Initial Evaluation and Follow Up for Patients with Hepatitis C

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Conflicts of Interest

- None

Objectives

- Discuss the initial laboratory testing for patients with Hepatitis C
- Describe the importance of and options for liver fibrosis staging
- Discuss monitoring during and post treatment

Hepatitis C Screening

Hepatitis C Screening

- ~ 3.5 million HCV-infected persons in the United States
  - 2.7 million in the general population
  - 800,000 incarcerated, institutionalized, or homeless persons
  - 50% of all infected people are unaware

Recommendations for One-time HCV Testing

- For all persons born between 1945 and 1965, without prior ascertainment of risk
  - 75% of people with hepatitis C born during these years
  - Increasing HCV associated morbidity and mortality
  - Testing based solely on elevated ALT is estimated to miss 50% of chronic infections

MMWR 2012; 61; 1-18

Recommendations for One-time HCV Testing

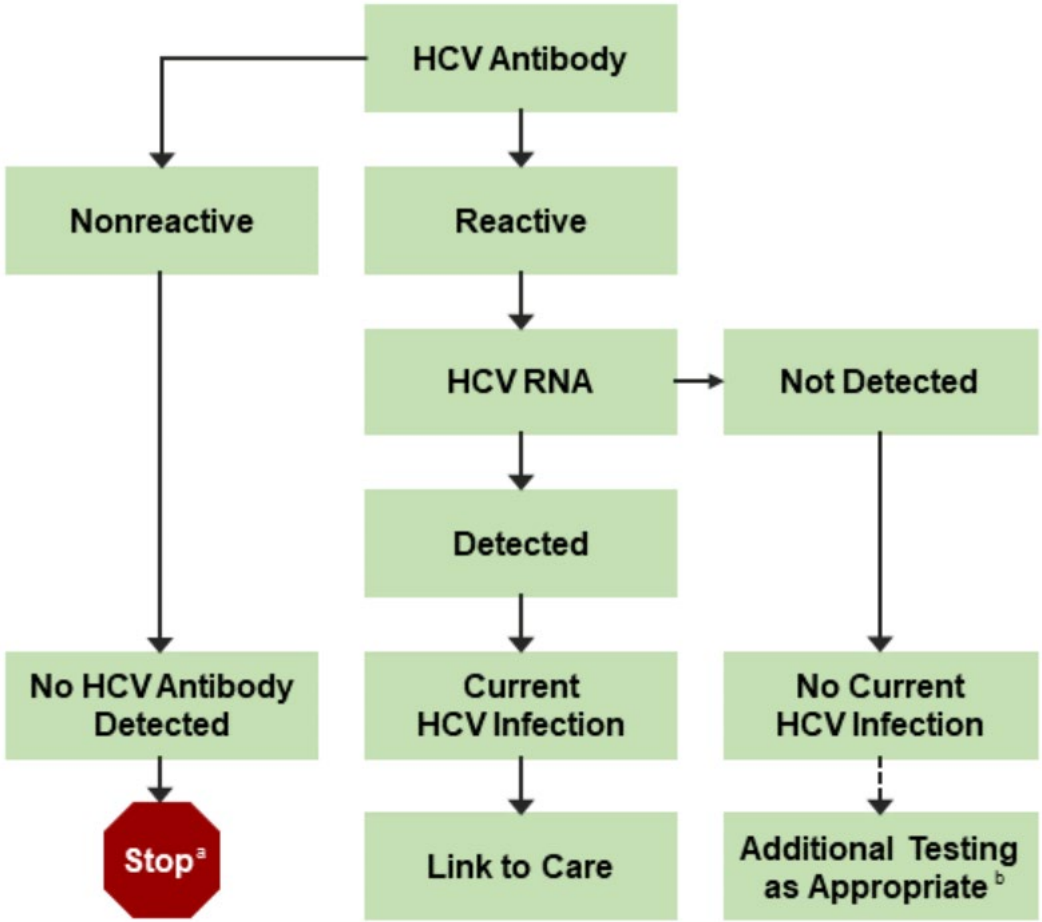
- Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed if present
  - Risk Behaviors
    - Injection Drug use
    - Intranasal illicit drug use
  - Risk exposures
    - Long term hemodialysis (ever)
    - Percutaneous/parenteral exposures to HCV infected blood
    - Children born to HCV infected women
    - Prior recipients of transfusions or organ transplants, including persons who
      - Received transfusion of blood products or underwent an organ transplant before July 1992
      - Received clotting factor concentrates produced before 1987
      - Were notified that they received blood from a donor who later tested positive for HCV
    - Incarceration
  - Other Considerations
    - HIV
    - Sexually active with persons about to start pre-exposure prophylaxis for HIV
    - Unexplained chronic liver disease and/or chronic hepatitis including elevated alanine aminotransferase levels
    - Solid organ donors

Recommendations for HCV Testing Those with Ongoing Risk Factors

- Annual testing for…
  - Persons who inject drugs
  - HIV positive men who have unprotected sex with men

- Periodic testing for…
  - Other persons with ongoing risk factors for exposure to HCV

Hepatitis C Testing



www.hcvguidelines.org

Hepatitis C Testing

What about universal screening?

HCV Screening – UK HealthCare Emergency Department

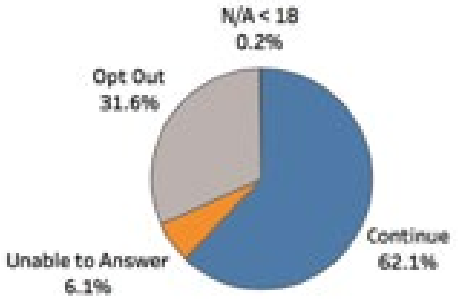
- Opt out screening for all adult patients coming through the emergency department
- Project funded by Gilead FOCUS
  - PI James Moore, MD

Project funded by Gilead FOCUS; PI James Moore, MD

HCV Screening – UK HealthCare Emergency Department

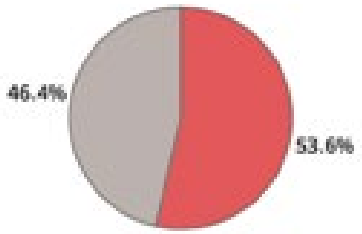
	Screened Date				
	July 2018	August 2018	September 2018	October 2018	Grand Total
Days Reported	16	31	30	7	84
Unique Patients Screened	2,012	3,893	3,814	888	9,708
Unique Continued Patients	1,242	2,582	2,513	575	6,516
Continue Rate	59.4%	62.9%	62.4%	63.5%	62.1%
HCV Ab Results Received	883	1,823	1,767	381	4,854
HCV Ab invalid/indeterminate/no result	1	1			2
HCV Ab+	101	203	217	44	565
HCV Ab+ Rate	11.5%	11.2%	12.3%	11.6%	11.7%
RNA Results Received	96	195	197	38	526
HCV RNA invalid/indeterminate/no result	23	28	22	2	75
HCV RNA+	51	107	105	19	282
HCV RNA+ Rate	53.1%	54.9%	53.3%	50.0%	53.6%

Screening



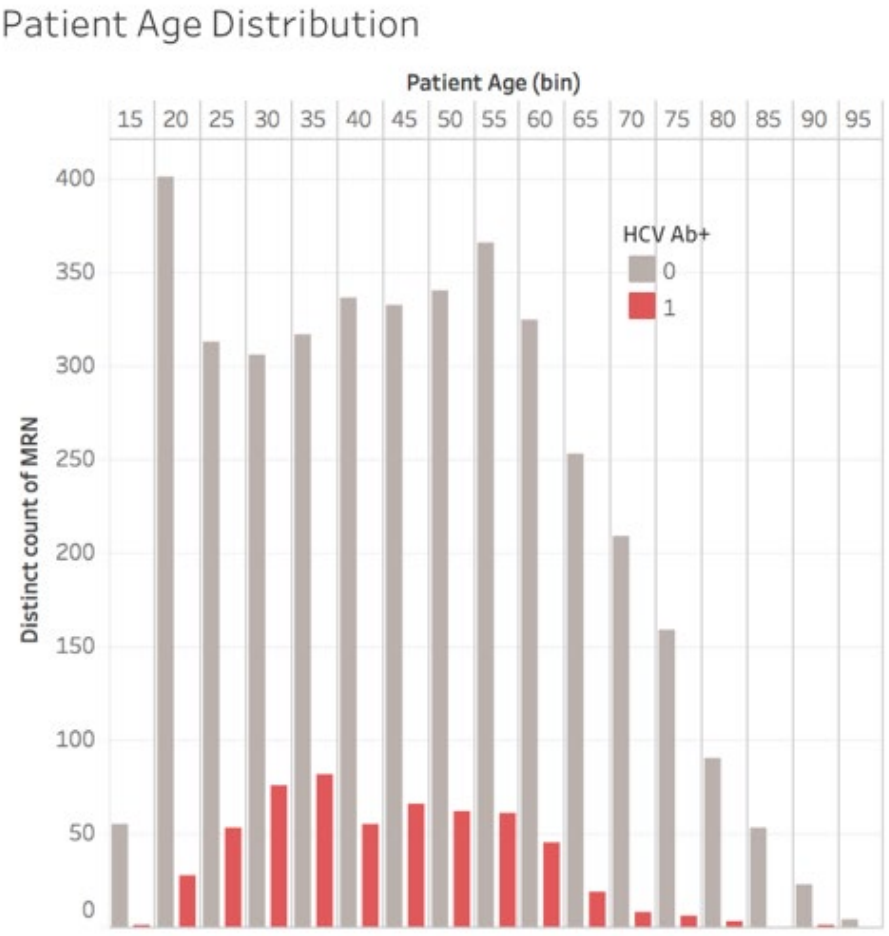
HCV Ab+

HCV RNA+



Preliminary Data

HCV Screening – UK HealthCare Emergency Department



Preliminary Data

HCV Screening – UK HealthCare Emergency Department

- ½ of patients are lost to follow up from diagnosis to initial visit
- Majority of HCV positive patients are outside of CDC recommended age cohort testing or targeted screening
- Overall HCV ab+ prevalence – 12%
  - Age 25-64 prevalence – 19%

HCV Screening – UK HealthCare Emergency Department

The Future…

- Real time HCV RNA testing
- Real time initiation of treatment
- Paired with medication assisted therapy

HCV Linkage to Care

- HCV screening will have minimal impact without improvements in linkage to care
- Patient related barriers
  - Lack of acceptance of treatment
  - Lack of access to treatment
- Clinician related barriers
  - Lack of expertise
  - Resistance to treating persons using illicit drugs
  - Concern about the cost of HCV treatment

HCV Linkage to Care

- Strategies
  - HIV care models
    - Use of case manager and patient navigators
  - Collaborate with specialists (telemedicine and Project ECHO)
  - Co-localization (integrated care)

Initial Assessment

History and Physical

- When and how diagnosed
- Risk factors
  - Injection drug use
  - Nasal drug use
  - Tattoos
  - Blood transfusions
  - Tattoos and piercings
  - Sexual exposures
  - Family exposures
- Prior work up
- Prior treatment
- Comorbidities
  - EtOH use, hepatotoxic drugs
  - Psychiatric
- Family hx of liver disease
- Current Medications

Initial Labs

- CBC
- INR
- Hepatic Function Panel
- Calculated GFR
- HCV genotype with subtype
- Quantitative HCV RNA
- HIV
- Total anti-HAV
- HBsAg / Anti-Hbs /Anti-HBc

Optional Screening Considerations

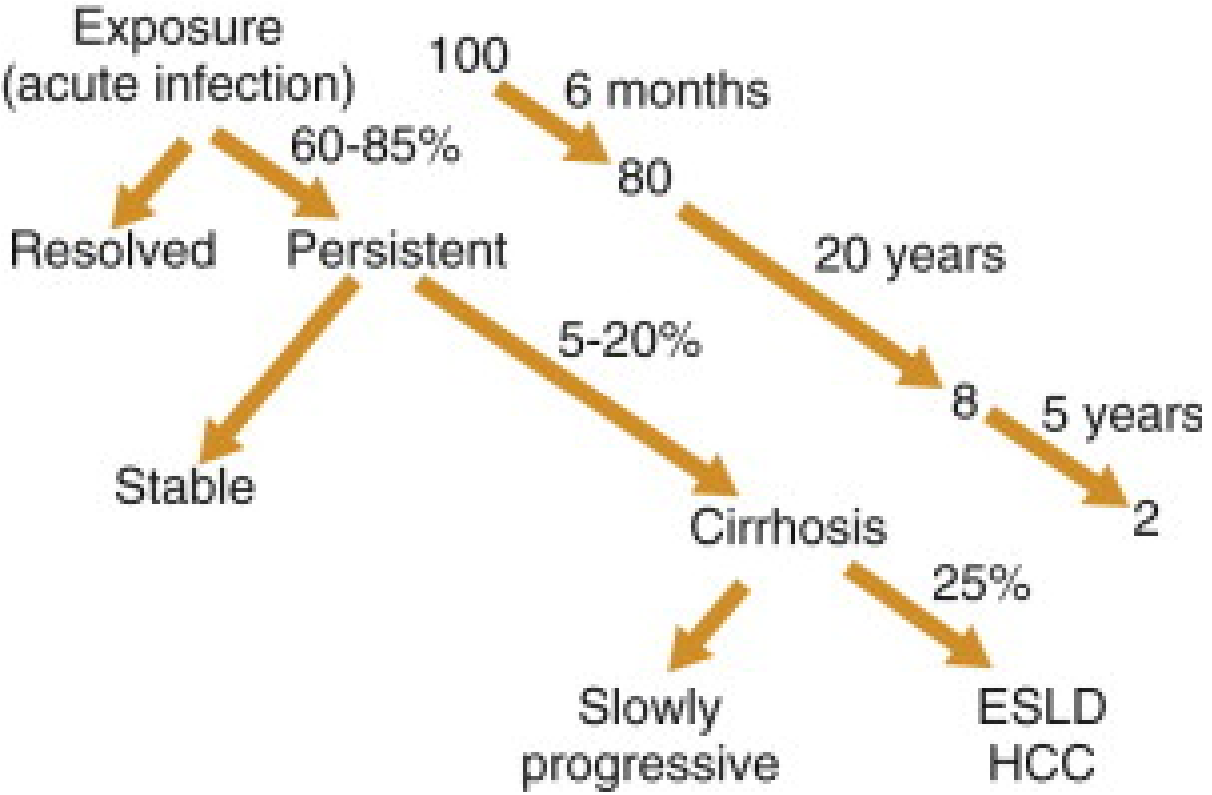
- Alpha-1 antitrypsin deficiency
  - Alpha-1 antitrypsin level
  - Alpha-1 antitrypsin phenotype
- Wilson's Disease
  - Ceruloplasmin
  - Urinary copper
- Autoimmune liver disease
  - ANA, anti-smooth muscle ab, antimitochondrial ab
- Genetic hemochromatosis
  - Ferritin, iron saturation

Transmission Reduction Counseling

Persons with Hepatitis C should…

- Avoid sharing razors/toothbrushes
- Be counseled to stop illicit drugs and enter substance abuse treatment
- Be advised not to donate blood and to discuss HCV status prior to donation of body organs, other tissue, or semen
- Be encouraged to use barrier precautions to prevent sexual transmission if they have HIV, multiple sexual partners, or sexually transmitted infections
- Clean and disinfect visible blood using a 1:10 household bleach dilution

Natural History of Hepatitis C



Ray, S et al. Ch 154 **Hepatitis C**. *Principles and Practice of Infectious Disease. 7th Ed*.

Pre-Treatment Assessment

- Other recommended assessments
  - Hepatic Fibrosis Staging
    - Liver biopsy, imaging, and/or noninvasive markers
  - Potential drug-drug interactions
    - Never too early to consider this

Hepatic Fibrosis Staging

Non-Invasive Fibrosis Staging

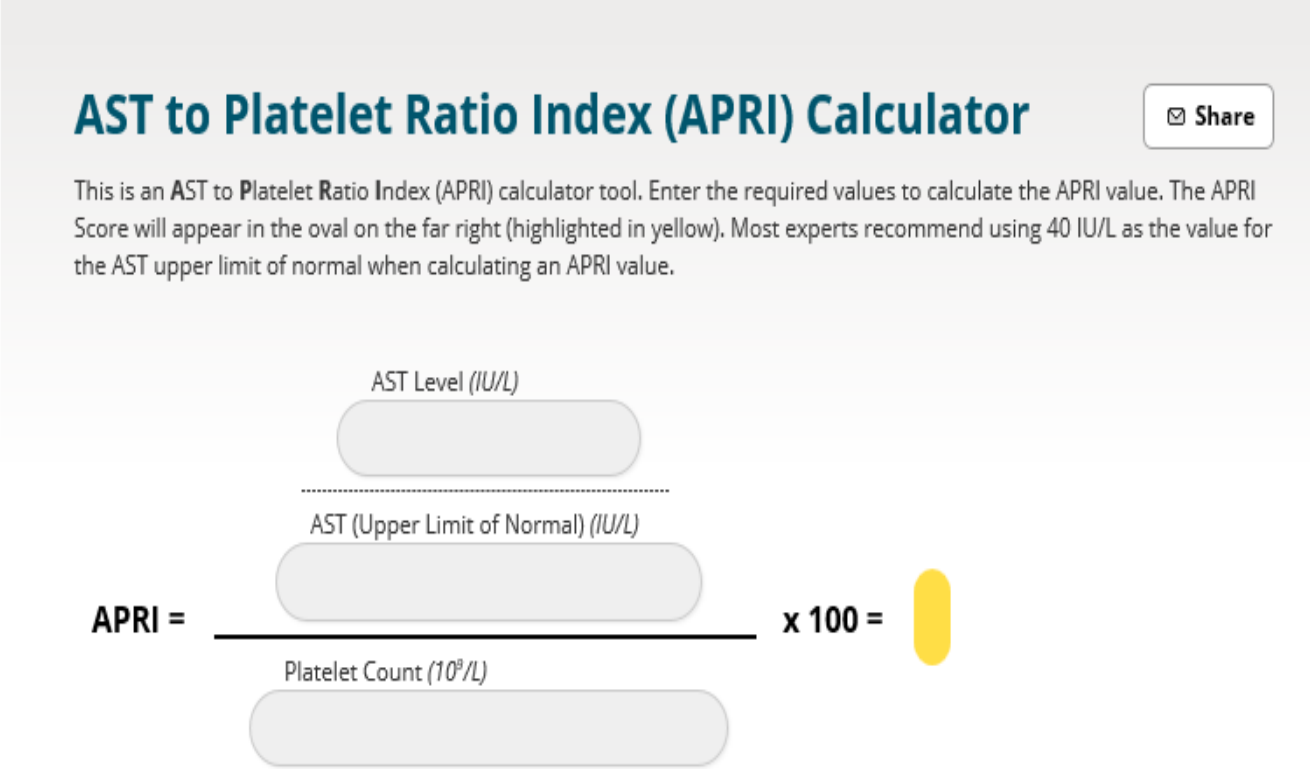
Blood Test

- FibroSure / FibroTest
- AST to Platelet Ratio (APRI)
- FIB-4

Imaging

- Transient Elastography
- MRI elastography
- MR Spectroscopy
- Diffuse weighted MRI

Non-Invasive Fibrosis Staging

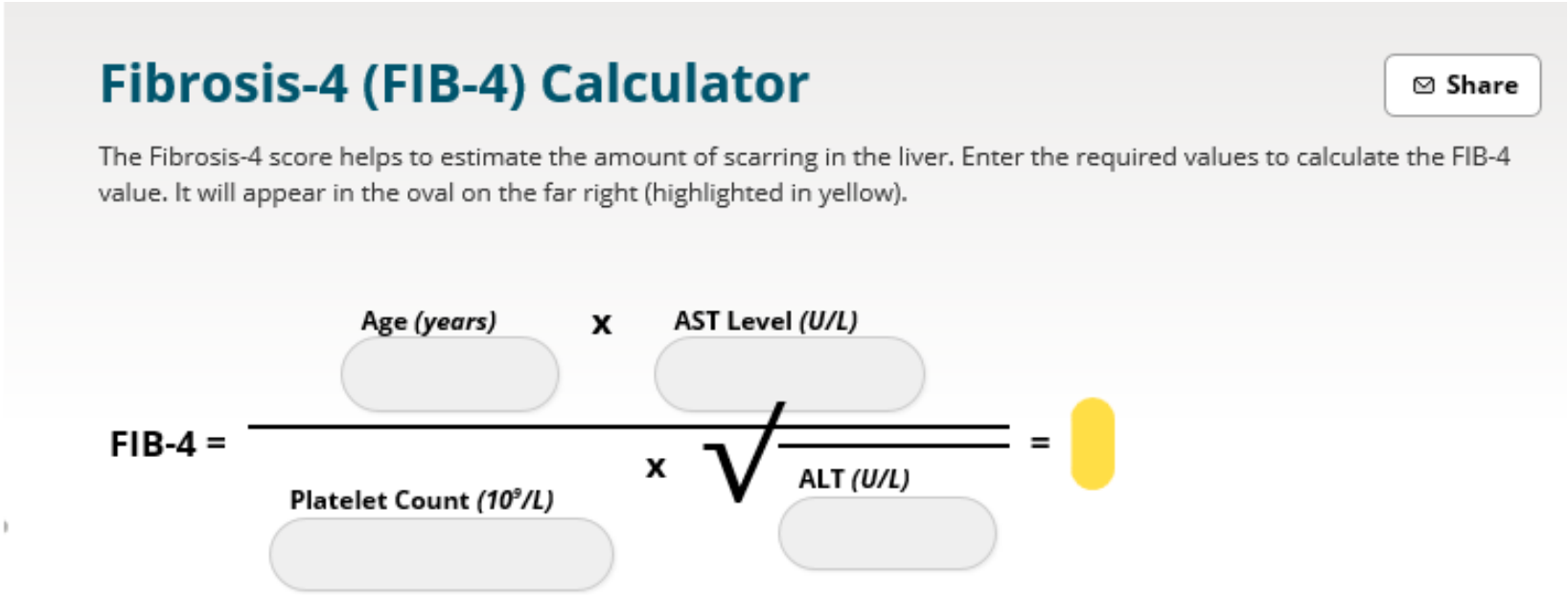


➢**1** = sensitivity of 76% and specificity of 72% for predicting **cirrhosis**

➢**0.7** = sensitivity of 77% and specificity of 72% for predicting **significant hepatic fibrosis**

www.hepatitisc.uw.edu

Non-Invasive Fibrosis Staging



< 1.45 = negative predictive value of 90% for **advanced fibrosis**

> 3.25= 97% specificity and positive predictive value of 65% for **advanced fibrosis**

Hepatic Fibrosis Staging

Table 1. Comparison of FIB-4 Index and Liver Biopsy Results

	Liver Biopsy (METAVIR)		
FIB4 Index	F0-F1-F2	F3-F4	Total
<1.45	94.7% (n = 521)	5.3% (n = 29)	550
1.45-3.25	73.0% (n = 168)	27.0% (n = 62)	230
>3.25	17.9% (n = 12)	82.1% (n = 55)	67
Total	82.8% (n = 701)	17.2% (n = 146)	847

Hepatology, Vol. 46, No. 1, 2007

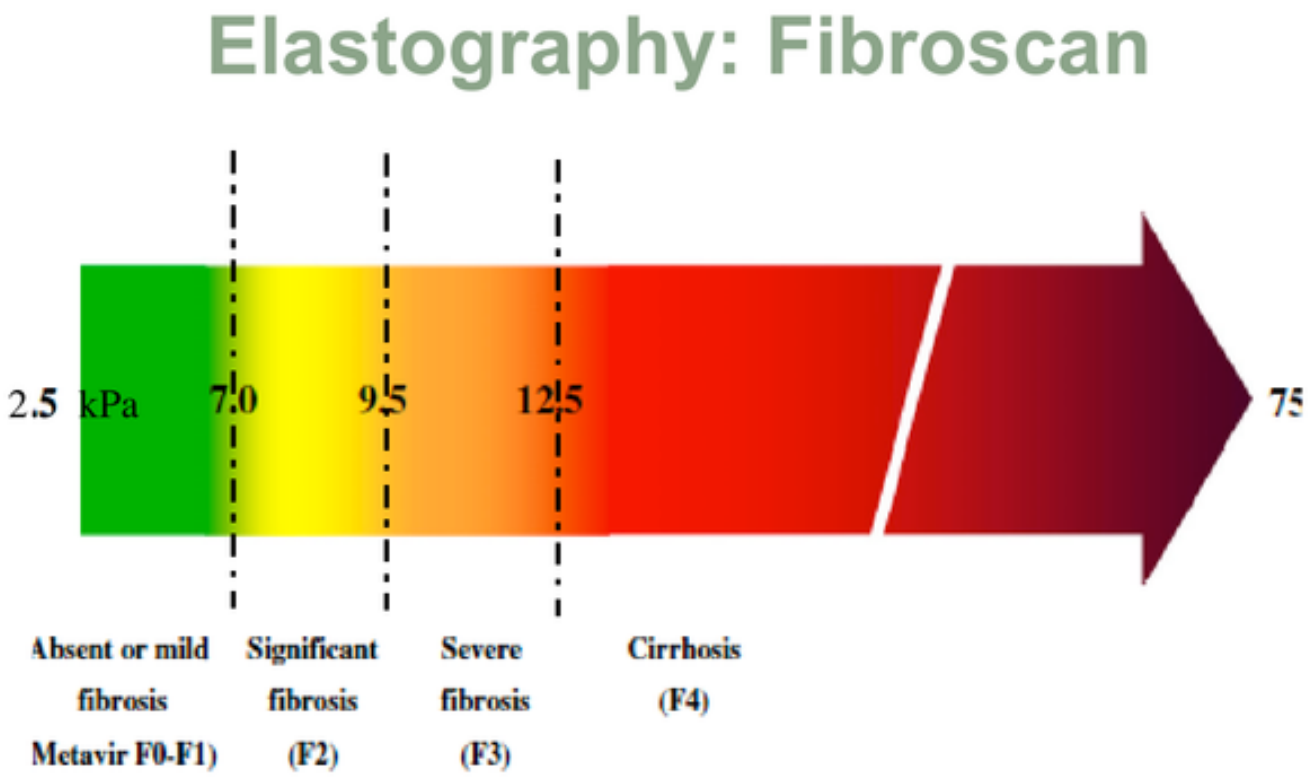
Hepatic Fibrosis Staging

Table 2. Comparison of FIB-4 Index and FibroTest Results

	FibroTest (METAVIR)		
FIB4 Index	F0-F1-F2	F3-F4	Total
<1.45	92.1% (n = 409)	7.9% (n = 35)	444
1.45-3.25	62.2% (n = 178)	37.8% (n = 108)	286
>3.25	24.0% (n = 12)	76.0% (n = 38)	50
Total	76.8% (n = 599)	23.2% (n = 181)	780

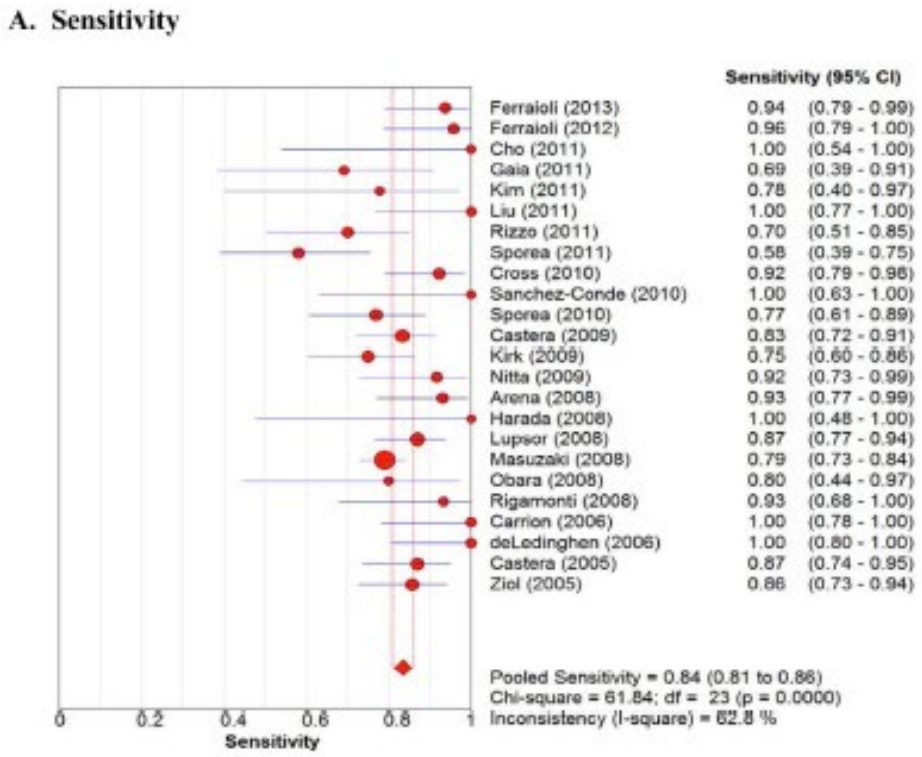
Hepatology, Vol. 46, No. 1, 2007

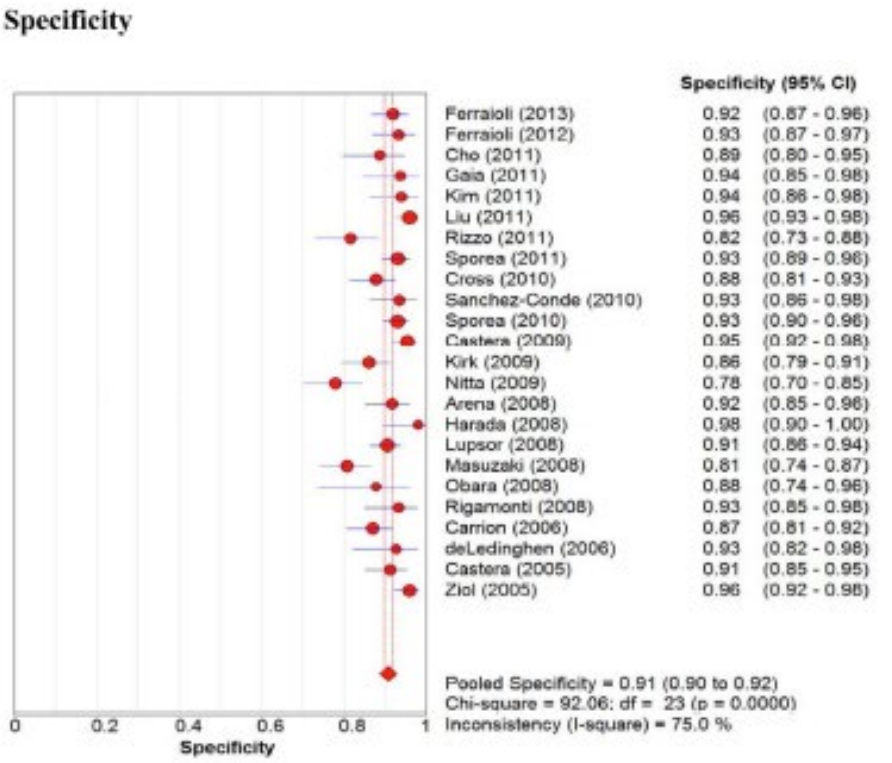
Hepatic Fibrosis Staging



Affected by weight, access of probe (2 cm), steatosis

Transient Elastography



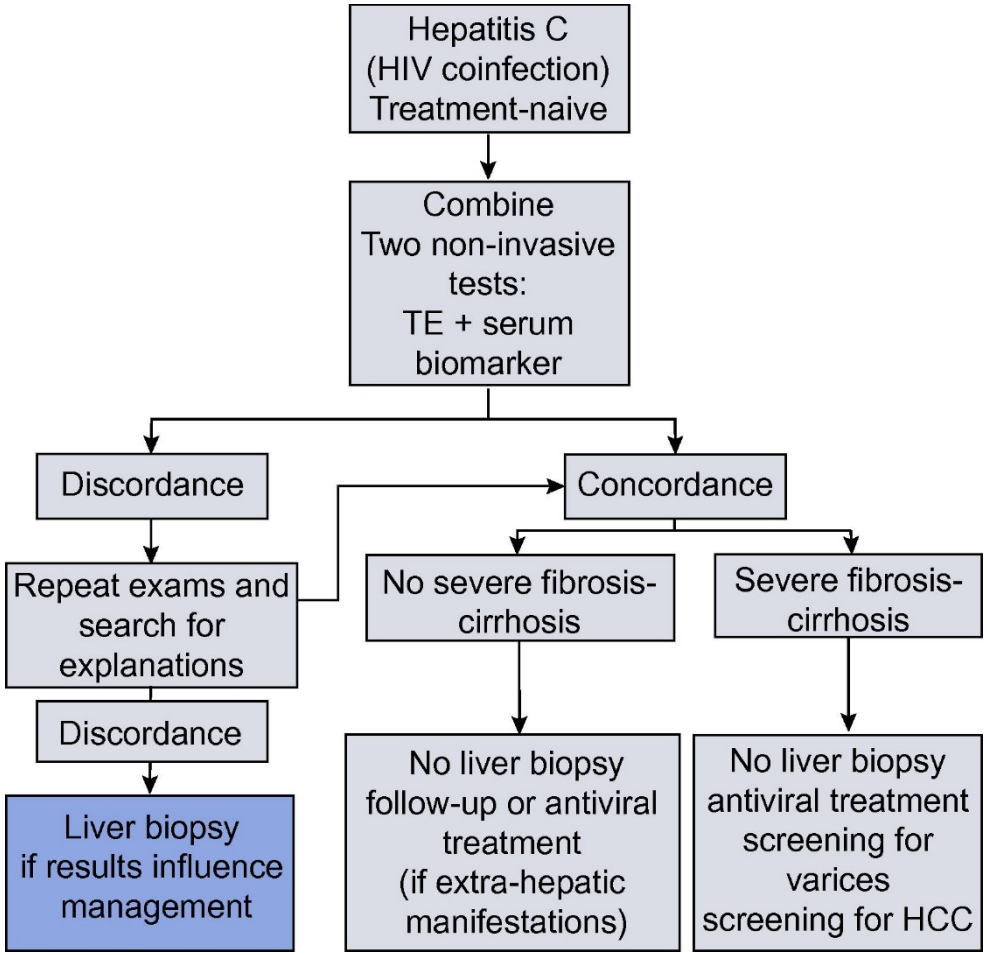


Sensitivity 84%

Specificity 90%

Clin Invest Med 2015; 38 (5): E150-160

Combining Blood Tests with Transient Elastography



Journal of Hepatology 2015 63, 237-264DOI: (10.1016/j.jhep.2015.04.006

Monitoring

Monitoring During Therapy

- Clinic visits or telephone contact as indicated to ensure
  - Medication adherence
  - Monitoring for adverse events
  - Assess for potential drug-drug interactions
- At Treatment Week 4
  - Creatinine level, calculated GFR, and a hepatic function panel
  - Quantitative HCV viral load

Monitoring During Therapy

- At End of Treatment (EOT)
  - Consider quantitative HCV viral load testing
- At 12 weeks post treatment
  - Quantitative HCV viral load testing
- At 24 weeks post treatment
  - Consider quantitative HCV viral load testing

Monitoring During Therapy

- Hepatitis B Surface Ag positive with HBV DNA level that does not meet AASLD criteria for treatment
  - Initiate prophylactic antiviral therapy until 12 weeks after completion of therapy

  OR

  - Monitor HBV DNA levels during and immediately after therapy
    - Start tx for HBV if DNA rises to >10 fold above baseline or > 1000 IU/mL if previously undetectable or unquantifiable

Monitoring During Therapy

- Discontinuation of Treatment Because of Lack of Efficacy
  - If HCV RNA detectable at week 4:
    - Repeat after 2 additional weeks
      - If HCV viral load has increased by > 10 fold, discontinue therapy
      - If lower but still positive, no recommendation to stop or extend is provided by the guidelines

Monitoring After Therapy

- Post treatment monitoring for patients in whom treatment failed to achieve SVR
  - Evaluate and consider for retreatment
  - Assess disease progression every 6 to 12 months with hepatic function panel, CBC, and INR
  - Screen for hepatocellular carcinoma and esophageal varices as indicated

Monitoring After Therapy

- Post treatment monitoring for patients who achieved a Sustained Virologic Response (SVR)
  - For patients without advanced fibrosis (F0-2), follow up is same as if they were never infected
  - Assess for recurrence if ongoing risk
  - For patients with advanced fibrosis (F3-4), assess for HCC with ultrasounds every 6 months
  - Baseline assessment for esophageal varices if cirrhosis is present

Summary

- Current recommendations include screening patients at risk for HCV based on risk factors and age
  - Consider additional screening if local rates of HCV infection are high
- Linkage to care is critical
- All patients need baseline hepatic fibrosis assessment
- Monitoring during therapy can vary but all patients should at least get labs at 4 weeks of treatment and at 12 weeks post treatment
- Hepatocellular carcinoma risk continues for patients with cirrhosis even after Sustained Virologic Response has been achieved
  - Screen with ultrasounds every 6 months