASIVE LIVER DISEASE ASSESSMENT TESTS

- NILDA
  - DIAGNOSTIC TESTS – NON INVASIVE
    - TO ASSESS FOR PRESENCE /RISK OF CHRONIC LIVER DISEASE
    - SERUM BASED MARKERS
    - IMAGING MODALITIES

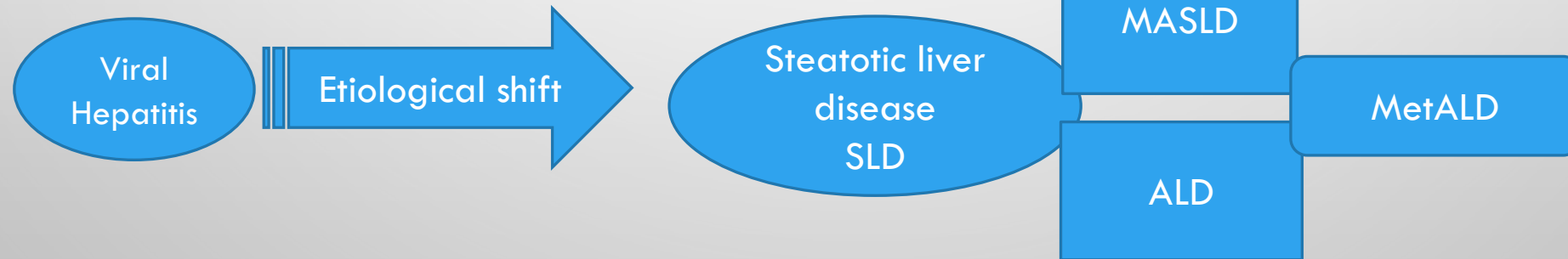
WHY NITS???

- CHRONIC LIVER DISEASE IS A PUBLIC HEALTH PROBLEM - NEEDING URGENT  
ACTIONS AND LARGE SCALE SCREENING

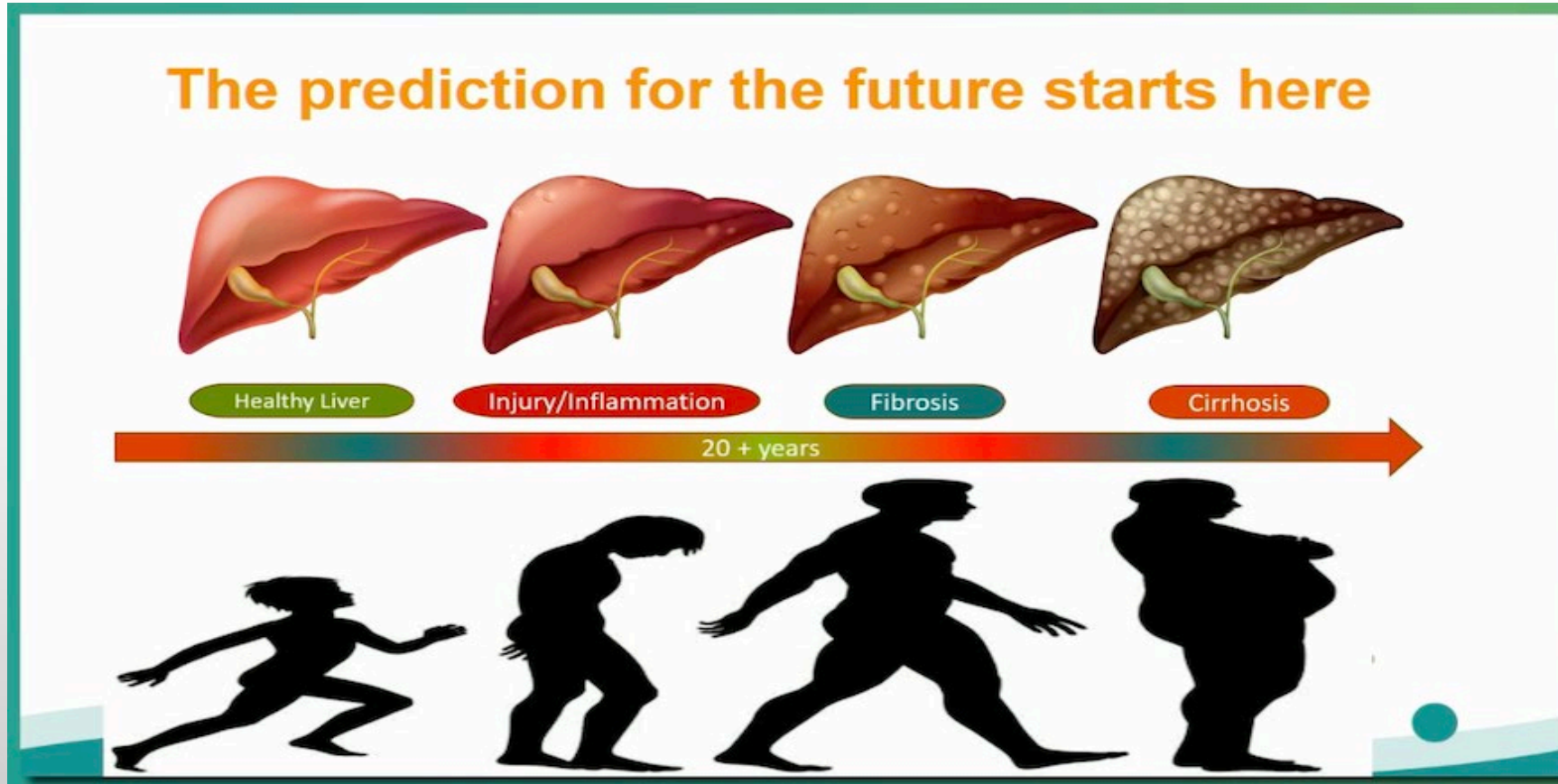
# GLOBAL BURDEN OF CHRONIC LIVER DISEASE FAST FACTS

- TWO MILLION DEATHS WORLDWIDE ANNUALLY (4% OF ALL DEATHS)
- CIRRHOSIS- 11TH LEADING CAUSE OF DEATH
- HCC- 4<sup>TH</sup> LEADING CAUSE OF CANCER RELATED DEATHS

- quarter of the global adult population
- 2nd leading cause of ESLD and liver transplant in North America and Europe



# WHY NITS?



Naudia L. Jonassaint

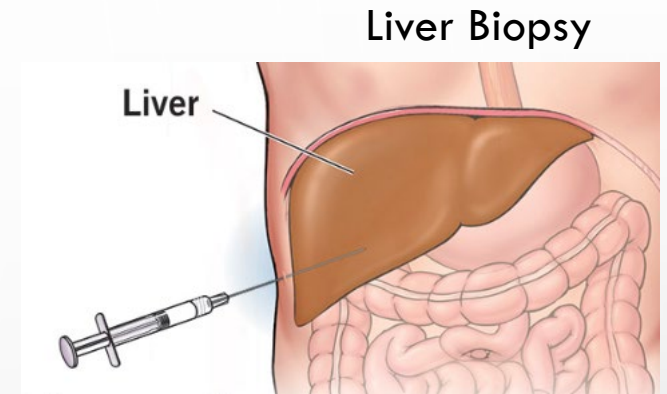
AASLD Liver Meeting 2023

[Epidemiology, disparities and social determinants of cirrhosis](#)

# NEED FOR LARGE SCALE SCREENING

## NON INVASIVE LIVER TESTS

- AFFORDABLE/ACCESSIBLE/AVAILABLE
- EASY TO PERFORM/MEASURE
- REPRODUCIBLE
- COST EFFECTIVE
- REPEATABLE
  
- EMERGING ROLES OF NITS
  - EARLY IDENTIFICATION- PRIMARY RISK STRATIFICATION
  - RISK ASSESSMENT OF SEC COMPLICATIONS /PREDICTING OUTCOMES
  - MONITORING RESPONSE



## Challenges:



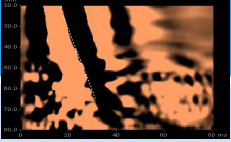
Access / availability

Affordability

Invasive nature

Not repeatable in clinical settings

# COMMONLY USED NITS

Serum based markers	Routine Imaging Modalities	Liver Stiffness Measurement
 <p>Simple</p> <ul style="list-style-type: none"> <li>- <b>FIB-4</b></li> <li>- AST to PLT Ratio Index (APRI)</li> <li>- NFS</li> </ul> <p>Commercial Lab tests</p> <ul style="list-style-type: none"> <li>- <b>ELF</b></li> <li>- <i>FibroSure</i></li> <li>- <i>FibroSpect II</i></li> </ul>	 <ul style="list-style-type: none"> <li>- US</li> <li>- CT scan</li> <li>- MRI</li> </ul>	 <ul style="list-style-type: none"> <li>- <b>Vibration Controlled Transient Elastography (VCTE)</b></li> <li>- <b>MR Elastography</b></li> <li>- Shear wave Elastography SWE</li> <li>- Acoustic Radiofrequency Impulse (ARFI)</li> </ul>
<p style="text-align: center;"><i>Composite tests</i></p> <p><i>FAST (FibroScan- AST)</i>  <i>MAST (MRI- AST)</i>  <i>MEFIB (MRE + FIB4)</i>  <i>AGILE 3+ and Agile 4+</i></p>		

# PRIMARY RISK STRATIFICATION

## FIB-4

- Most Validated serum based marker.
- HCV, HBV, MASLD, AUD
- Recommended by most societies (AASLD, EASL, AGA, AACE) as the first line test
- No additional cost

Low Risk	High Risk (Need Referral)	Cirrhosis
<1.3	≥ 2.67	≥ 3.48

- Limitations
  - Indeterminant zone
  - Age
  - Inflammation

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}} = 2.73$$

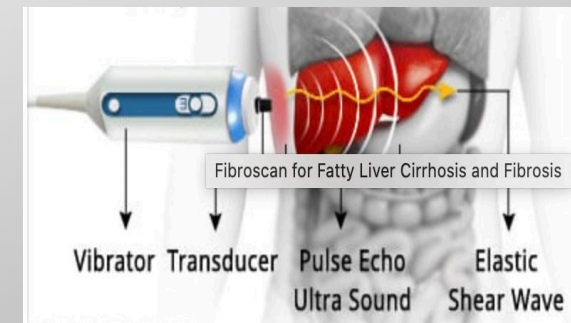
The calculation uses the following values: Age (years) = 46, AST Level (U/L) = 55, Platelet Count (10<sup>9</sup>/L) = 100, and ALT (U/L) = 86. The result 2.73 is highlighted in a yellow circle.



# VIBRATION CONTROLLED TRANSIENT ELASTOGRAPHY - VCTE

- Second line test
- US waves through the liver to measure liver stiffness (KPa)  
Higher speed → Higher stiffness
- Robust POC test (can be performed at bedside, OP setting)
- PATIENT FRIENDLY
- IMMEDIATE RESULTS
- COST
- ROLE IN PREDICTING OUTCOME AND LIVER RELATED EVENTS  
(DECOMPENSATION, HCC, DEATH)

THE TOTAL VOL OF TISSUE THAT IS EVALUATED THROUGH THIS TECHNIQUE IS  $3\text{CM}^3$  -- AT LEAST 100 TIMES LARGER THAN A STANDARD LIVER BIOPSY SPECIMEN



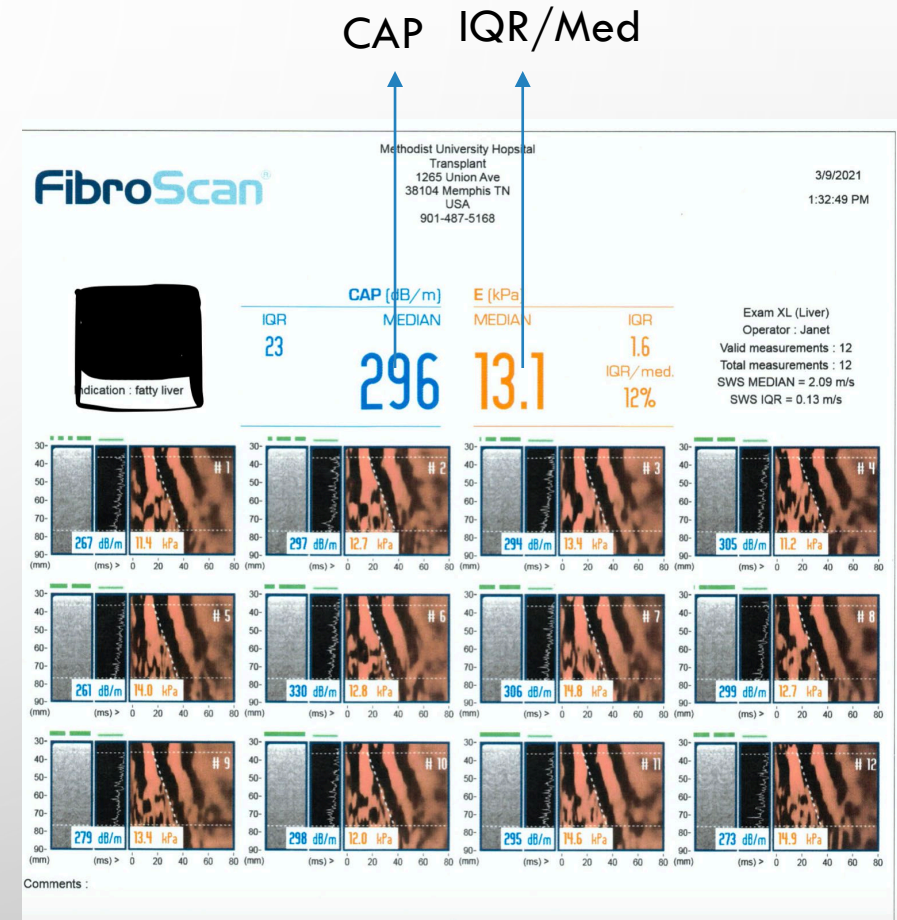


- LSM values range from 1.5 to 75 kPa; lower values indicate a more elastic liver

Liver stiffness	Interpretation	CAP	Steatosis
<8 KPa	Advance Fibrosis less likely	248 dB/m	S1 (11%-33%)
8-12 KPa	Intermediate (May be associated with Fibrotic NASH)	268 dB/m	S2 (34% - 66%)
>12KPa	Likely advance Fibrosis	280 dB/m	S3 ( $\geq$ 67%)
> 20 Kpa	Cirrhosis		

Consideration:

- Satiety
- Presence of inflammation
- Venous congestion (CHF)
- Ascites
- Body habitus (XL probe for BMI >30)

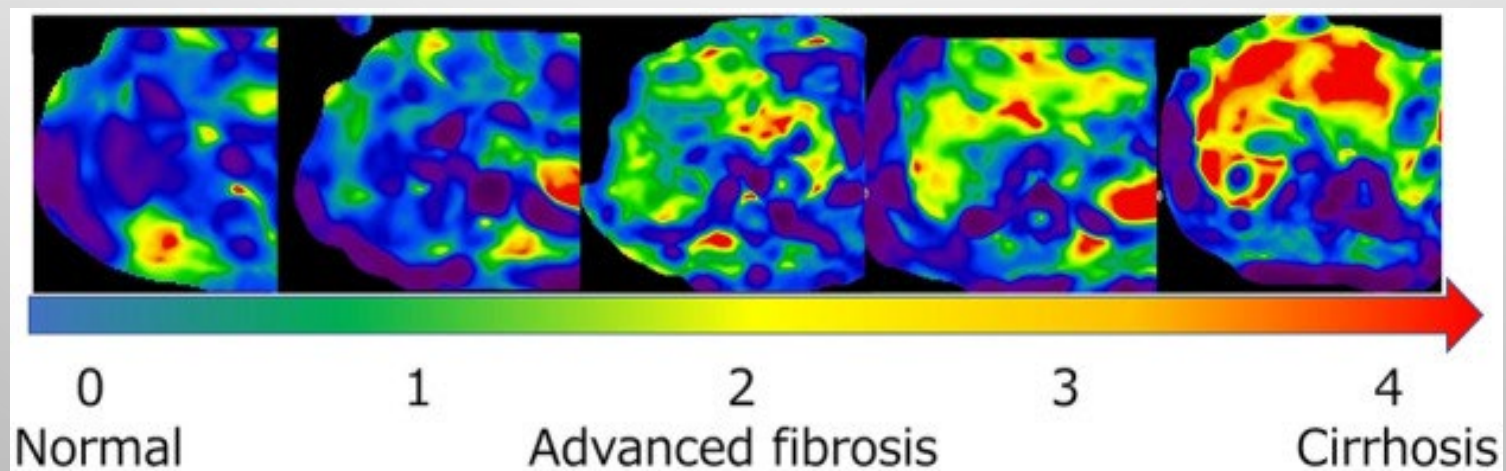


10 measurements with IQR/med <30%

# MR ELASTOGRAPHY

- HIGHEST ACCURACY
- USEFUL IN INDETERMINANT NIT RESULTS
- MEASUREMENT OF STEATOSIS (PDFF)

AF less likely	AF Likely	Cirrhosis
$< 2.55 \text{Kpa}$	$\geq 3.63$	$\geq 5 \text{Kpa}$



## RISK ASSESSMENT FOR SECONDARY COMPLICATIONS AND PREDICTING OUTCOMES

- Patients with Advance chronic Liver disease
  - cACLD
  - Cirrhosis and CSPH (decompensation )

Non-invasive staging of chronic liver disease	No cACLD	Possible cACLD	Highly suggestive of cACLD	cACLD	
Liver stiffness (kPa)	<10	10-15	15-20	20-25	>25
Platelet count (K/mm <sup>3</sup> )	NR	NR	If <110 = CSPH	If <150 = CSPH	CSPH**

Risk of decompensation

Baveno VI Criteria:

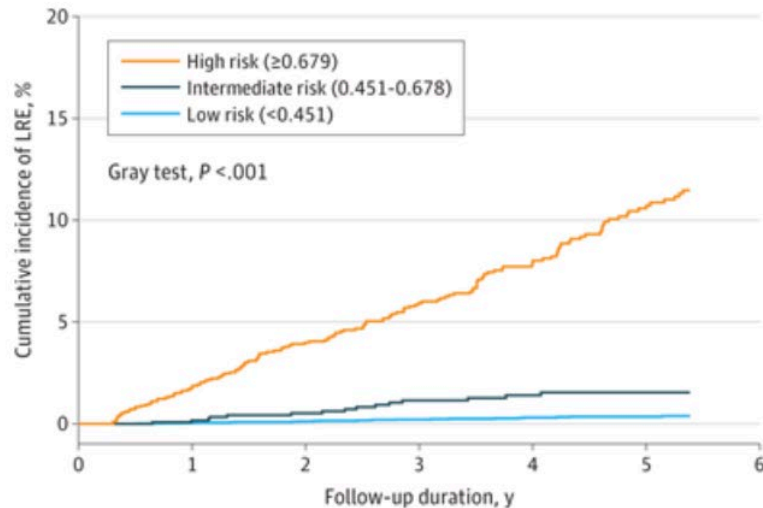
**LSM <20 KPa and PLT >150,000/mm<sup>3</sup> → Likelihood of high risk varices is low → Screening EGD can be avoided**

# Vibration-Controlled Transient Elastography Scores to Predict Liver-Related Events in Steatotic Liver Disease

## LRE

- HCC
- Hepatic Decompensation
  - Ascites
  - VH
  - HE
  - HRS

B Cumulative incidence of LREs stratified by Agile 3+ score in the baseline model



No. at risk	0	1	2	3	4	5	6
High risk	1858	1673	1430	1203	916	620	
Intermediate risk	1314	1183	1022	868	703	479	
Low risk	9776	8585	7134	5879	4742	3582	

a positive nonlinear association between changes in Agile scores or LSM and the risk of LREs (eFigure 12 in Supplement 1). Regardless of baseline Agile scores and LSM, a 10% or greater relative decrease in the test results was associated with a lower risk of LREs, whereas an increase in the test results was associated with increased risk of events (Figure 3B;

**CONCLUSIONS AND RELEVANCE** Findings of this study suggest that single or serial Agile scores are highly accurate in predicting LREs in patients with MASLD, making them suitable alternatives to liver biopsy in routine clinical practice and in phase 2b and 3 clinical trials for steatohepatitis.

# CURRENT PROGRESS AND FUTURE OPPORTUNITIES

- Adoption of AI based technologies into application of NITs
  - More accurate quantification of fibrosis, NASH
  - DL of raw US data for cost effective and precise quantification of fat fraction
  - Automatic classification for focal lesions based on MRI and risk factors
  - Automated reads for MRE, MRI PDFF, SWE and iron quantification



# CASE

- A 46 Y OLD HISPANIC FEMALE WITH ELEVATED LIVER ENZYMES
- PMHX OF T2DM, HLD AND OBESITY – CURRENT BMI 36
- SH- A GLASS OF WINE 1-2 TIMES/MONTH

Na 136, K 4.0, Albumin 4.1, creatinine 0.8, Bilirubin 0.6, **AST 55, ALT 35, ALP 132, FBG 310**, H/H:14.5/36.2, WBC 5.0, **PLT 125**, INR 0.9

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}} = 3.42$$



## IMPRESSION:

1. Cirrhosis. Possible mass in the lateral segment left hepatic lobe.
2. Unremarkable interrogation of the hepatic and portal vasculature.
3. Borderline splenomegaly.

This report was dictated at Workstation ID: PLA1126

Signature Line

The background is a light gray gradient with several realistic water droplets of various sizes scattered across it. The droplets have highlights and shadows, giving them a three-dimensional appearance. The text 'THANK YOU' is centered in the middle of the image.

**THANK YOU**