Non-Alcoholic Fatty Liver Disease

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What is more likely to develop into fibrosis or cirrhosis, fatty liver or NASH?
Background

Non-alcoholic fatty liver disease first reported in 1980. There are two histologic subtypes:

- Isolated hepatic steatosis with or without mild inflammation (fatty liver)
  - Most prevalent form of liver disease in the U.S.
- NASH \(\rightarrow\) Non-alcoholic steatohepatitis
  - Hepatocellular injury with or without fibrosis
  - 20% of patients will develop cirrhosis during their lifetime
  - Diagnosis of NASH is strongest predictor for development and progression of liver fibrosis
Risk Factors for NAFLD

- Central obesity (BMI $\geq 30$)
- Hypertension
- Insulin resistance
- Low level of HDL
  - $<40$ mg/dL in men
  - $<50$ mg/dL in women
- FBG $\rightarrow 110$ mg/dL
- Waist circumference
  - $>40$ inches in men
  - $>35$ inches in women

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Box 1. Established Risk Factors Associated With Nonalcoholic Steatohepatitis and More Progressive Disease

**Risk Factors**
- Obesity (central)
- Hypertension
- Dyslipidemia
- Type 2 diabetes
- Metabolic syndrome

**Adult Treatment Panel III Definition of the Metabolic Syndrome**

Patient must have 3 or more of the following:
- Waist circumference of greater than 102 cm in men and greater than 88 cm in women
- Level of triglycerides of 150 mg/dL or greater
- High-density lipoprotein cholesterol level of less than 40 mg/dL in men and less than 50 mg/dL in women
- Systolic blood pressure of 130 mm Hg or greater or diastolic blood pressure of 85 mm Hg
- Fasting plasma glucose level of 110 mg/dL or greater
Diagnosing NAFLD

- Often found incidentally on imaging
  - Asymptomatic or non-specific symptoms
    - May have RUQ pain
  - Central obesity and hepatomegaly common
- Approximately 75 to 100 million people in the U.S. have NAFLD
  - Worldwide median incidence of 20%
Are liver enzymes a good predictive test to diagnose NASH?
Diagnosing NAFLD

No

- 30% - 60% of patients with NASH have a normal ALT level
- Sensitivity and specificity of ALT as a predictor of NASH is 45% and 85% respectively
Diagnosing NAFLD

Need to rule out other causes of fatty liver

- Alcohol
- Hepatitis C
- Wilson’s disease
  - Alpha-1 antitrypsin deficiency
- Acute fatty liver of pregnancy
- Medications
  - Amiodarone, steroids, methotrexate, tamoxifen, valproate, anti-retroviral agents, TPN
Diagnosing NAFLD

Abdominal ultrasound

- Ultrasound has a 93% sensitivity for steatosis when greater than 1/3 of the liver is involved
- Preferred first line diagnostic imaging study
  - Can’t differentiate between steatosis and NASH
  - Steatosis could be fibrosis or early cirrhosis
- MRI best predictor of steatosis \(\rightarrow\) Expensive!
What is the most important factor in patients with NAFLD that affect outcome?
Diagnosing NAFLD

Non-invasive fibrosis test

- NAFLD fibrosis score (NFS)
  - Age
  - BMI
  - Presence or absence of hyperglycemia
  - Platelet count
  - Albumin level
  - Ratio of AST to ALT

- Best at ruling out advanced fibrosis (98% accurate < 0.675)
  - Not significant at predicting F2 or F1 vs. no fibrosis

http://nafldscore.com
Diagnosing NAFLD

Non-invasive fibrosis test

- Transient elastography (FibroScan)
  - Can be done in an office setting
  - Best used to rule out advanced fibrosis
  - Can be obscured by obesity
  - Similar to the lab test (NFS), cannot differentiate well between F1 and F2

- MR elastography
  - Has an 86% sensitivity and 91% specificity for advanced fibrosis
  - Expensive!
Diagnosing NAFLD

Liver biopsy

- Gold standard to determine:
  - NASH (steatosis, hepatocyte ballooning, and lobular inflammation)
  - Fibrosis/Cirrhosis
    - Patients with significant fibrosis or cirrhosis, regardless of cause are at higher risk for hepatoma and need U/S every 6 months with AFP level

- Limited by
  - Invasive test
  - Sampling error → can be seen in up to 40% of patients
Liver Biopsy

A. Steatosis alone (isolated hepatic steatosis)

B. Steatosis with mild lobular inflammation

C. Steatosis with lobular inflammation and cellular ballooning (inset)

D. Fibrosis

E. Cirrhosis

Rinella, ME, Jama 2015
Treatment

- Diet and exercise are the main ways to treat NAFLD
- Weight loss of 10% can result in histologic improvement (Mediterranean diet, DASH diet)
- Abstain from alcohol
- Optimize blood glucose control
- No medication has shown clear, defined improvement (Vitamin E and Actos (pioglitazone))
Treatment

Statins

- Lowering cholesterol can improve fatty liver
- Low incidence of liver toxicity with statins
  - Hydrophilic statins accumulate less in the liver
    - Pravachol (pravastatin) and Livalo (pitavastatin)
    - Crestor (rosuvastatin) has both hyrdophhic and lipophilic properties
  - May be elevations of LFT’s, usually occurs within the first 3 months of treatment → dose dependent
    - ALT > 3x ULN → change medication
- Contraindicated in patients with decompensated cirrhosis or acute liver failure
What is more likely to develop into fibrosis or cirrhosis, fatty liver or NASH?
NASH
References