An Update on Nonalcoholic Fatty Liver Disease (NAFLD)

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ABSTRACT

Nonalcoholic fatty liver disease (NAFLD) is a common chronic disease that is strongly associated with metabolic syndrome but can also be seen in nonobese, nondiabetic patients. This poster reviews the pathophysiology, clinical presentation, diagnosis, and management of NAFLD.

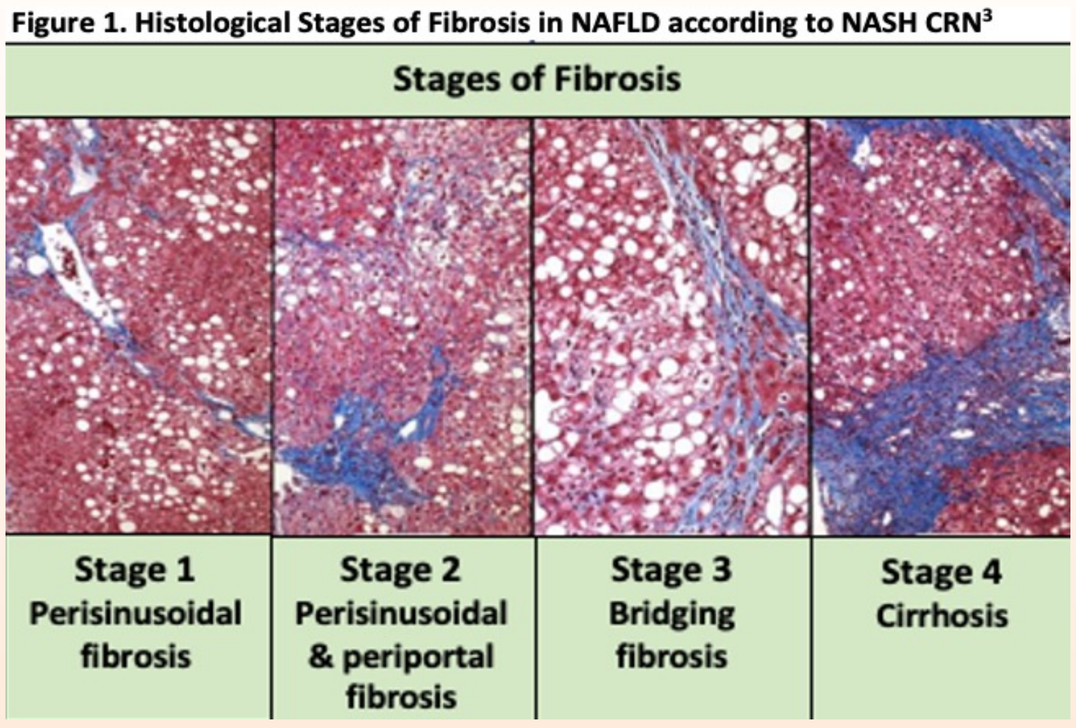
INTRODUCTION

According to the American Association for the Study of Liver Diseases (AASLD), NAFLD is an umbrella term that includes two conditions: nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH).[1] NAFL is defined as the presence of ≧5% hepatic steatosis (HS) without evidence of hepatocellular injury or fibrosis. NASH is defined as the presence of ≧5% of HS with inflammation and hepatocyte injury (e.g. ballooning), with or without fibrosis.[1] NASH can advance to cirrhosis and is a risk factor for hepatocellular carcinoma.[1]

PATHOPHYSIOLOGY

- **Insulin resistance** → failure to suppress hepatic glucose production and FFA release by adipocytes[2] → excessive TGs accumulate in the liver → steatosis, ↑ BG, ↑ TGs
- **Steatosis** → inflammatory factors → metabolic/oxidative stress in fatty hepatocytes → **lipotoxicity** → hepatotoxic repair response → further injury / damage → **NASH** → worsening **fibrosis**[2] → **cirrhosis**

Figure 1. Histological Stages of Fibrosis in NAFLD according to NASH CRN[3]



CONCLUSIONS

- Fibrosis is the key prognostic factor in NAFLD and is correlated with liver-related outcomes and mortality.[7]
- Current pharmacologic treatments aim to improve metabolic components (i.e. treat dyslipidemia, lower IR, combat oxidative stress).[8]
- AASLD Practice Guidelines for NAFLD Care (January 2018):[1]
  - **Weight loss** of ≤ 3-5% of body weight improves steatosis, but a greater weight loss (7-10%) is needed to improve NASH and fibrosis
  - The most common cause of death in NAFLD is cardiac-related → aggressive modification of CVD risk factors should be considered in all NAFLD.[1]
    - **Statins** can be used to treat dyslipidemia in patients with NAFLD and NASH but should be avoided in decompensated cirrhosis.[1]
    - **Omega-3 fatty acids** should not be used to specifically treat NAFLD or NASH but may be used to concurrently treat hypertriglyceridemia.[1]
  - **Pioglitazone** is recommended in patients with biopsy-proven NASH with and without T2DM. SE: weight gain, increased risk of CHF.[1]
  - **Vitamin E** is only recommended in patients with biopsy-proven NASH without diabetes or cirrhosis. SE: increased risk of prostate cancer.[1]
  - Patients with NAFLD should **avoid alcohol**.[1]
  - **Bariatric surgery** should not be used to specifically treat NASH but can be considered in otherwise eligible obese NAFLD or NASH patients.[1]
  - Patients with advanced fibrosis (stages 3 and 4) should be considered for esophageal varices and hepatocellular carcinoma screening.[1,9]
- Emerging treatment: Oleoylethanolamide (OEA, sold as Riduzone) (PPAR-α agonist) stimulates lipid metabolism, induces satiety, and helps control weight.[6]

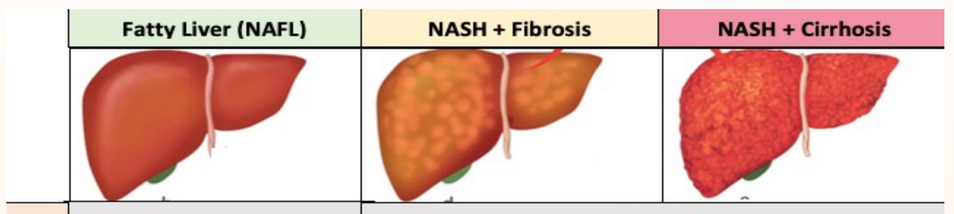
CLINICAL PRESENTATION

- Most patients with NAFLD are asymptomatic; those with NASH may complain of malaise, fatigue, and RUQ discomfort.
- Diagnosis is frequently considered by incidental discovery of elevated liver aminotransferases or hepatic steatosis on imaging.

DIAGNOSIS

- **Rule out:** Hep B (HBsAg, anti-HBc, anti-HBs); Hep C (anti-HCV, HCV RNA); ETOH (AST:ALT > 3); hepatotoxic medications[4,5]
- **Ask:** Is fibrosis present? If so, how advanced? → **Test**
- **Radiographical Imaging[6]**
  - Conventional—US, CT, MRI
  - Elastography—transient elastography (TE), acoustic radiation force impulse (ARFI), magnetic resonance elastography (MRE)
- **Noninvasive Fibrosis Scores[6]**
  - FIB-4 = *(age x AST) / (PLT x √ALT)*
  - NFS = NAFLD fibrosis score
    - Age, BMI, DM, alb, plt, AST, ALT
    - Must pair with TE
    - Intermediate scores require bx
  - APRI = AST-to-platelet ratio index
- **Invasive Biopsy = gold standard[3]**
  - NASH must be confirmed with bx (US-guided-transjugular measures hepatic venous pressure gradient)

MANAGEMENT, Figure 2[1]



	Fatty Liver (NAFL)	NASH + Fibrosis	NASH + Cirrhosis
Weight loss	• Weight loss 3-5% of body weight to improve steatosis	• Weight loss 7-10% of body weight to improve NASH and fibrosis	
Dietary options	• Reduce daily caloric intake by 500-1,000 kcal • Avoid **snacking** / Encourage a regular meal pattern • Mediterranean diet yielded significant improvement in steatosis on MRI • Consider daily and moderate **coffee** consumption • Encourage abstinence from alcohol • Limit **fructose**/sugar intake to <10% of total calories/day (especially sugary drinks)		
Exercise	• Moderate-intensity exercise in combination with hypocaloric diet for better likelihood for sustained weight loss over time • Exercise alone may prevent or reduce HS in NAFLD but its ability to improve other aspects of liver histology remains unknown		
Pharmaceuticals	• Omega-3 fatty acids (if treating dyslipidemia)	• Vitamin E: 800 units/day in non-diabetic NASH • Pioglitazone (+ T2DM)	• NOT Vitamin E • Pioglitazone: (+ T2DM)
	• Metformin NOT recommended		
	• Statins but NOT for decompensated cirrhosis		
Surgery	• Bariatric surgery in eligible obese but NOT to specifically treat NASH		• Bariatric surgery • Liver transplantation
Screen -ing	• Routine screening for NAFLD in high-risk groups NOT advised • NFS, fibrosis-4 index (FIB-4), vibration controlled transient		• Screen all for HCC and esophageal varices

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