Invasive & Non-Invasive Tests of Liver Fibrosis

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Invasive Testing

Liver Biopsy

Gold Standard but subject to sampling error due to sample size.

Reasons to do Biopsy:

- 1) for diagnosis (especially if atypical features, or co-existing disorders),
- 2) for assessment of prognosis (disease staging), and/or
- 3) to assist in making therapeutic management decisions.

Pre-Biopsy Evaluation and Testing:

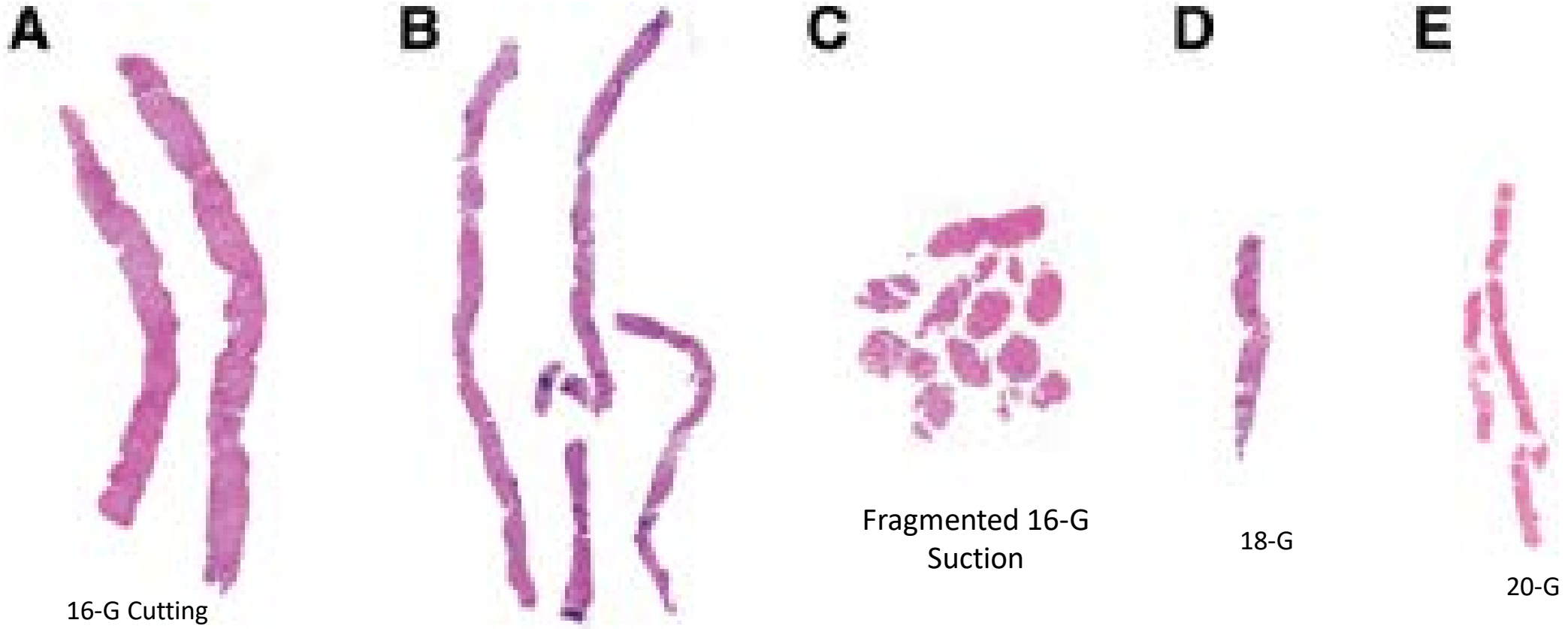
- Platelet count (platelet transfusion or thrombopoietin analogs); goal > 50,000-56,000),
- Fibrinogen level (cryoprecipitate); goal > 120 mg/dL,
- Imaging to R/O Focal lesions or biliary dilation,
- Anti-coagulant/anti-platelet management plan.

Liver Biopsy: Minimization of Sampling Error

- Approaches and tissue sample goals:
  - **Pathology Adequacy: defined as 11 or more complete portal tracts**
  - Laparoscopic/Surgical: 2 lobe needle biopsy or wedge biopsy + surface inspection
  - Percutaneous: with >/= 16 G needle; Total core > 2 cm (3 cm is best);
  - EUS guided with 19 G aspiration needle of both lobes; total core >/= 5 cm is best;
  - Transjugular: 19 G x >/= 3 passes + pressure gradient measurement;

Effect of Liver Biopsy Gauge

AASLD Position Paper: “Liver Biopsy” Hepatology 2009; 1017-1044



Liver Biopsy Complications

- Pain in up to 84%;
- Bleeding requiring intervention in 1/10,000 to 1/2,500;
- Minor bleed in 1/500;
- Mortality 1/10,000 in percutaneous and 9/10,000 in trans-jugular;
- Others: pneumothorax, hemothorax, bacteremia specially post hepatico-jejunostomy, bile peritonitis, hemobilia, etc.

Non-Invasive Testing

Goals of Non-Invasive Tests

Minimize Liver Biopsy Need	Separate patients in whom the test(s) can reliably identify cirrhosis (no need for liver biopsy), and Patients with “inconclusive or incongruent result”, who need Liver Biopsy.
Define Need for Varices Screening with EGD	Serve as a triage (screening) to decide who needs upper endoscopy to evaluate due to “high risk” for varices. Patients who do not fulfilling criteria will not need EGD (will continue non-invasive monitoring).

Goals of Non-Invasive Tests

Identify Clinically Significant Portal Hypertension

Serve as a triage (screening) for patients with cirrhosis requiring elective, non-hepatic surgery, to decide if they do not have “clinically significant portal hypertension” (defined as HVPG > 10 mm Hg).

Other patients will require hepatic venous pressure gradient measurement.

Commonly Used Non-Invasive Tests for Liver Fibrosis

Laboratory Tests

- **Non-Patented:** APRI, FIB-4, NAFLD Fibrosis Score (NFS), PGA Index, Fibro Index, Forns Index, BARD Score
- **Patented:** FibroTest/ActiTest (FibroSure), FibroSpect II, ELF, FibroMeter

Imaging Tests

- Transient Elastography
- Acoustic Radiation Force Impulse imaging (ARFI or pSWE)
- Two-Dimensional Shear Wave Elastography (2D-SWE)
- Magnetic Resonance elastography (MR Elastography)

EASL Practice Guideline:

Non-Invasive Tests for Liver Fibrosis 2015 (modified)

Journal of Hepatology 2015 vol. 63; 237–264

Non-invasive tests should always be interpreted by specialists in liver disease, according to the clinical context, considering the results of other tests (biochemical, radiological and endoscopic) and taking into account the recommended quality criteria for each test and its possible pitfalls.

The most important clinical end-point if the non-invasive tests is **detection of cirrhosis.**

EASL Practice Guideline:

Non-Invasive Tests for Liver Fibrosis 2015 (modified)

Journal of Hepatology 2015 vol. 63; 237–264

Detection of cirrhosis indicates that patients should be monitored for complications related to Portal Hypertension and regularly screened for HCC.

Serum biomarkers can be used in clinical practice due to their high applicability (>95%) and good inter-laboratory reproducibility.

Serum biomarkers should be preferably obtained in **fasting** patients (particularly those including **hyaluronic acid**) and following the manufacturer's recommendations for the patented test.

APRI (AST to Platelet Ratio Index)

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

- AST to Platelet Ratio (APRI) = (AST relative elevation/platelet count) x 100
  - Unknown if influenced by age.
- Better in Predicting F4 vs F2-F4.
- **Hepatitis C:**
  - F4: cut-off > 1.5 has AUROC of 0.8; vs
  - F4: cut-off > 2 has AUROC of 0.89 (Sensitivity 46%;Specificity 91%)
  - F2-4: Cut-off > 0.7 (Sensitivity 77%; Specificity 72%)
  - Less accurate for HCV/HIV coinfection.
- **Hepatitis B:**
  - WHO (2015) recommends APRI > 2 for Cirrhosis
- **NAFLD:**
  - APRI > 1.5 predicts liver related events with AUROC of 0.8;
  - For F4 the AUROC is 0.75 and for F3/F4 is 0.74

FIB-4 Index

- Combines laboratory values (platelet count, ALT, and AST) and age.
- Was initially develop to assess Fibrosis in HCV/HIV coinfection.
- **In HCV:**
  - Index > 3.25 indicates F3-F4 (sensitivity 82%; specificity 98.2%) (AUROC 0.85).
- **For HIV/HCV:**
  - Index > 3.25 indicates F3-F4 (sensitivity 70%; specificity 97%) (AUROC is 0.76).
  - Thrombocytopenia due to HAART exaggerates Fibrosis stage.
- **In NASH:**
  - Index > 2.67 for F3-F4 with an AUROC of 0.88;
  - Index < 1.3 (< 2 if age >/= 65**) indicates absence of advanced fibrosis (stage F2 or lower). Am J Gastroenterol. 2017 May; 112(5): 740–751

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

Impact of pre-screening with Fibrosis-4 index on a referral pathway for patients with suspected NAFLD

Aim:

To assess the potential impact of implementing a *FIB-4 first* strategy to triage patients using a clinical referral pathway for suspected non-alcoholic fatty liver disease (NAFLD) (abnormal ALT or steatosis on ultrasound)

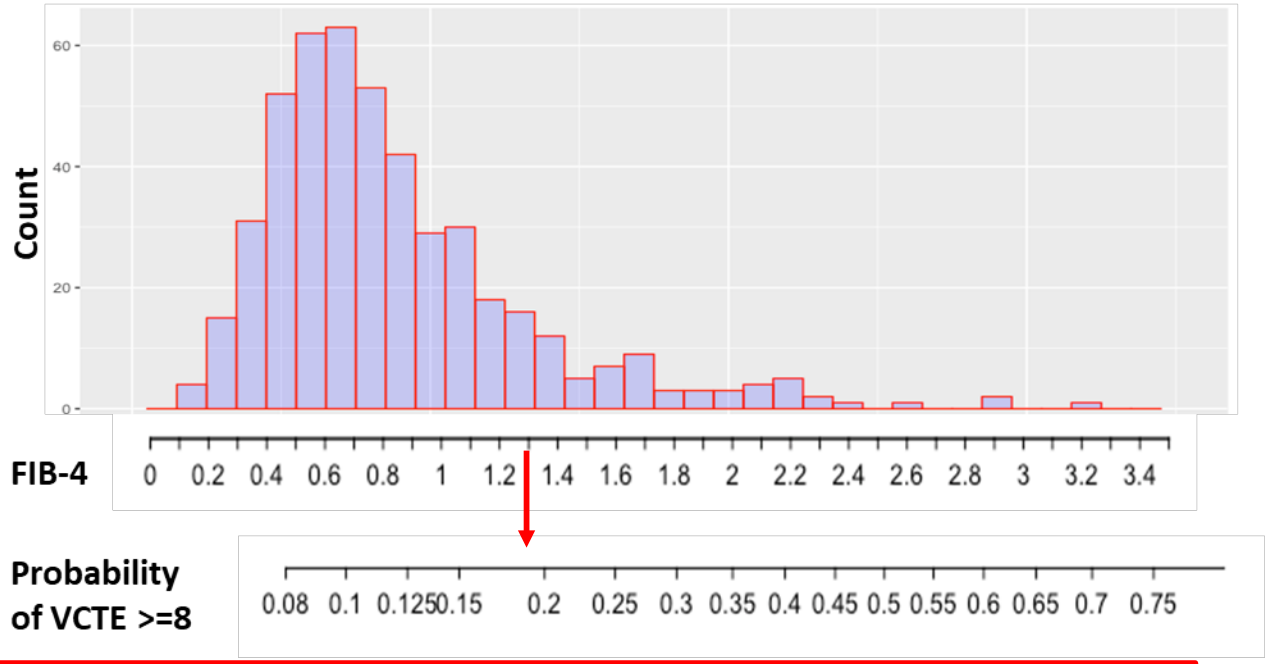
Methods:

All referred patients were risk stratified using FIB-4 and VCTE. The risk of finding a VCTE ≥8 kPa according to FIB-4 values was modelled with logistic regression.

Conclusions:

As compared with a referral pathway in which all patients with suspected NAFLD undergo VCTE for risk stratification, a *FIB-4 first* strategy with a threshold of 1.3 would save 85% of VCTE assessments.

Distribution of FIB-4 values in 481 patients using the referral pathway and predicted risk of VCTE ≥8 kPa

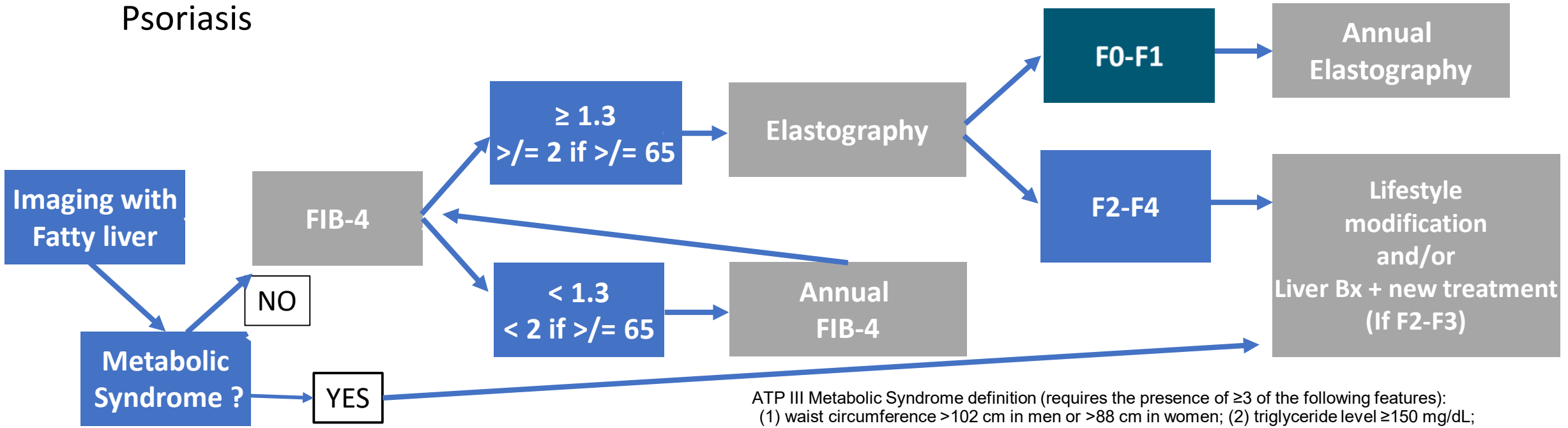


Davyduke TM, et al., Abstract 69
AASLD 2018

FIB-4 of >/= 1.3 identifies > 82% of VCTE >/= 8 kPa that means >/= F2, and saves 85% of TE tests

Screening for NAFLD in Patients with Fatty Liver in Imaging

- Metabolic Syndrome* (ATP III)
- Elevated liver enzymes, or Signs or Symptoms of Liver Disease.
- Normal Liver enzymes and absent Sings/Symptoms of liver disease, but presence of:
  - Obesity, Diabetes Mellitus, Dyslipidemia, or PCOS
  - OSA, Hypothyroidism, Hypopituitarism, Hypogonadism, Pancreato-duodenal resection, or Psoriasis



ATP III Metabolic Syndrome definition (requires the presence of ≥3 of the following features):
(1) waist circumference >102 cm in men or >88 cm in women; (2) triglyceride level ≥150 mg/dL;
(3) HDL cholesterol level <40 mg/dL in men and <50 mg/dL in women;
(4) SBP ≥130 mm Hg or DBP ≥85 mm Hg; and (5) fasting plasma glucose level ≥110 mg/dL.

NAFLD Fibrosis Score

Only used in NAFLD

Based on age, body mass index (BMI), blood glucose levels, aminotransferase levels, platelet count, and albumin.(Influenced by age).

NAFLD fibrosis score cutoff > 0.676 predicts stage F3-F4 (sensitivity 43%, specificity 96%) (AUROC = 0.85)

NAFLD Fibrosis Score < -1.455 (or < 0.12 if >/= age 65) indicates absence of advanced fibrosis (scores F0 to F2) (sensitivity 77% and specificity 71%) Am J Gastroenterol. 2017 May; 112(5): 740–751

FibroTest/ActiTest and FibroSure

Proprietary tests including alpha-2-macroglobulin, alpha-2-globulin (haptoglobin), gamma globulin, apolipoprotein A1, GGT, total bilirubin, gender and age.

- High Bili due to HAART or Gilbert's exaggerates Fibrosis Score.
- Nevirapine and alcohol also increases score due to GGT induction.

FibroSure and FibroTest are the same Test.

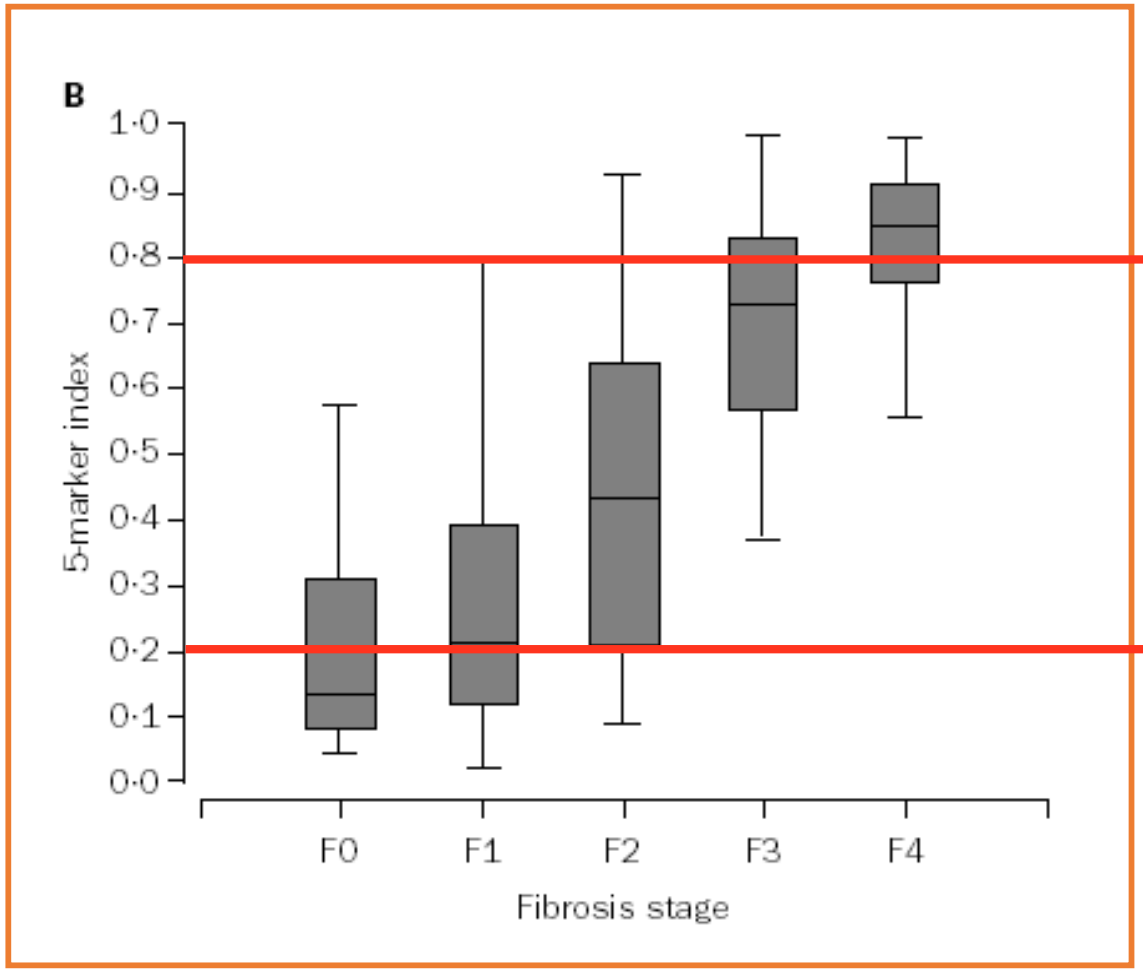
- **Quest and Mayo**: FibroTest/ActiTest (HCV and HBV)
- **LabCorp**: HCV FibroSure, NASH FibroSure, ASH FibroSure
  - For HCV F4: the AUROC is 0.86
  - For HBV F4: the AUROC is 0.80; and for F2-4: AUROC is 0.80
  - For NASH, the AUROC for F4 is 0.91 and for F3-4 the AUROC is 0.80

ActiTest adds ALT to incorporate an inflammatory component to the fibrosis panel.

FibroSure/FibroTest Types

TYPE	Height	Weight	Age	Gender	A2 Macroglobulin	Haptoglobin	Apo-A1	Bilirubin	GGT	ALT	AST	Cholesterol	Triglycerides	Glucose
HCV			X	X	X	X	X	X	X	X				
NASH or ASH	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Up to 50% of Biopsies May Be Avoidable with FibroTest



FT > 0.80
Spec 97%
PPV 92%

Indeterminate
54%

FT ≤ 0.20
Sens 92%
NPV 87%

n=134
F2-F4 fibrosis: 45%

Imbert-Bismut. Lancet 2001;357:1069-75

Enhanced Liver Fibrosis panel (ELF)

Proprietary algorithm using hyaluronic acid level, amino-terminal propeptide of type III collagen level, and TIMP-1.

Used in liver diseases with different etiologies. Not commercially available in USA.

In general AUROC is 0.78

In NAFLD AUROC is 0.86

Other Laboratory-based Tests – Not Patented

- **PGA Index** – Combines the measurement of the prothrombin index, GGT level, and apolipoprotein A1 level.
  - **Used in Alcoholic Liver Disease**.
- **Fibro Index** – Derived from the platelet count, AST, and gamma globulin measurements.
  - **Used in Hepatitis C** [1.738 - 0.064 x (platelets [104/mm3]) + 0.005 x (AST [IU/L]) + 0.463 x (gamma globulin [g/dl])] (AUROC 0.83).
  - Score > 2.25 is consistent with F4.

Other Laboratory-based Tests – **Not Patented**

- **Forns Index** – Combines age, GGT, cholesterol, and platelet count.
  - **Used in Hepatitis C**. [7.811 - 3.131 x ln(platelet count) + 0.781 x ln(GGT) + 3.467 x ln(age) - 0.014 x (cholesterol)] (AUROC 0.81).
  - Scores less than 4.2 excludes advanced Fibrosis (F2-F4) with NPV of 96%.

- **BARD Score** –Takes into account BMI, the AST/ALT ratio, and the presence of diabetes mellitus.
  - **Used in NAFLD** (BMI ≥28 = 1; AST/ALT ratio ≥0.8 = 2; diabetes = 1);
  - If score ≥2, odds ratio for advanced fibrosis = 17.

Other Laboratory-based Tests – **Patented**

- **FibroMeter** – Patented Formula (Echosense Lab).
  - Combines platelet count, prothrombin index, AST, alpha-2-macroglobulin, hyaluronic acid, blood urea nitrogen, and age.
  - Done by ARUP Laboratories in USA.
  - Used in Viral Hepatitis (**FibroMeter Virus**) (AUROC = 0.89) and NAFLD (**FibroMeter NAFLD**).
  - **ASH FibroMeter** not available in USA.

- **FibroSpect II** - Patented Formula (Prometheous Lab).
  - Uses a combination of serum hyaluronic acid, tissue inhibitor of metalloproteinase-1 (TIMP-1), and alpha-2-macroglobulin.
  - **Used in Hepatitis C**. (AUROC = 0.83)

FibroMeter Components

FibroMeter	Parameter Score	Age	Gender	Weight	A2 Macroglobulin	Hyaluronic Acid	PT Index	Platelets	AST	Urea	GGT	ALT	Ferritin	Glucose
Viral	Fibrosis	X	X		X		X	X	X	X	X	X		
	Cirrhosis	X	X		X	X	X	X	X	X	X	X		
	Activity				X		X	X				X		
ALD	Fibrosis	X	X		X	X	X							
	Area of Fibrosis				X	X	X	X						
NAFLD	Fibrosis	X	X	X				X	X			X	X	X
	Area of Fibrosis					X	X	X	X			X		X

Imaging Tests

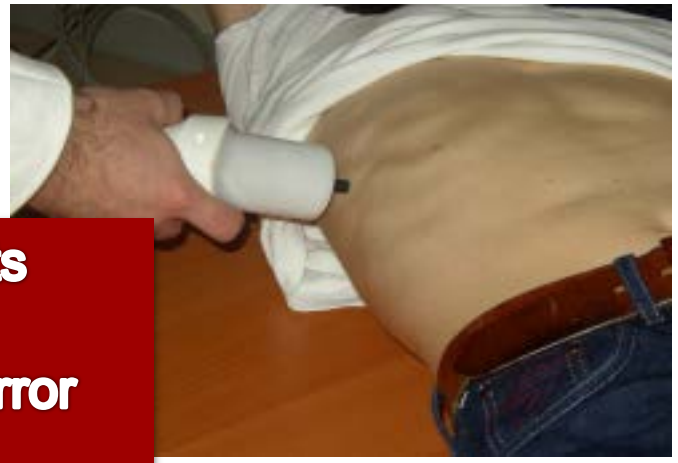
- Transient Elastography
- Acoustic radiation force impulse imaging (ARFI or pSWE)
- Two-dimensional shear wave elastography (2D-SWE)
- Magnetic resonance elastography (MR Elastography)

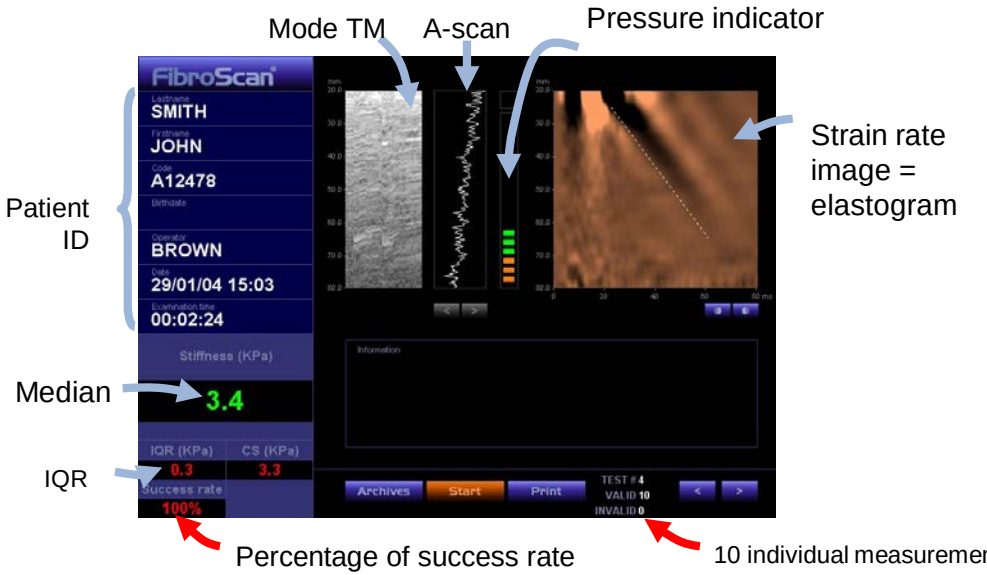
Transient Elastography

Immediate results

Less sampling error

Bedside procedure





Transient Elastography (TE)

or

Vibration Controlled Transient Elastography (VCTE)

Uses shear wave imaging to estimate liver stiffness

A mechanical vibrating source is applied to tissue, and shear waves created by the excitation are measured with an ultrasound detector.

The stiffer the tissue, the faster the wave travels.

Unreliable in: Ascites, ALT or AST > 5 x ULN, extrahepatic biliary obstruction, extrahepatic vascular (arterial or venous) obstruction, or congestive heart failure.

TE should be performed by an experienced operator (>100 examinations) following a standardized protocol

-patient, fasting for at least 2 hours,

-supine position,

-right arm in full abduction,

-mid-axillary line with the probe-tip placed in the 9th to 11th intercostal space

-a minimum of 10 shots

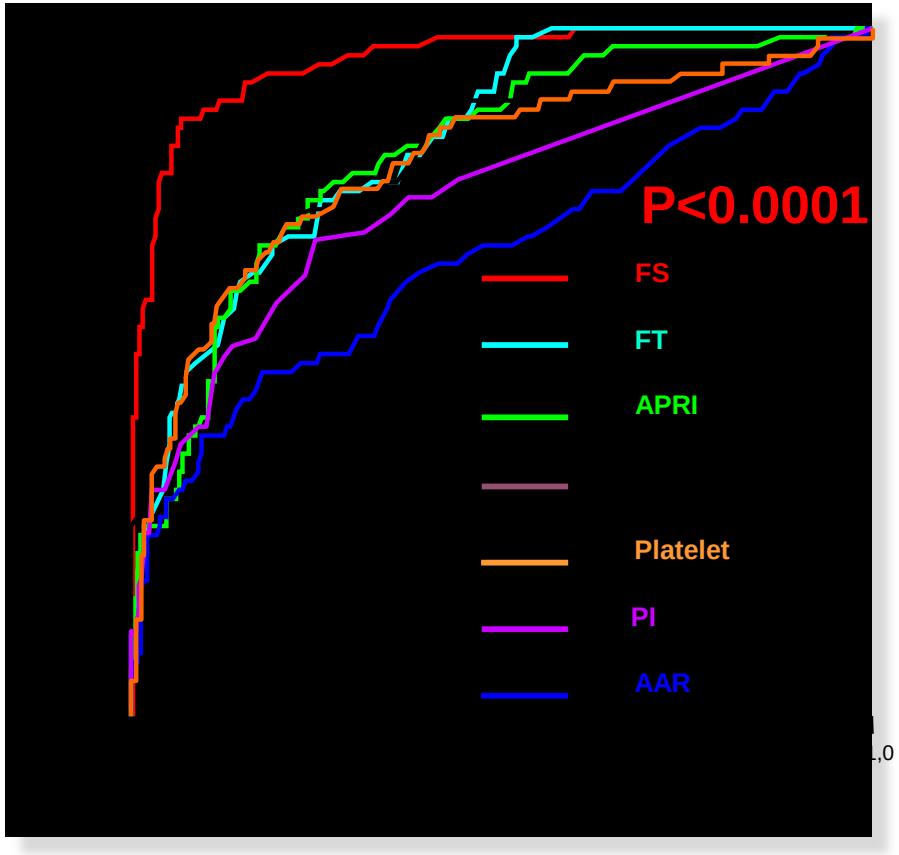
Parameters Needed for Correct Interpretation of TE & CAP

- IQR/ median value (<30%),
- Serum aminotransferases levels (<5 x ULN),
- Absence of extra-hepatic cholestasis,
- Absence of right heart failure, or other causes of congestive liver
- Absence of ongoing excessive alcohol intake,
- BMI (use XL Probe above BMI of 30 kg/m^2 or if skin-to-capsule distance is >25 mm),
- Presence of Diabetes Mellitus
- Presence of NAFLD or NASH

Transient Elastography (TE)

- TE is reliable for the diagnosis of cirrhosis in patients with chronic liver diseases.
- Most extensively studied and validated imaging technique, with high intra- and inter-observer reproducibility.
- TE is **better at "ruling out"** than "ruling in" cirrhosis (NPV = 96% and PPV = 74%)
- Correctly classifies cirrhosis in 80 to 98% of patients (AUROC 0.8-0.99); less accurate for lesser fibrosis.
- Cut-offs are different by diagnosis.
- TE is better validated in viral (HCV, HCV/HIV, HBV) than in NAFLD.
  - If ALT higher than 5 x ULN, repeat test after hepatitis is controlled.
- In Alcoholic Liver Disease the values are not very reliable while actively drinking.
  - If AST is > 100 U/mL, repeat the Test after 2 weeks or more of abstinence.

Diagnosing Cirrhosis: TE *vs.* Biomarkers



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Degos et al. J Hepatol 2010; 53: 1013-21

Castera et al. J Hepatol 2009; 50: 59-68

Transient Elastography (TE) in HCV

In patients with **active** HCV:

- TE >/= 12.5 kPa reliably identifies cirrhosis (< 5% False Negative rate).

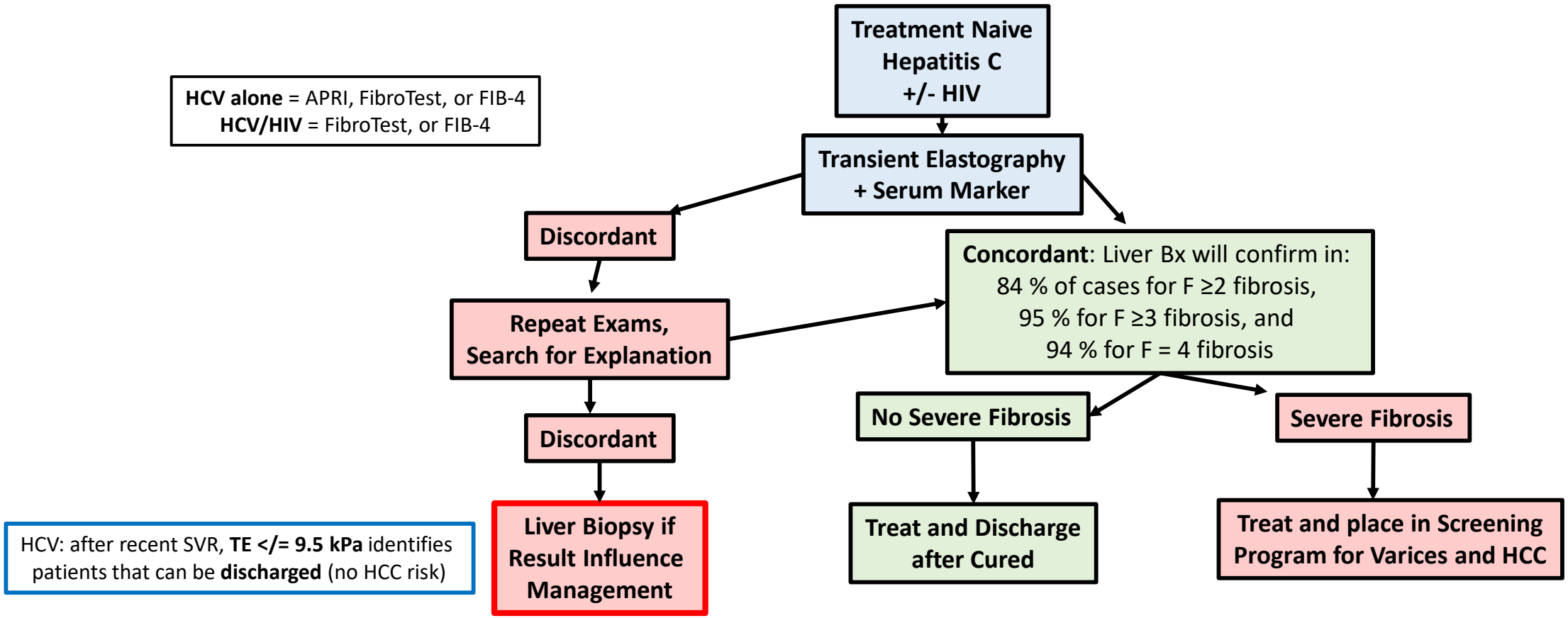
In patients with HCV **after SVR**:

- TE < /= 9.5 kPa, reliably identifies patient who can be discharged (< F3, with < 7% False Negative rate; no need for surveillance).

MR elastography is NOT superior to TE in patients with Hepatitis C.

Sequential Algorithm for Fibrosis Evaluation (SAFE) in Hepatitis C

Modified from: Journal of Hepatology 2015 vol. 63; 237–264 and Gastroenterology 2017 Vol. 152, 1536–1543



Transient Elastography (TE) in HBV

In patients with HBV:

- TE >/= 11 kPa reliably identifies cirrhosis (AGA 2017)
  - False negative rate < 5% (sens 81%; specif 83%);
  - All patients with cirrhosis should be treated.
- If **ALT is elevated** but < 5 x ULN, either HBeAg(+) or HBeAg(-), and independently of HBV-DNA level:
  - TE with kPa 6-9 (likely > 6 but < 11 kPa in USA) should lead to liver biopsy, if likely to change management.

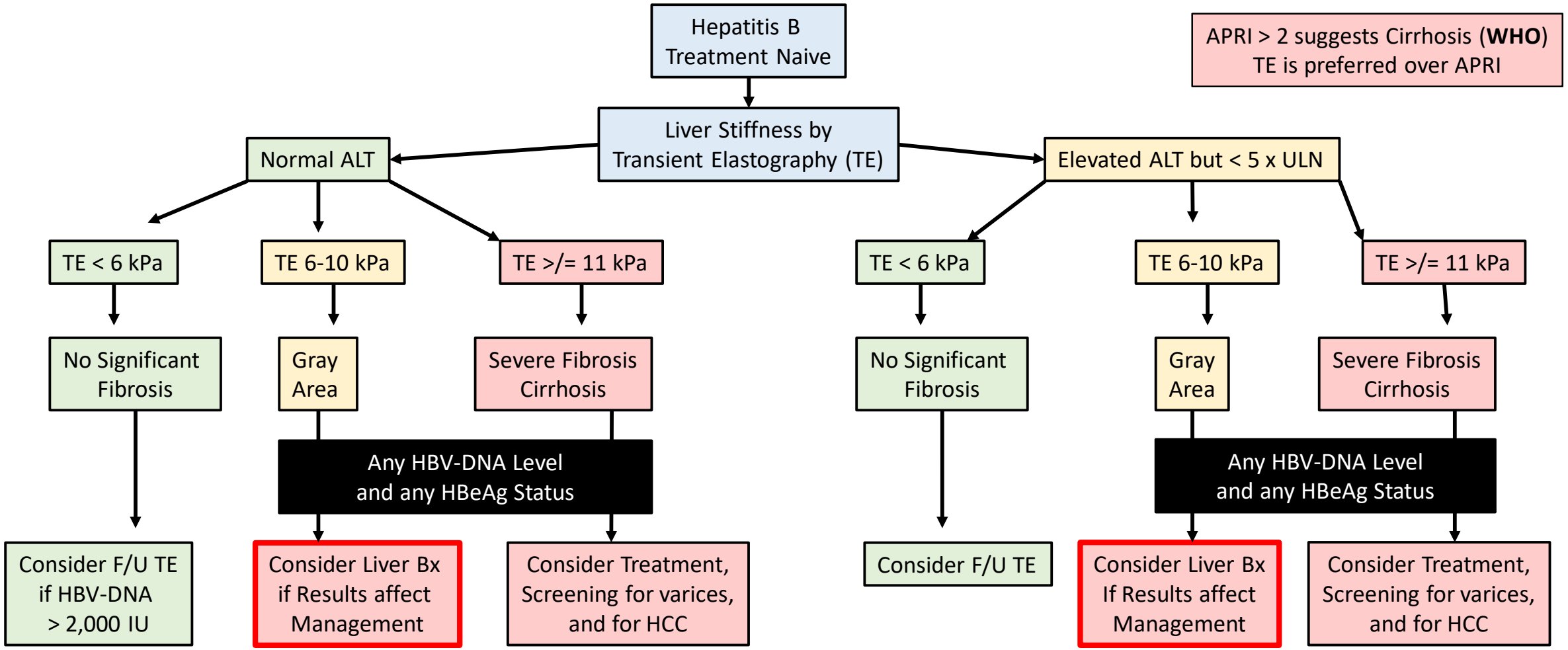
Transient Elastography (TE) in HBV

In patients with HBV:

- If **ALT is normal** but TE > 9 kPa (indicating cirrhosis in Europe; or >/= 11 kPa per AGA guidelines), strongly consider therapy + varices surveillance.
  - All patients with cirrhosis should be treated.
- In **patients older than 35** with normal ALT, and either HBeAg(+) or HBeAg(-):
  - TE with 6 to 9 kPa in Europe (likely > 6 kPa to < 11 kPa in USA) should lead to liver biopsy to decide if treatment is needed (EASL 2015).

Sequential Algorithm for Fibrosis Evaluation (SAFE) in HBV by ALT Elevation & TE

Modified from: Journal of Hepatology 2015 vol. 63; 237–264 and Gastroenterology 2017 Vol. 152, 1536–1543



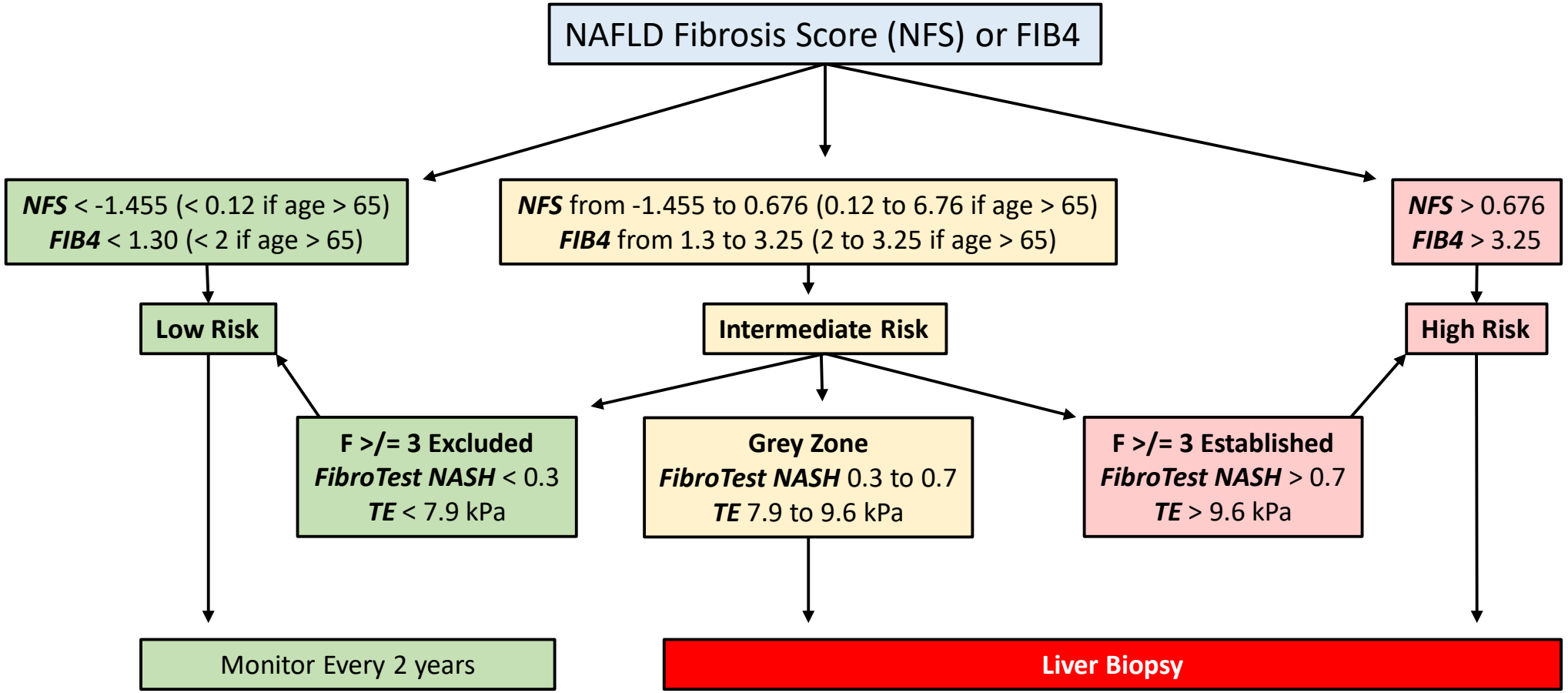
Transient Elastography (TE) in NAFLD

In patients with NAFLD, TE nor APRI nor FIB-4 are reliable enough to diagnose cirrhosis

- In **populations with high prevalence of cirrhosis** (subspecialty clinic) **MR Elastography** is superior to TE to diagnose cirrhosis in NAFLD (less “False Positives”).
- **Liver Biopsy** is needed for accurate diagnosis, and before drug-therapy.

Sequential Algorithm for Fibrosis Evaluation (SAFE) in NAFLD

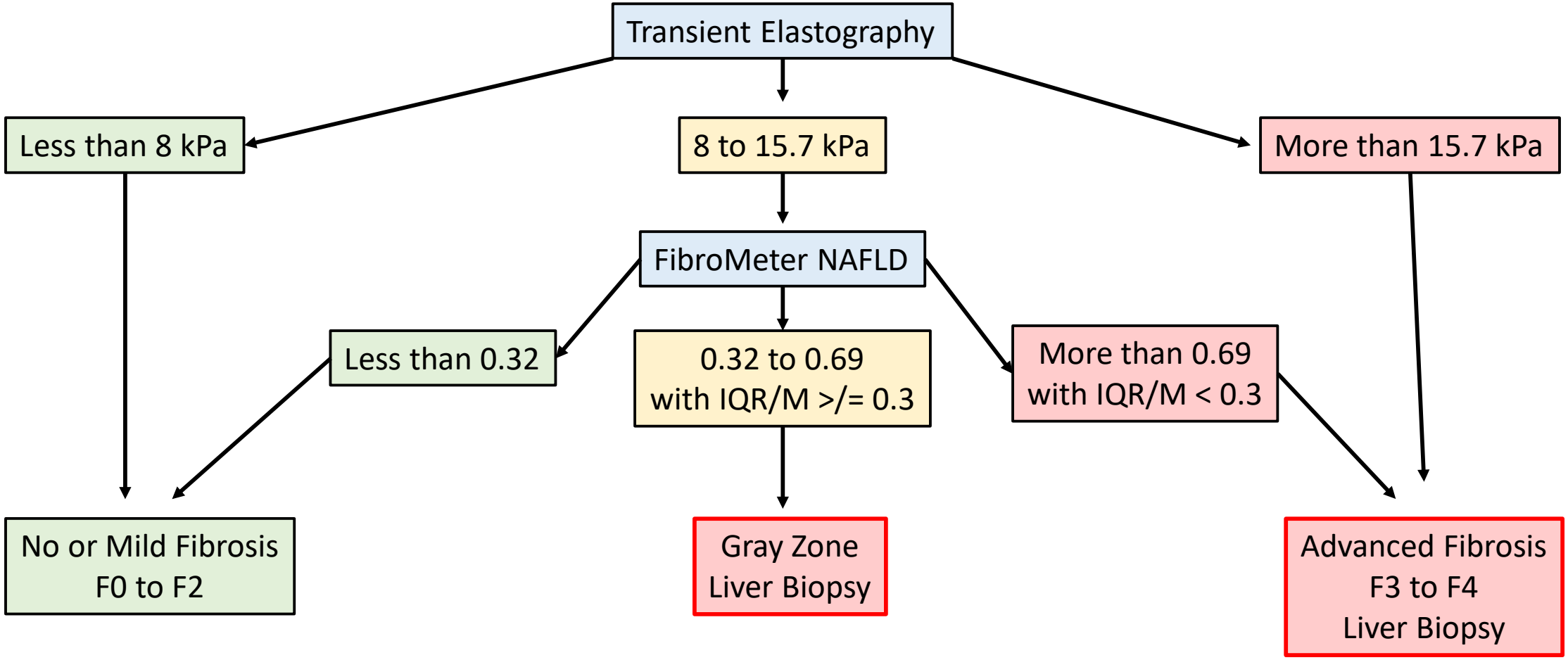
Modified from: J Hepatol 2016; 64:1388-1402; J Hepatol 2019; 71:389-396; Am J Gastroenterol 2017;112:740-751



TE = Transient Elastography

SAFE for NAFLD with Transient Elastography + FibroMeter

Modified from: Journal of Hepatology 2019 vol. 71: 389–396



Transient Elastography (TE) in ALD

TE is NOT reliable to diagnose cirrhosis in Acute Alcoholic Hepatitis.

In Alcoholic Liver disease (not actively drinking) a cut-off of **12.5 kPa** detects cirrhosis with low “false negative” rates (< 1.5%) but relatively high false “positive rate” (27.5% and 20.3%) in low vs high prevalence groups, respectively, most of the false (+) being F3.

In Alcoholic Hepatitis, TE > 30 kPa indicates cirrhosis.

Transient Elastography (TE) in Cirrhosis

In patients with cirrhosis, a TE >/= 19.5 kPa identifies patients at higher risk of esophageal varices (AGA Guidelines, 2017).

- Baveno VI Consensus recommended TE > 20 kPa or platelet count < 150,000 as triggers for screening EGD
- A TE of >/= 50.7 kPa suggests high risk of variceal bleed.

A TE < 17 kPa is indicative of absence of “clinically significant portal hypertension” (no varices) with misclassification rate < 6.8%.

UofL TE Interpretation Summary

Modified from: Bonder A, Afdhal N. Current Gastroenterology Reports 2014; 16:372, Lim JK et al. Gastroenterology 2017; 152:1536-1543, Moreno C et al. J of Hepatology 2019(70): 273-283; Wu S et al. Hepatology International (2019) 13:91–101

	F0-F1 (kPa)	F2 (kPa)	F3 (kPa)	F4 (kPa)
HBV	</= 6	6.1 to 9	9.1 to 10.9	**>/= 11***
HCV	</= 7	7.1 to 9.4	9.5 to 12.4	**>/= 12.5***
HCV-HIV	</= 7	7.1 to 10	10.1 to 13.9	>/= 14
Cholestatic Liver Disease	</= 7	7.1 to 9.9	10 to 16.9	>/= 17
Autoimmune Hepatitis	</= 6.2	6.3 to 8.4	8.5 to 12.3	>/= 12.4
NAFLD/NASH	</= 7	7.1 to 9.9	10 to 13.9	>/= 14
Alcoholic Liver Disease (without alcoholic hepatitis (AH))	</= 6	6.1 to 7.9	8 to 12.4	**>/= 12.5*** [>/= 30 kPa if with AH]
High Probability of varices				**>/= 19.5***
Low probability of CSPH				**< 17***

HBV: -Liver Biopsy if it could change management
-With NORMAL ALT, consider treating if > 9 or 11 kPa (vs Bx)

HCV: after recent SVR, TE </= 9.5 kPa identifies patients that can be discharged (no HCC risk)

Baveno VI Consensus recommended:
TE >/= 20 kPa, or Platelets < 150,000

***AGA 2017 Guideline**

Point Shear Wave Elastography (pSWE) or Acoustic Radiation Force Impulse (ARFI)

Uses strain imaging to estimate fibrosis (short-duration, high-intensity acoustic pulse is applied and tissue displacement in the direction of the stress is measured).

Is better for detection of F4 (AUROC 0.8) than for “advanced fibrosis” F2-F4 (AUROC 0.74).

Not affected by ascites

Sensitivity for F4 is 92% and specificity is 87% with a cut-off of 1.9 m/s

Quality criteria not as well defined as for TE

2D-Shear Wave Elastography (2-D SWE)

Integrates real-time, gray-scale U/S imaging + Shear Wave Elastography.

You can monitor the volume of tissue being examined.

Is more accurate to detect Cirrhosis (F4) (AUROC 0.8) than “advanced fibrosis” (F2-F4) (AUROC 0.75).

Quality criteria not well defined

MR Elastography

MRE interrogates the entire liver and is not limited to a defined target volume for sampling.

Procedure:

- Mechanical waves are generated by an "active driver" (located outside the scanner room) and transmitted via tubing to a nonmetallic "passive driver" placed against the patient’s right anterior chest wall overlying the liver.
- A flexible membrane on the surface of the passive driver conducts the vibrations into the body to generate propagating mechanical waves.
- Imaging with fast pulse sequences measures the speed of the shear waves through the liver and thereby estimates tissue stiffness.

MR Elastography

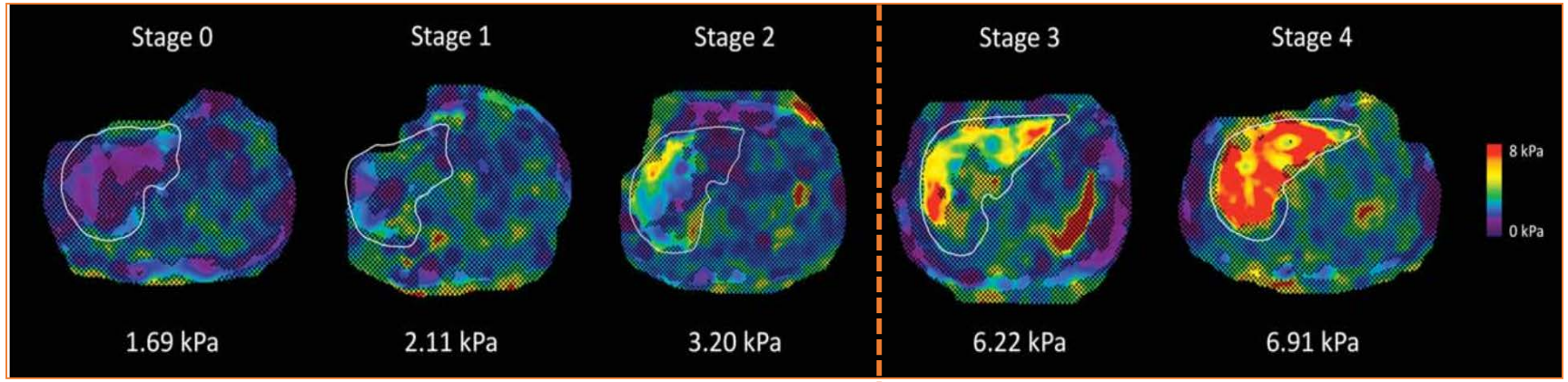
In HCV:

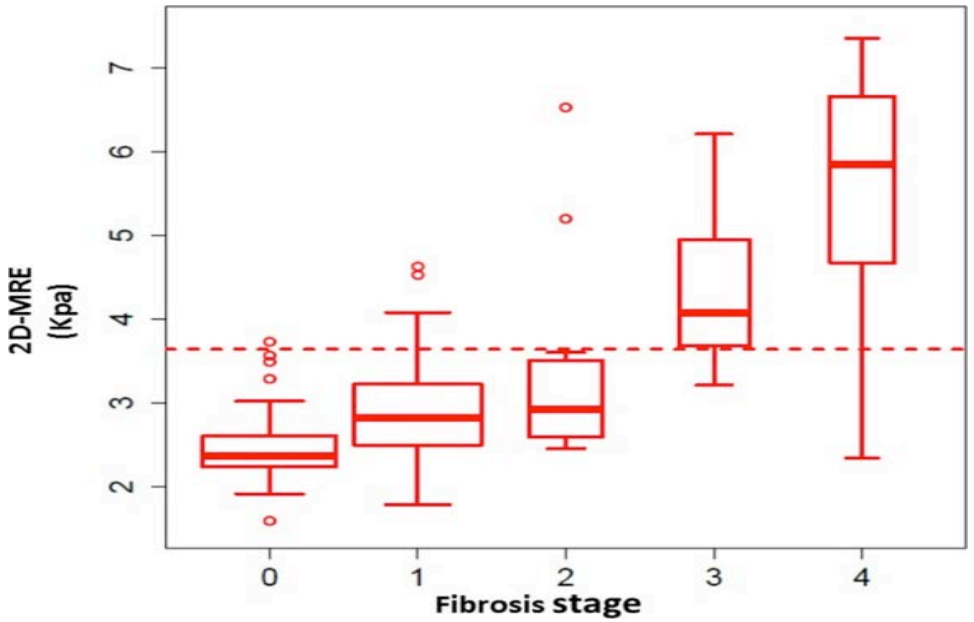
- MRE is inferior to TE in identifying cirrhosis (higher “false (+)” rate).

In NAFLD:

- **In populations at high risk of cirrhosis (referral center), MRE is superior to TE by giving less “false (+)” cirrhosis diagnosis.**
- In populations with low risk for cirrhosis (primary care), both TE and MRE, have high “false (+)” diagnosis of cirrhosis.

MR Elastography Diagnoses Advanced Fibrosis





- Stiffness cutoff: 3.63 kPa
  - Sensitivity 0.86
  - Specificity 0.91
- AUC for diagnosis of advanced fibrosis: 0.924

Loomba et al 2014

Evaluation of Hepatic Steatosis Degree

FibroScan Controlled Attenuation Parameter (CAP) Interpretation

Meta-analysis of 2735 patients comparing histology and CAP with BMI </= 35: **Karlas T et al. J Hepatol. 2017 May;66(5):1022-1030****

CAP measures the increased **attenuation** of ultrasound waves when travelling through steatotic hepatic tissue, compared to normal liver.
Interpretation is based in studies of CAP results paired with liver biopsy samples.

Steatosis Degree	S0	S1	S2	S3
Affected Hepatocytes (%)	< 10%	10-33%	34-66%	> 66%
CAP (dB/m)	< 248	248-267	268-279	> 280

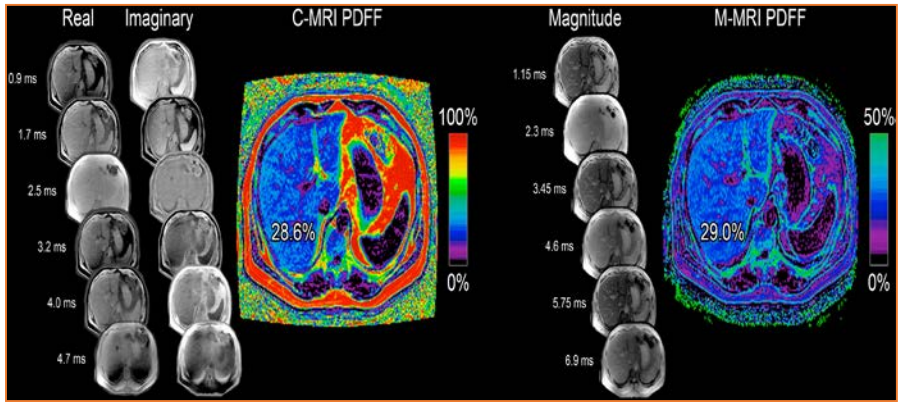
CORRECTIONS:
Deduct 10 dB/m for NAFLD/NASH
Deduct 10 dB/m for Diabetes
Deduct 4.4 dB/m for each BMI point below 25 (max 22 dB/m)
Add 4.4 dB/m for each BMI point above 25 (max 22 dB/m)

**Patients with BMI > 35 were excluded

CAP validity is lower if the IQR of CAP is ≥ 40 dB/m (AUROC 0.77 vs 0.9 if < 40)

MR Imaging Methods to Estimate Proton Density Fat Fraction (PDFF)

- Fat (TG) has a chemical signature
- This chemical signature can be detected by magnetic resonance spectroscopy (MRS)
- MRS quantifies the *proton density fat fraction (PDFF),* a standardized measure of liver tissue [TG]
- Limitations of MRS
- One 8cm^3 voxel
- Not available on routine scanners
- Requires expertise



- MRI-PDFF addresses confounding factors, unlike conventional in-phase and opposed-phase
- MRI-PDFF ***not*** affected by
  - Scanner field strength
  - Patient factors: age, sex, BMI, etiology of liver disease
  - Concomitant liver abnormalities: iron overload, necro-inflammation

Thomsen MRI 1994, Hamilton JMRI 2009, Hamilton NMR Biomed. 2011. Reeder JMRI 2011, Yu MRM 2008, Bydder MRI 2008, Bydder MRI 2010, Hansen MRI 2012, Kang Invest Radiol 2012, Kuhn Radiology 2012, Tang Radiology 2013, Dulai, Sirlin, Loomba J Hep 2016

Thank you for your attention

EASL: Sequential Algorithm for Fibrosis Evaluation (SAFE) in NAFLD

EASL–EASD–EASO CPG NAFLD. J Hepatol 2016;64:1388–402
Journal of Hepatology 2019 vol. 71: 389–396
Am J Gastroenterol. 2017 May; 112(5): 740–751 **

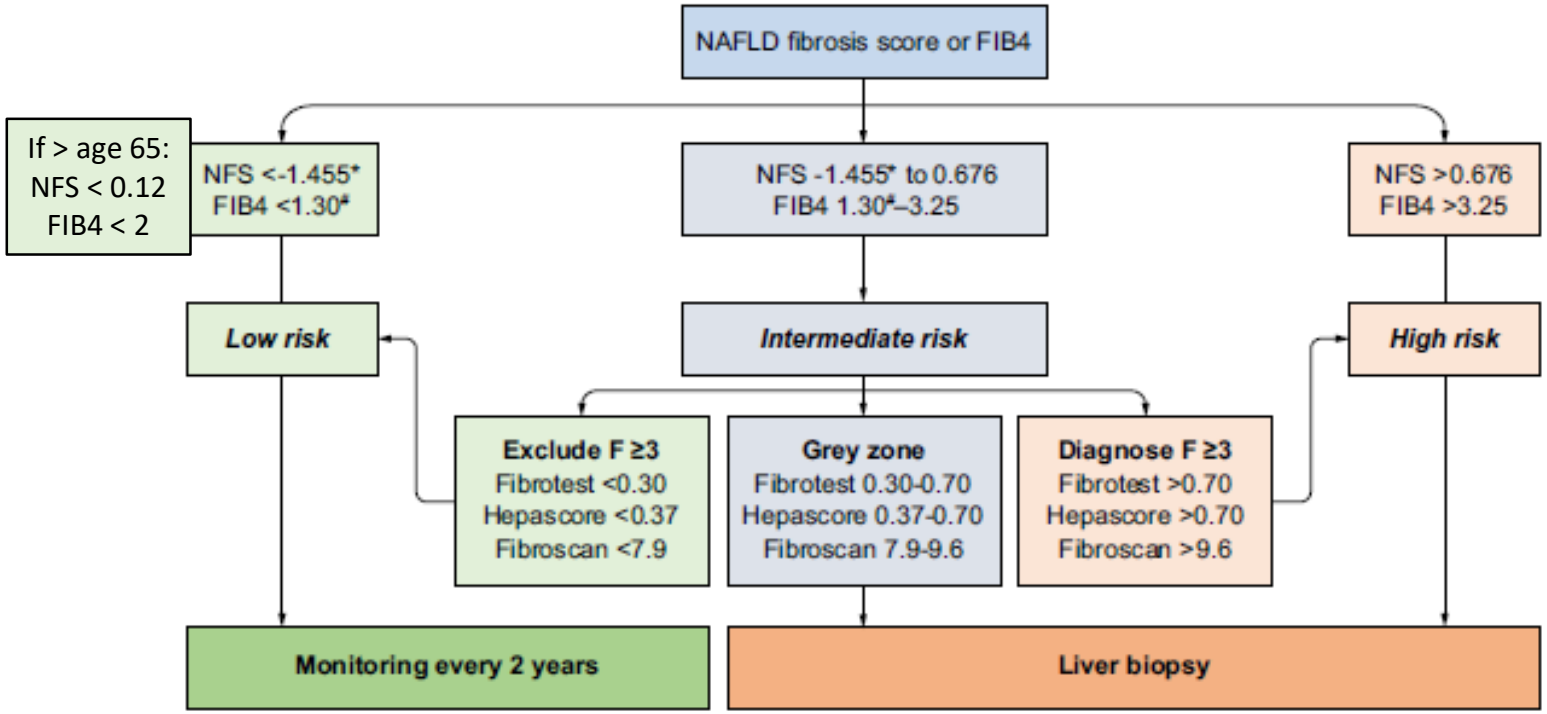
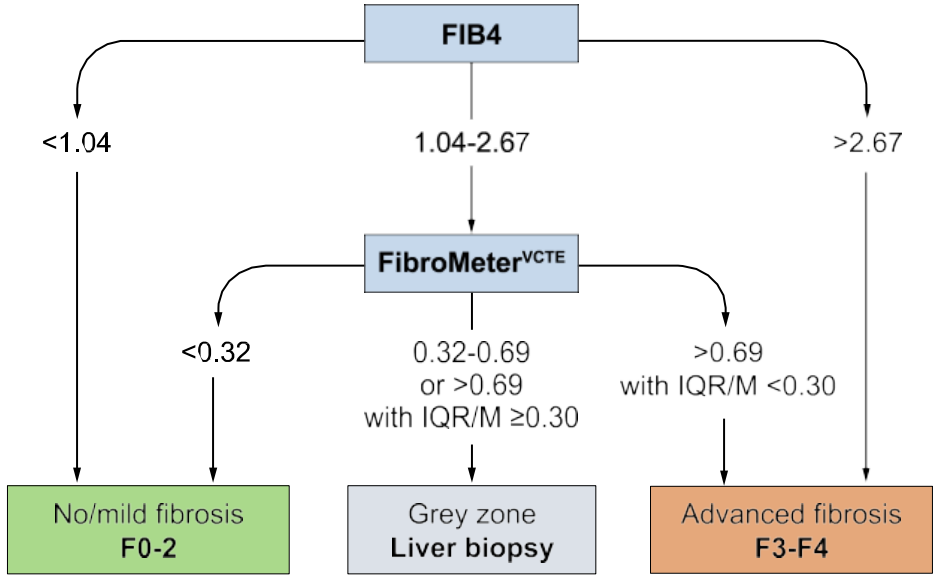


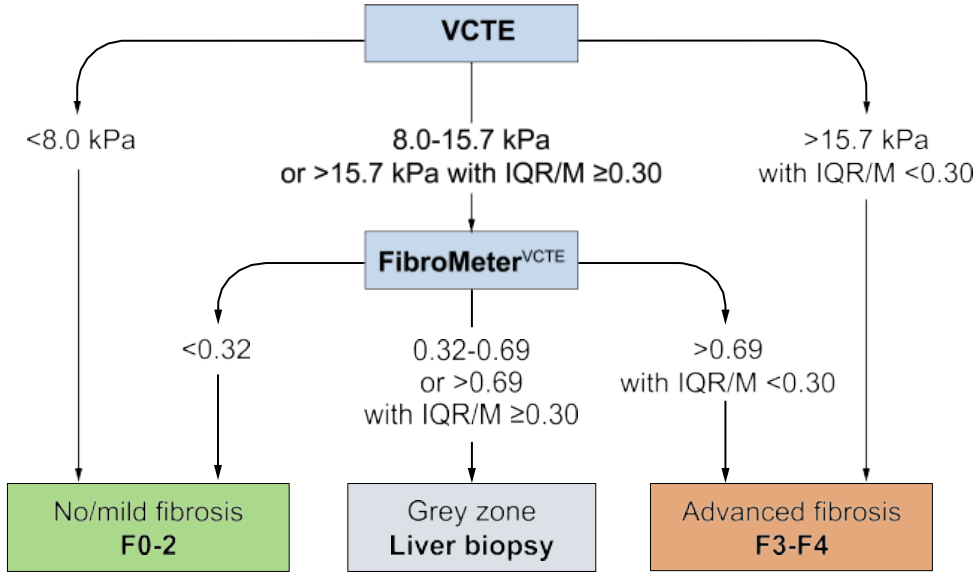
Fig. 1. Diagnostic algorithm proposed by the European Association for the Study of the Liver to non-invasively assess advanced liver fibrosis in patients with NAFLD.[11,12] *NFS threshold: −1.455 in patients <65 years old, 0.12 in patients ≥65 years old. #FIB4 threshold: 1.30 in patients <65 years old, 2.0 in patients ≥65 years old. FIB4, Fibrosis-4; NAFLD, non-alcoholic fatty liver disease; NFS, NAFLD fibrosis score.

Cut of for age >/= 65: **NFS < 0.12 (instead of < -1.455) and **FIB4** < 2 (instead of < 1.3)

FibroMeterVCTE (VCTE + Blood Marker) in NAFLD

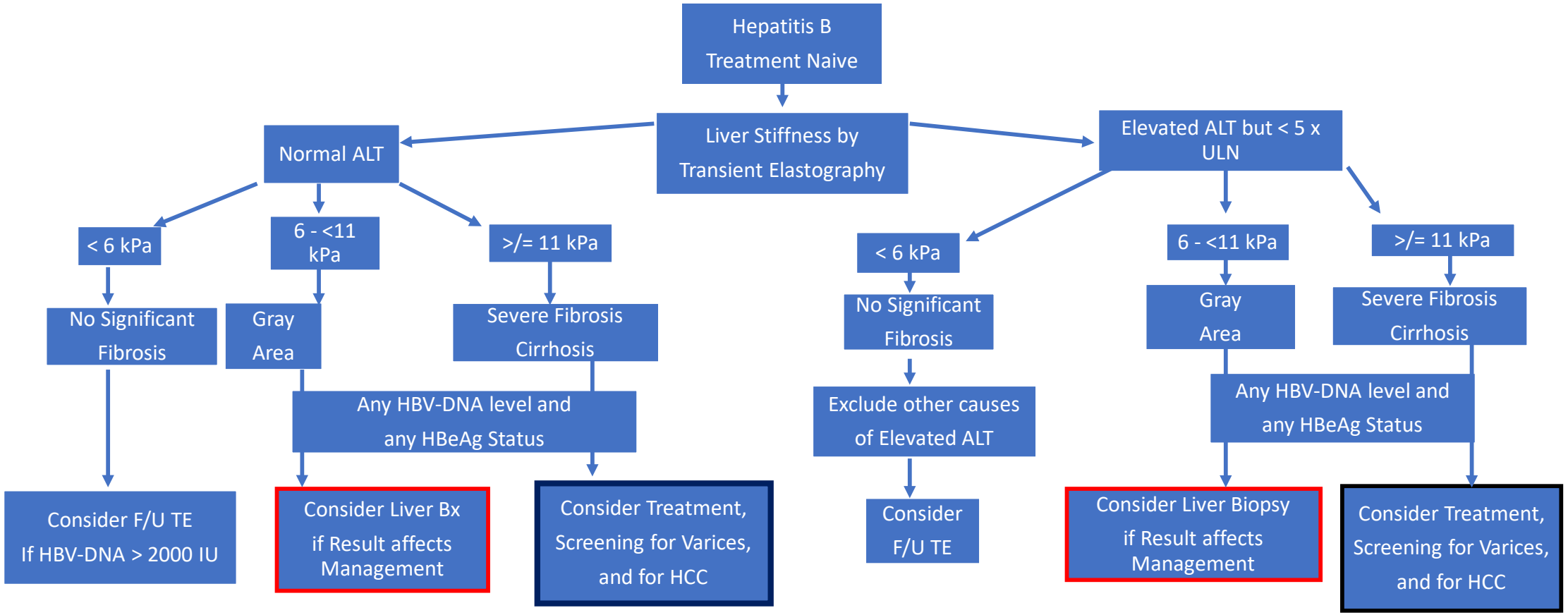
Journal of Hepatology 2019 vol. 71: 389–396





Sequential Algorithm for Fibrosis Evaluation (SAFE) in HBV by ALT Elevation & TE

Journal of Hepatology 2015 vol. 63; 237–264 and Gastroenterology 2017 Vol. 152, 1536–1543



APRI > 2 suggests Cirrhosis (WHO)
TE is preferred over APRI