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When Is a Liver Biopsy Necessary?

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Disclosures

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No financial relationships to disclose.

Liver Biopsy Indications

- Liver biopsy currently has three major roles:
  1. For diagnosis
  2. For assessment of prognosis (disease staging)
  3. To assist in making therapeutic management decisions

https://aasldpubs.onlinelibrary.wiley.com/doi/10.1002/hep.22742

Liver Biopsy Indications

- Liver biopsy is particularly useful in patients with atypical clinical features; diagnostic dilemma
- Parenchymal liver disease and staging
  - Alcohol-related liver disease/ nonalcoholic steatosis
  - Viral vs. autoimmune hepatitis
  - Heavy metal storage disorders (hemochromatosis, Wilson disease)
  - Suspected rejection or other complication after liver transplant
  - Unexplained intrahepatic cholestasis (primary biliary cholangitis vs. primary sclerosing cholangitis vs. drug induced liver injury)
  - Drug induced liver injury (hepatotoxic drugs, i.e methotrexate)
- Chronic abnormal liver tests of unknown etiology after noninvasive evaluation
- Fever of unknown origin
- Abnormalities on imaging studies

https://www.uptodate.com/contents/approach-to-liver-biopsy?search=liver+biopsy

Complications

- Pain
- Bleeding
- Infection
- Injury
- Seeding a tumor
- Intra-abdominal hemorrhage
- Bile peritonitis
- Lacerated liver
- Hospitalization
- Death

**Complications usually become evident within 3-4 hours

Contraindications

- Severe thrombocytopenia <50,000
- Bleeding tendency (INR > 1.5)
- Suspected vascular lesion (e.g., hemangioma)
- Patient's inability to remain still, uncooperative patient
- Profound anemia
- Peritonitis, infection of the hepatic bed
- Marked ascites
- Right pleural infection or effusion
- Morbid Obesity

Lindenmeyer, C. L. *Liver Biopsy*. 2019, December. Merck Manual. https://www.merckmanuals.com/professional/hepatic-and-biliary-disorders/testing-for-hepatic-and-biliarydisorders/liver-biopsy; Liver Biopsy: When Are Other Liver Tests Appropriate? *Love*. https://labblog.uofmhealth.org/rounds/alternatives-to-liver-biopsy-when-are-other-tests appropriate; Rockey, D. C., Caldwell, S. H., Goodman, Z. D., Nelson, R. C., & Smith, A. D. *Liver Biopsy*. *Hepatology*. 2008; 49(3), 1017-1044. doi:10.1002/hep.22742.

Complications Continued…

Factors that May Influence Complication Risk with Liver Biopsy Patient:

- Cooperation
- Coagulation status
- Operator experience
- Use of image guidance
- Type of technique (percutaneous/transvenous)
- Number of needle passes
- Needle diameter
- Type of needle

Rockey, D. C., Caldwell, S. H., Goodman, Z. D., Nelson, R. C., & Smith, A. D. Liver biopsy. *Hepatology.* 2008; 49(3), 1017-1044. doi:10.1002/hep.22742.

Limitations

- Sampling error (many liver diseases do not uniformly affect the liver)
- Sampling size (at least 3cm in length, 16g or larger core needle)
- Occasional errors
- Risk of complications vs. noninvasive methods
- Varying interpretations by pathologist
- Expense, costly
- Need for interventional radiologist

Lindenmeyer, C. L. *Liver Biopsy*. 2019, December. Merck Manual. https://www.merckmanuals.com/professional/hepatic-and-biliary-disorders/testing-for-hepatic-and-biliarydisorders/liver-biopsy; Liver Biopsy: When Are Other Liver Tests Appropriate? *Love*. https://labblog.uofmhealth.org/rounds/alternatives-to-liver-biopsy-when-are-other-tests appropriate; https://www.uptodate.com/contents/approach-to-liver-biopsy?search=liver+biopsy.

Alternatives

- Fibroscan
- APRI (AST to Platelet Ratio Index)
- Fib 4 (Fibrosis-4)
- Liver imaging: Ultrasound, CT, MRI, MRCP, ERCP
- Liver workup: ANA, ASMA, AMA, Quantitative Immunoglobulin panel, Ferritin, Alpha 1 antitrypsin/phenotype, viral workup

Alternatives Continued…

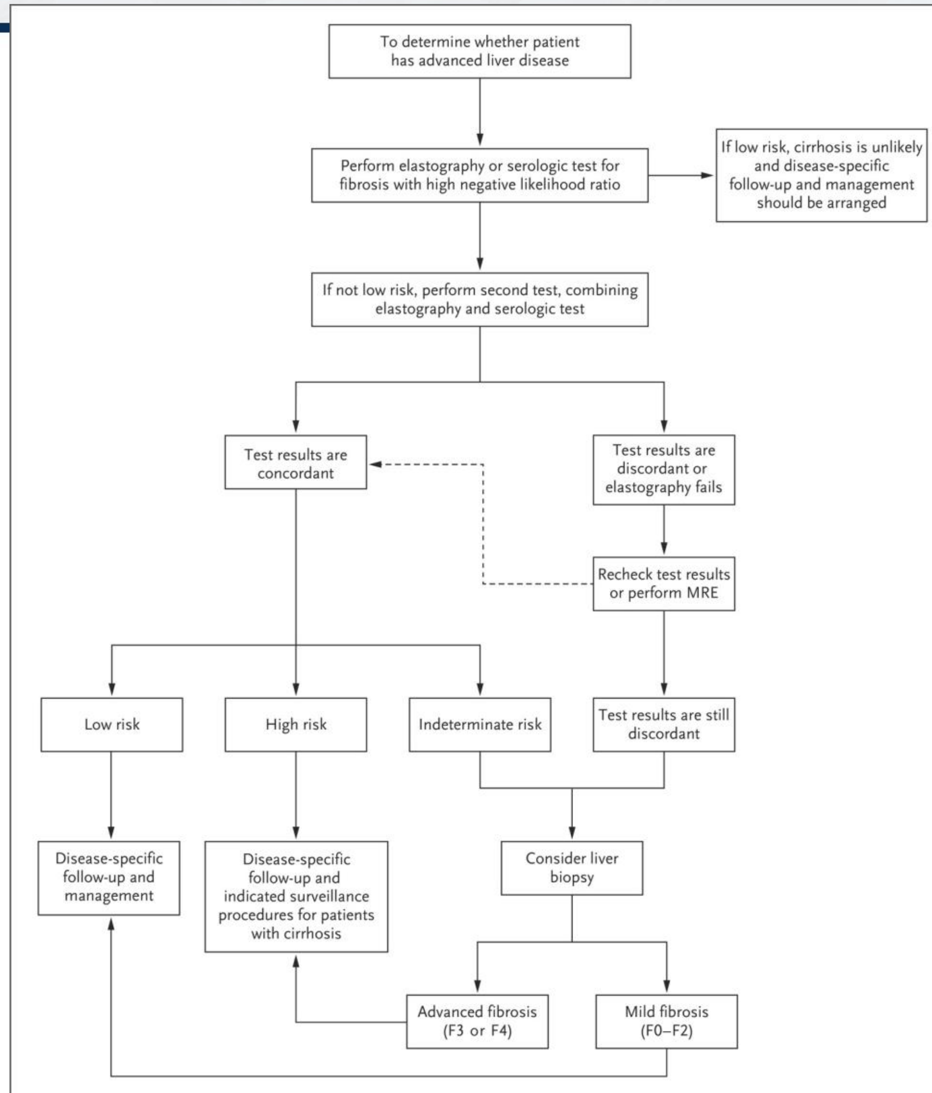
$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count } (10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}}$$

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

- <1.45 excludes severe fibrosis (F3-F4) with high negative predictive value
- >3.25 has high predictive value for significant (F3-F4 fibrosis)

- APRI<0.5 will rule out cirrhosis
- All non-invasive tests do not work as well with intermediate levels of fibrosis

Vallet-Pichard A, et al. *Hepatology*. 2007;46:32-6; Ding D, et al. *Int J Clin Exp Med.* 2015;8:20876-82.



The NEW ENGLAND JOURNAL of MEDICINE

Tapper EB, Lok AS-F. *N Engl J Med*. 2017;377:756-768.

Case #1-LG

- New patient: 56 year Hispanic female
- Referred by PCP after patient presented to a local ED for abdominal pain
- Complete abdominal US noted hepatic steatosis
- Elevated LFTs

Case #1 – Med Hx and Medications

Medical History

- Hypertension
- Diabetes mellitus, type 2
- Obesity, BMI 40
- Obstructive sleep apnea

Medications

- Metformin 1000 mg BID
- Glipizide 5 mg daily
- Amlodipine 10 mg daily
- Ibuprofen 200 mg PRN

Case #1 Diagnostic Testing and Labs

Diagnostic Tests:

- Complete abdominal US: hepatomegaly with fatty infiltration. Spleen normal in size, no ascites
- Fibroscan: 14.5 kPa, CAP 300

Labs:

- AST 75/ALT 44
- Alkaline phosphatase 175
- Total bilirubin 0.4
- Albumin 3.7
- INR 1.1
- PLT 250,000
- HbA1c 9.8
- Creatinine 1.0

Case #1 Discussion

- What's your diagnosis?
- Do you have enough information to confidently make a diagnosis? If not, what more do you need?
- Do you need a liver biopsy? Why?

Case #1 Biopsy

- Biopsy performed to confirm diagnosis and fibrosis staging due to inconsistent findings between Fibroscan and indirect markers (US, PLT, etc)
- Biopsy: hepatic steatosis with steatohepatitis (NASH), NAS 4/8, stage 2/4 fibrosis

Case #2 – BS

- 66 year old White female, status post liver transplantation in 2015 for primary biliary cholangitis (PBC).
- Has done well.
- Immunosuppression decreased 3-4 weeks ago due to rising creatinine.
- Last liver biopsy (2016): mild, chronic, nonspecific inflammation, no fibrosis or steatosis, no findings to suggest biliary issues.
- On routine labs, patient noted to have elevated alkaline phosphatase, AST/ALT. Repeat testing continues to show elevations.

Case #2 Med History and Medications

Medical History

- Liver Transplant – 2015
- Hypertension
- Impaired fasting glucose
- Asthma
- Chronic back pain
- Arthritis
- Hyperlipidemia

Medications

- Tacrolimus 2mg BID
- Ursodiol 500 mg BID
- Lisinopril 10 mg daily
- Acetaminophen 500 mg prn
- Tramadol 50 mg prn
- Atorvastatin 40 mg daily

Case #2 Diagnostic Testing and Labs

Diagnostic Tests

- Complete abdominal US: normal appearing liver. Enlarged spleen. No ascites.
- Fibroscan: 7.5 kPa, CAP 240

Labs

- Alkaline phosphatase 180
- AST 77, ALT 89
- Total bilirubin 0.8
- INR 1.0
- Albumin 3.5
- PLT 160,000
- HbA1c 7.1
- Tacrolimus level 6.1
- Creatinine 1.4

Case #2 – Discussion

- What's your diagnosis?
- Do you have enough information to confidently make and diagnosis? If not, what more do you need?
- Do you need a liver biopsy? Why?

Case #2

Biopsy was performed.

- Pathology describes active inflammation, no steatosis, no fibrosis. Findings consistent with acute cellular rejection.

Case #3 AM

- 26 y/o white male who presents to clinic for initial evaluation of chronic HCV
- Unknown fibrosis stage and elevated AST/ALT
- Sober from injection drug use and intranasal drug use for the past 3 years, but admits to taking illicitly obtained Suboxone and Gabapentin

Case #3 – PMH and Medications

Medical History

- Hypertension
- Tobacco Use
- Substance use history
- Obesity
- Schizoaffective Disorder
- Depression
- Obesity

Medications

- Melatonin 10mg qhs
- Nortriptyline 300mg qhs
- Olanzapine 15mg qhs
- Propanolol 20mg TID
- Duloxetine 60mg daily

Case #3 Labs and Diagnostic Testing

- HCV RNA 4,480,000
- HIV Nonreactive
- AST 194 / ALT 466
- Albumin 4.4
- Alk phos 73
- Total bilirubin 0.2
- Creatinine 0.6
- Plts 279,000
- INR 1.0
- APRI 0.669. Fib 4 0.47
- Abd U/S: no focal liver lesions, spleen normal, borderline increased liver echogenicity suggesting mild hepatic steatosis, no ascites, no intrahepatic biliary dilation. Likely reactive peripancreatic lymph node.
- Fibroscan 6.5 kPa, 217 CAP

Case #3 Labs and Diagnostic Testing Cont…

- Hep A IgG nonreactive
- Hep B sAg nonreactive
- **Hep B core Ab total reactive**
- Hep B surface Ab >1000
- CMV IgM negative
- EBV IgM negative
- HSV IgM negative
- Hep a IgM nonreactive

- Ferritin 49
- AMA <20
- Actin smooth muscle AB 17
- Alpha-1 antitrypsin 155
- Ceruloplasmin 32.9
- Immunoglobulin G 1423, IgA 224, IgM 119

Case #3 Discussion

- What are the differential diagnoses?
- Do you have enough information to make a diagnosis?
- Do you need a liver biopsy? Why?

Case #3 Biopsy

- Biopsy performed due to marked elevation in liver enzymes, concerns of drug induced liver injury (Zyprexa vs. street drug contamination) vs. other liver disorder such as autoimmune hepatitis.
- Biopsy: Chronic hepatitis with mild activity, mild steatosis with no steatohepatitis, portal fibrosis (stage 1).

Case # 4 DS

- 60 y/o African American male with genotype 1B chronic HCV and HIV co-infection presents to clinic for initial evaluation.
- His fibrosis score is unknown.
- He drinks 5-6 24oz beers daily.
- He attends AA meetings “here and there” and verbalizes he “probably needs to go more.”
- He complains of itchy skin, but otherwise has no other complaints.

PMH and Medications

- HIV/AIDS
- Depression
- Hx of HSV
- Hypothyroid
- Sleep Apnea
- Alcohol Dependence
- Tobacco use
- Schizophrenia, not taking meds
- Chronic HCV

- Sulfamethoxazole Trimethoprim DS 800mg-160mg 1tab daily
- Tenofovir Alafenamide 200mg-25mg 1tab daily
- Dolutegravir 50mg daily

Labs and Diagnostic Testing

- Creatinine 1.0
- Albumin 4.1
- Total bili 0.7
- Alk phos 82
- AST 57 / ALT 33
- Plt 171,000
- INR 1.0
- APRI= 1.150, Fib 4=3.40 (>3.25 suggestive of advanced fibrosis)
- Fibroscan: 5 kPa, 198 CAP
- CD4 54
- HIV viral load 100
- HCV RNA 7,370,000, Genotype 1b
- Hep A IgG reactive
- Hep B sAg nonreactive
- Hep B core IgG nonreactive
- Hep B sAb <3.1
- AFP 2.3

Case #4 Discussion

- What are the differential diagnoses?
- Do you have enough information to make a diagnosis?
- Do you need a liver biopsy? Why?

Case #4 Biopsy

- APRI Fib 4 scores do not correlate with the Fibroscan results. Also, length of HCV infection, coinfection with HIV and daily alcohol use suggest more advanced liver disease or cirrhosis.
- Biopsy: No definite hepatocellular ballooning or Mallory hyaline is observed. Chronic hepatitis with minimal activity and periportal **fibrosis (stage 2**). No significant steatosis. No definite hepatocellular ballooning or Mallory hyaline is observed.

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Q&A