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

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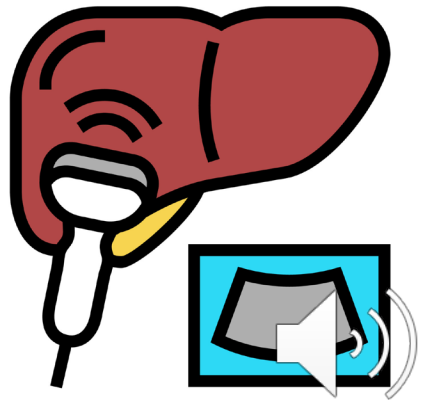


NON INVASIVE TESTS/NON INVASIVE LIVER DISEASE ASSESSMENT TESTS

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

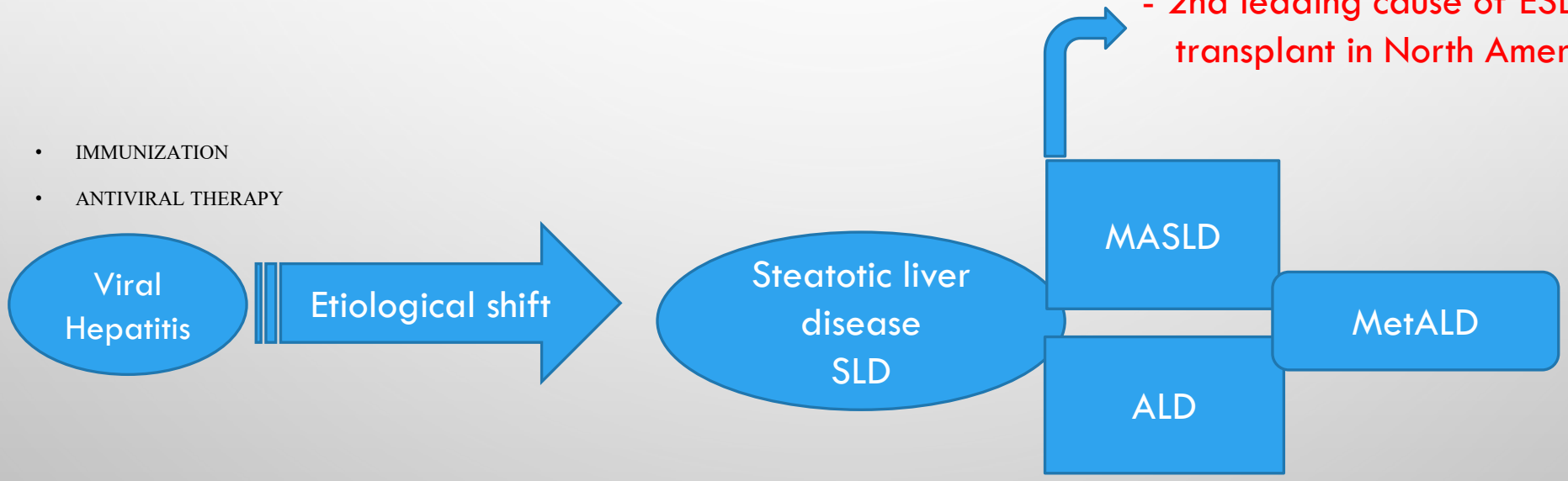
WHY NITS???

- 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- 4TH LEADING CAUSE OF CANCER RELATED DEATHS

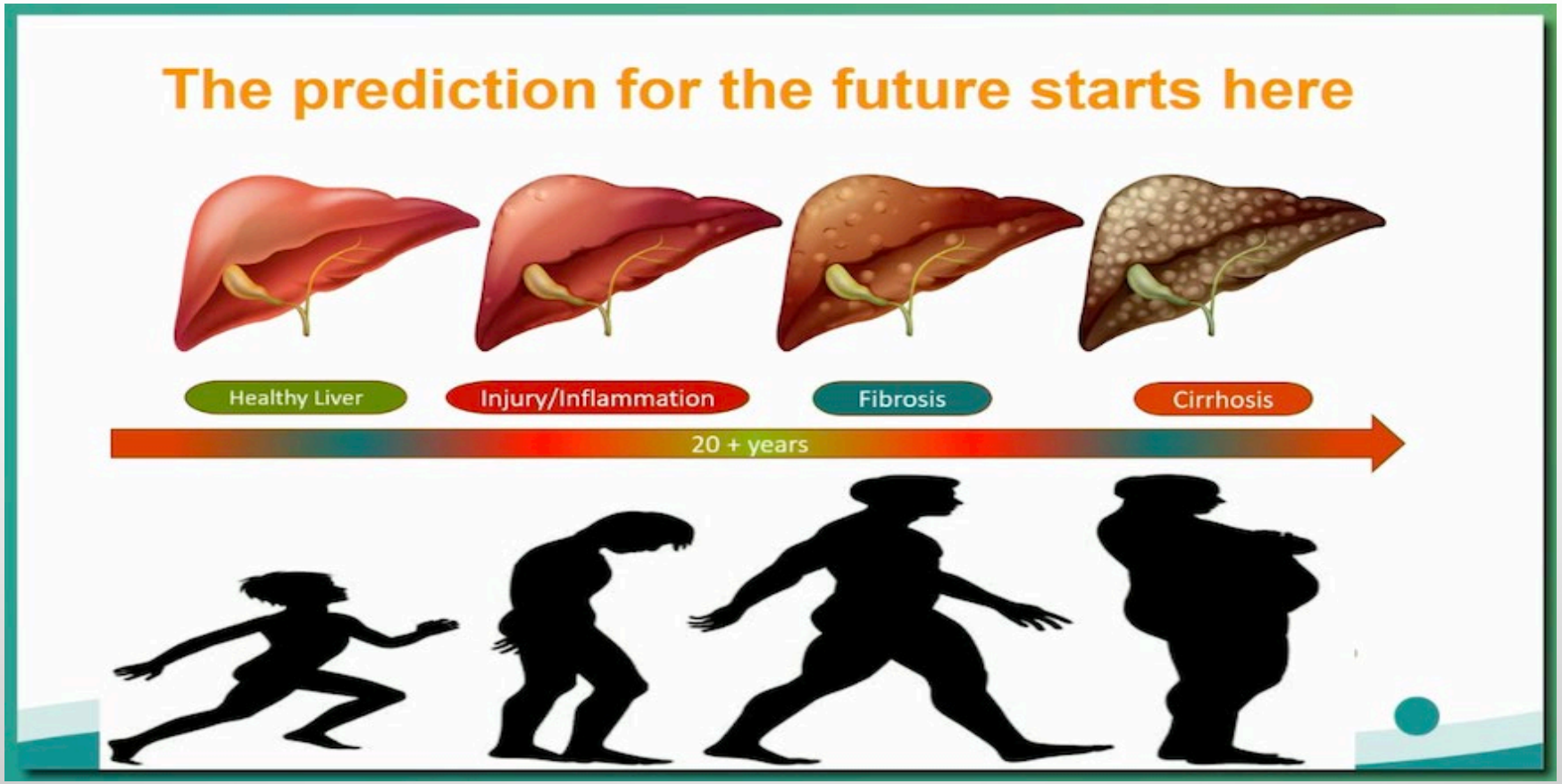
- IMMUNIZATION
- ANTIVIRAL THERAPY



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

(DEVARBHAVI H, ASRANI SK, ARAB JP, NARTEY YA, POSE E, KAMATH PS. GLOBAL BURDEN OF LIVER DISEASE: 2023 UPDATE. J HEPATOL. 2023 AUG;79(2):516-537. DOI: 10.1016/J.JHEP.2023.03.017. EPUB 2023 MAR 27. PMID: 36990226.)

WHY NITS?



Naudia L. Jonassaint
AASLD Liver Meeting 2023
Epidemiology, disparities and social determinants of cirrhosis

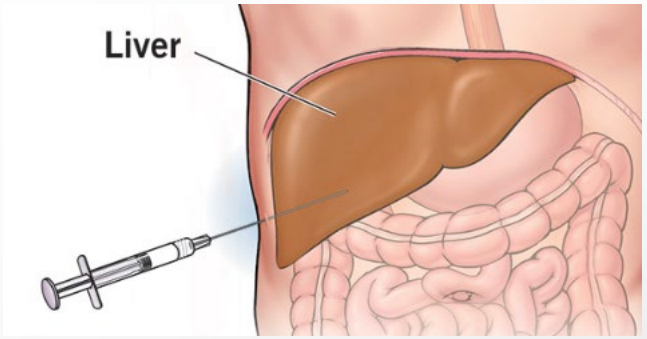
NEED FOR LARGE SCALE SCREENING

NON INVASIVE LIVER TESTS

- AFFORDABLE/ACCESSIBLE/AVAILABLE
- EASY TO PERFORM/MEASURE
- REPRODUCIBLE
- COST EFFECTIVE
- REPEATABLE

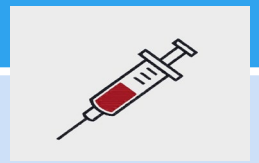
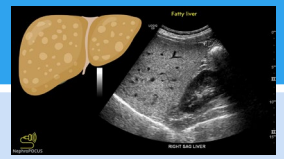
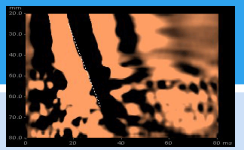
- EMERGING ROLES OF NITS
  - PRIMARY RISK STRATIFICATION
  - SEC RISK ASSESSMENT FOR COMPLICATIONS OF LD/PREDICTING OUTCOMES
  - MONITORING RESPONSE

Liver Biopsy



Challenges:
Access / availability
Affordability
Invasive nature
Not repeatable in clinical settings

COMMONLY USED NITS

Serum based markers	Routine Imaging Modalities	Liver Stiffness Measurement
 Simple - **FIB-4** - AST to PLT Ratio Index (APRI) - NFS Commercial Lab tests - ***ELF*** - *FibroSure* - *FibroSpect II*	 - US - CT scan - MRI	 - **Vibration Controlled Transient Elastography (VCTE)** - Shear wave Elastography SWE - Acoustic Radiation force Impulse (ARFI) - **MR Elastography**
Composite tests *FAST (FibroScan- AST)* *MAST (MRI- AST)* *MEFIB (MRE + FIB4)* *AGILE 3+ and Agile 4+*		

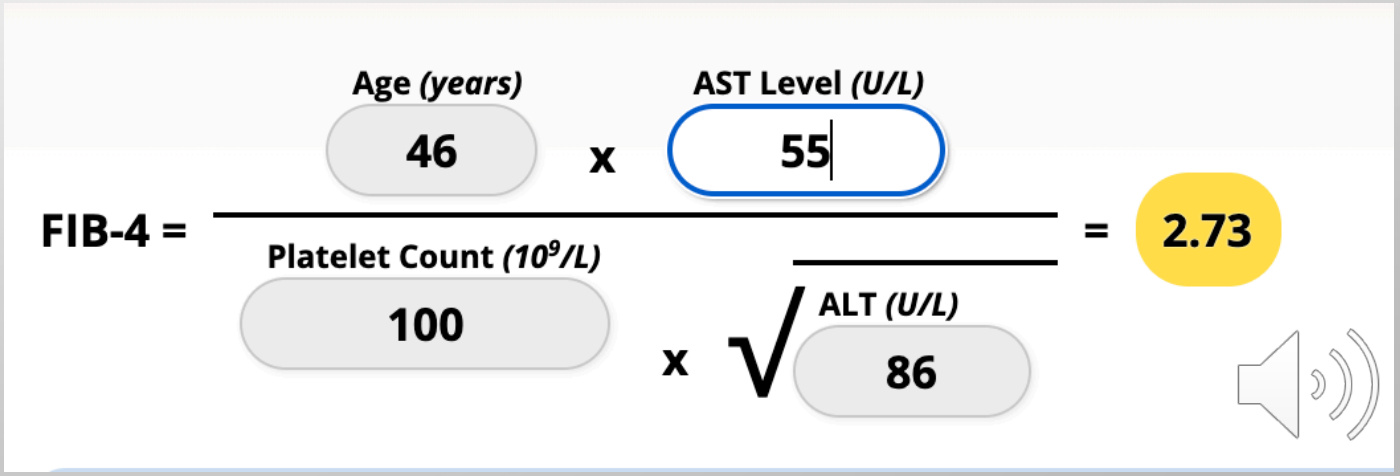
PRIMARY RISK STRATIFICATION

FIB-4

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

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

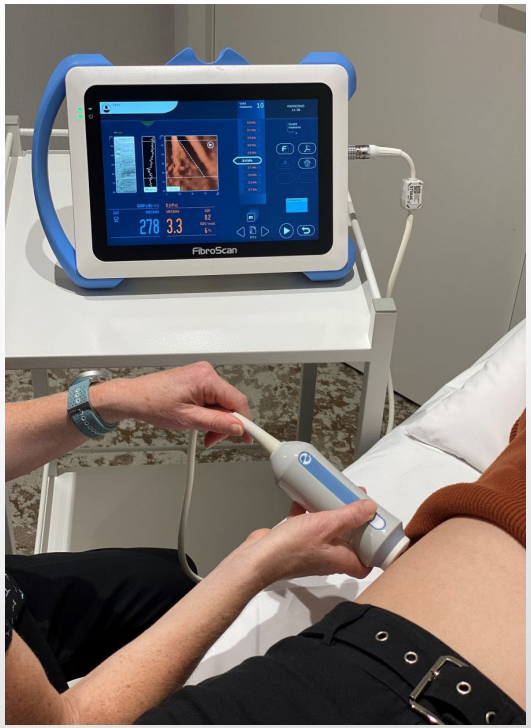
- Limitations
  - Indeterminant zone
  - Age 35-65y
  - Inflammation



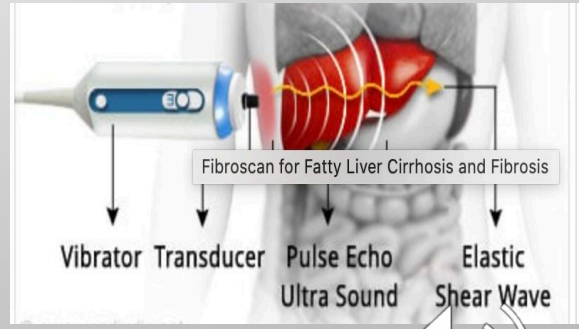
VIBRATION CONTROLLED TRANSIENT ELASTOGRAPHY - VCTE

- Second line test
- US waves through the liver to measure liver stiffness (KPa)

  Higher speed → Higher stiffness



- POC test (can be performed at bedside, OP setting)
- PATIENT FRIENDLY
- IMMEDIATE RESULTS
- COST EFFECTIVE
- ROLE IN PREDICTING OUTCOME AND LIVER RELATED EVENTS (DECOMPENSATION, HCC)

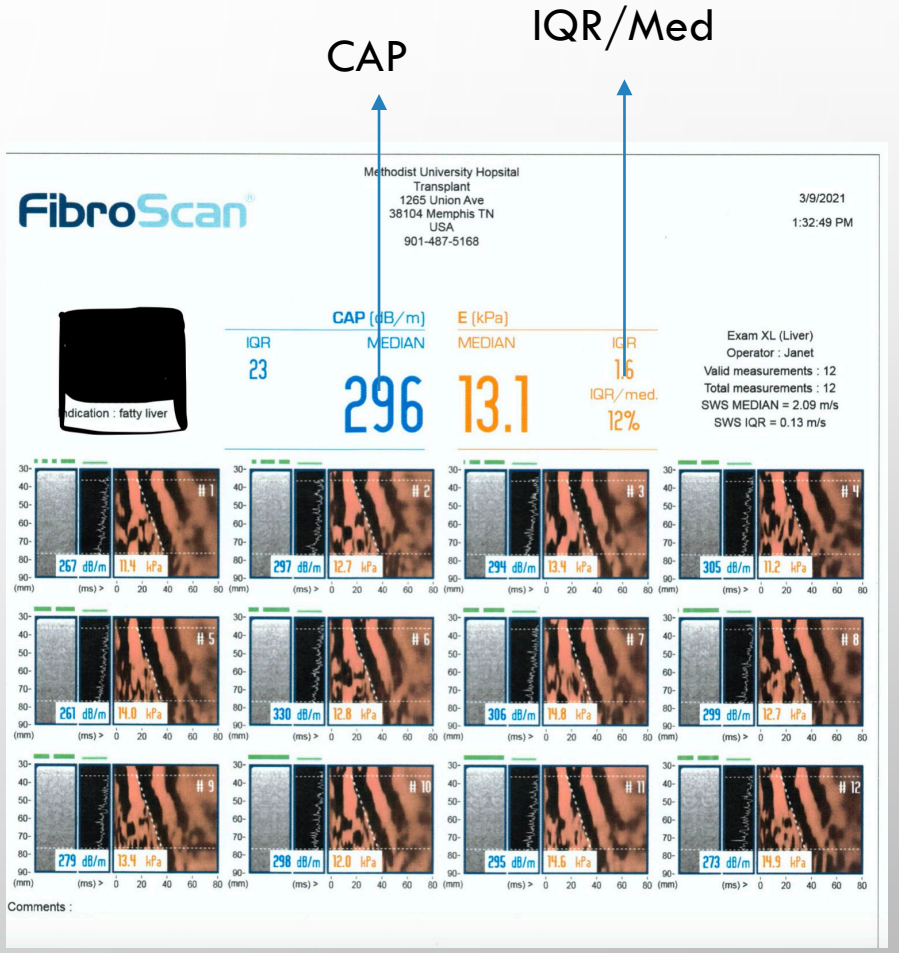


THE TOTAL VOL OF TISSUE THAT IS EVALUATED THROUGH THIS TECHNIQUE IS $3CM^3$ -- AT LEAST 100 TIMES LARGER THAN A STANDARD LIVER BIOPSY SPECIMEN

Sterling, et al., AASLD Practice Guideline on imaging-based non-invasive liver disease assessments of hepatic fibrosis and steatosis. Hepatology March 15, 2024.

- 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 (≥67%)
> 20 Kpa	Cirrhosis		



Consideration:

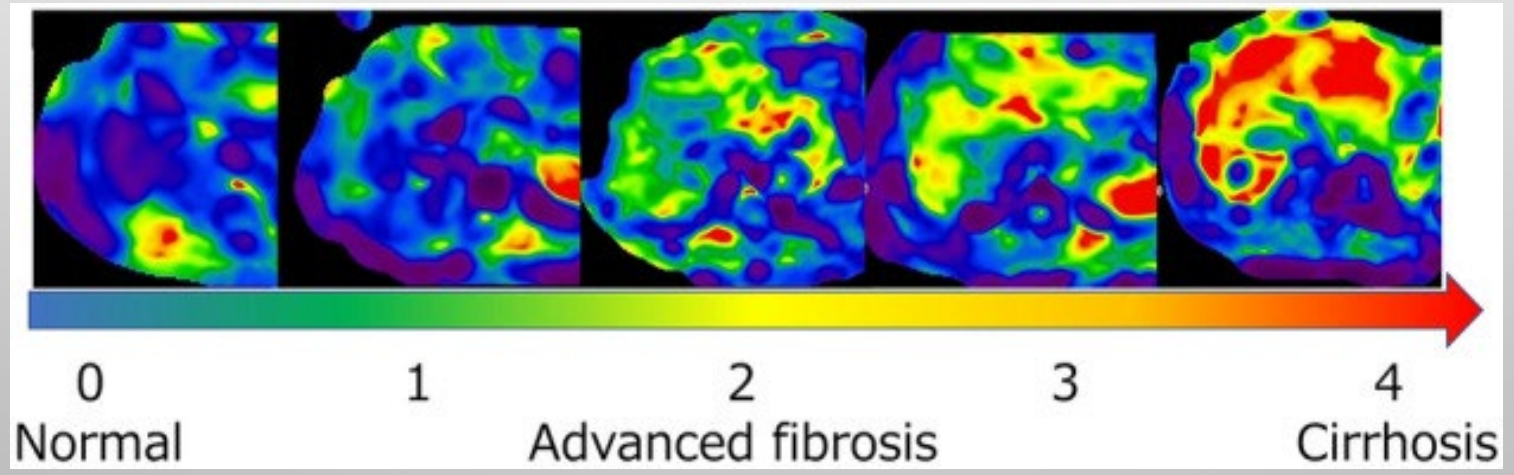
- Satiety
- Presence of inflammation
- Venous congestion (CHF)
- Ascites
- Body habitus (XL probe for BMI >30)

10 measurements with IQR/med 0%

MR ELASTOGRAPHY

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

AF less likely	AF Likely	Cirrhosis
<2.55Kpa	≥ 3.63	≥ 5Kpa



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/mm³)	NR	NR	If <110 = CSPH	If <150 = CSPH	CSPH**

Risk of decompensation

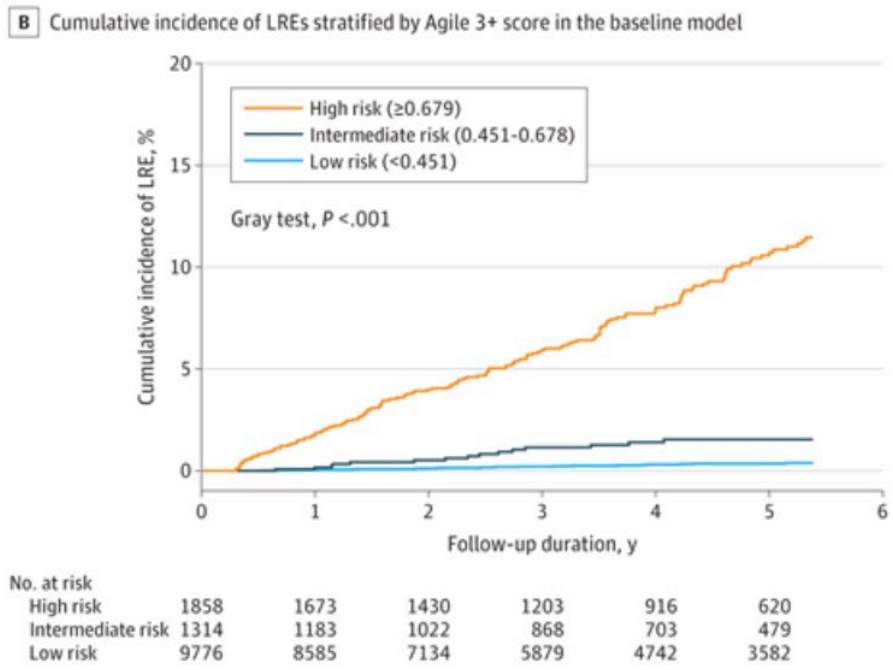
Baveno VI Criteria:

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

JAMA | Original Investigation

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

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



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.

Lin H, Lee HW, Yip TC, et al. Vibration-Controlled Transient Elastography Scores to Predict Liver-Related Events in Steatotic Liver Disease. *JAMA*. 2024;331(15):1287–1297. doi:10.1001/jama.2024.1447

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

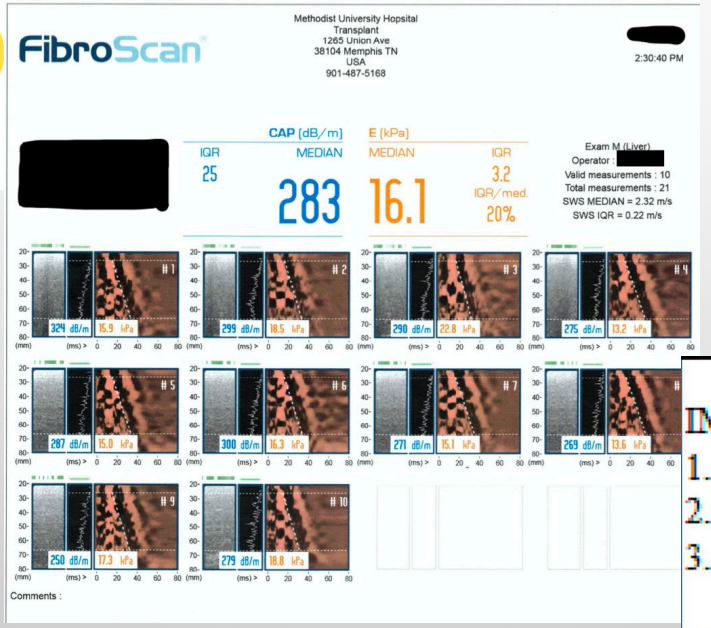
CASE

- 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

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

$$\text{FIB-4} = \frac{46 \times 55}{125 \times \sqrt{35}} = 3.42$$



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

This report was dictated at Workstation ID: PLA1126

Signature Line

THANK YOU