Assessing liver disease progression for better patient outcomes

A noninvasive way to assess risk of NASH disease progression

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease, affecting at least a quarter of the global adult population.[1] It's a condition characterized by the presence of hepatic steatosis, typically associated with type 2 diabetes mellitus and obesity.[2] If left undiagnosed, many patients with NAFLD progress to nonalcoholic steatohepatitis (NASH),[3,4] which includes inflammation and liver damage.[5] Additionally, NASH is strongly linked to liver fibrosis and can lead to life-threatening outcomes.[3,4]

For these reasons, identifying patients who are developing liver disease is vitally important, especially in light of growing obesity rates. The 2022 American Association of Clinical Endocrinology (AACE) guidelines recommend specialized blood tests and imaging to determine risk of significant fibrosis.[6] For patients in high-risk groups with an indeterminate or high fibrosis-4 (FIB-4) index, the Enhanced Liver Fibrosis Score, or ELF™ Score, is a recommended option.[6] This is a newer blood test that can assess risk of NASH disease progression and can be a less invasive solution than biopsy when making patient care decisions.

This paper outlines key considerations for improved outcomes as decision-makers and healthcare providers work to identify patients with liver disease who need urgent specialized interventions.

NAFLD and NASH:
a looming crisis

Due to higher rates of obesity, an increasing number of patients have a range of cardiometabolic conditions, including insulin resistance, metabolic syndrome, hyperlipidemia, hypertension, and type 2 diabetes. Patients with these underlying conditions have a greater risk of developing NAFLD and progressing to NASH.[5]

While most patients with NAFLD have simple fatty liver or simple steatosis, about 20% have NASH.[3,4] As a result, they have an increased risk of disease progression and poor outcomes, such as cirrhosis, liver transplantation, and possibly even death.[3,4]

Because NAFLD has a silent presentation in its early phases, the challenge of diagnosis poses a risk for patients.[7] It is estimated that less than 10% of cases are detected.[8]

20%

of patients with NAFLD progress to NASH[3,4]

1 in 5

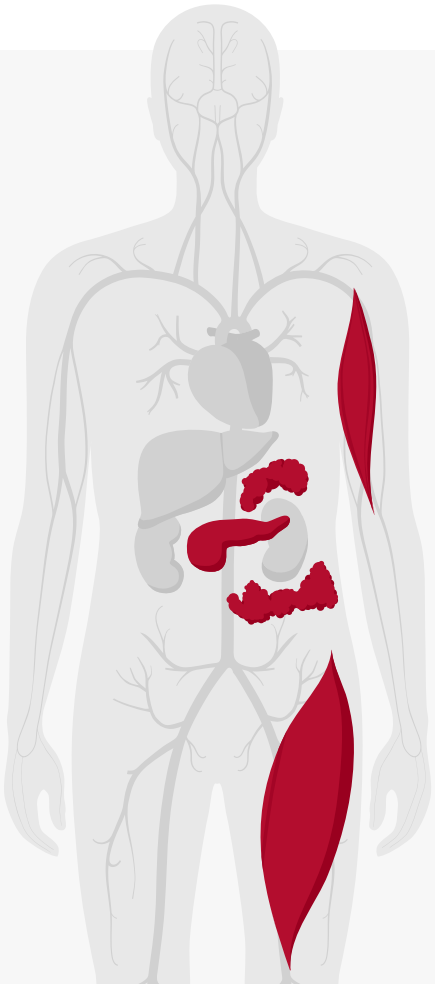
patients with advanced fibrosis progress to cirrhosis in 2.5 years[9]

#1

NASH is the #1 reason for liver transplants in women in the US, and will likely rise to be the #1 reason in men[10]

Metabolic dysfunction can lead to NAFLD

Early metabolic dysfunction rooted in insulin resistance is a foundational and prevalent driver of cardiovascular disease and associated chronic conditions such as prediabetes/diabetes, chronic kidney disease, and NAFLD.



Metabolic

Cardiovascular

Hepatic

Renal

Guidelines for identifying and managing **NAFLD/NASH risk**

In 2022, AACE and American Association for the Study of Liver Disease (AASLD) released new guidelines for the diagnosis and management of NAFLD and NASH. Here are the key takeaways:[6]

1. Signs that patients are likely to have NAFLD and should be considered at high risk for liver fibrosis:
   a. Obesity and/or features of metabolic syndrome
   b. Prediabetes or type 2 diabetes
   c. Hepatic steatosis on any imaging study and/or persistently elevated plasma aminotransferase levels (over 6 months)

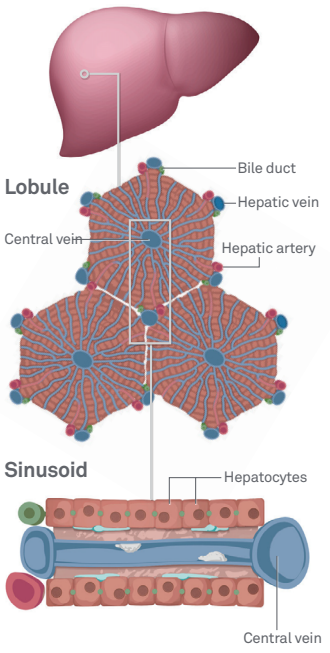
2. Recommended blood tests to assess the risk of NAFLD with liver fibrosis:
   a. The FIB-4 index is the preferred noninvasive way to assess risk of NASH disease progression
   b. Repeat testing every 2 years is suggested for patients with a low FIB-4
   c. Patients in the high-risk groups with an indeterminate or high FIB-4 index should be considered for further testing with the ELF Score

3. Patients should be referred to a liver specialist when they present with:
   a. Persistently elevated ALT or AST levels and/or with hepatic steatosis on imaging and indeterminate risk or high risk based on blood tests and/or imaging
   b. Other clinical evidence of advanced liver disease

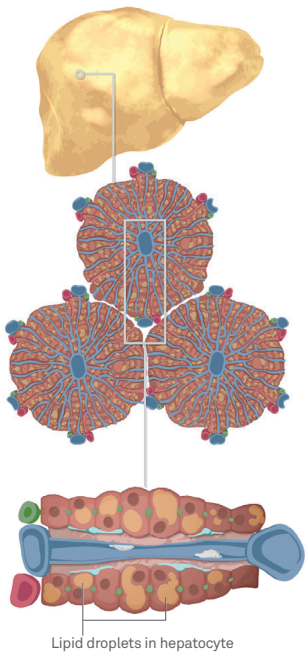
Progression of NAFLD

The disease can be prevented or even reversed with lifestyle changes if risk is identified early.

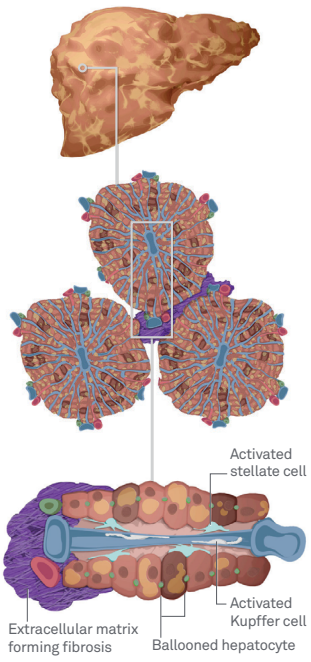
Healthy liver



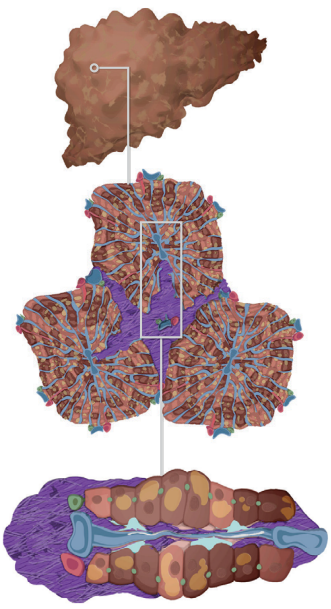
Steatosis (fatty liver)



Early NASH



Late NASH with fibrosis



Assessing available **diagnostic tools**

Liver biopsy

- Official method to diagnose NASH
- Considered undesirable due to the variability in interpretation of results and risk to patients

Imaging

- Ultrasound and magnetic resonance elastography can be used to assess fibrosis
- Access to the technology is often limited

FIB-4 index

- A noninvasive, indirect/mixed marker blood test
- Relied on by more specialists due to the limits of other options

A newer option: The ELF Score

- First routine, standardized, direct biomarker blood test for prognostic risk assessment in advanced NASH
- ELF Score test code: 10350
- FIB-4 Index Panel with Reflex to Enhanced Liver Fibrosis (ELF) Score test code: 12734

Final takeaways

With new therapies becoming available, it will be important to identify patients at risk of developing cirrhosis and liver-related clinical events early on so they can be appropriately monitored and treated. While there are a number of diagnostic tools available, the ELF Score provides an easier way to identify those patients most in need of specialized intervention.

Key advantages of the ELF Score

The ELF Score is recommended by AACE guidelines,[6] as its measurements have proven valuable for identifying patients with advanced fibrosis (F3 or F4) at risk of progressing to cirrhosis and liver-related events. In cases where FIB-4 is ≥1.3, this option can be used to exclude advanced fibrosis.[11]

A noninvasive blood test requiring only a single nonfasting tube of serum, the ELF Score is based on 3 direct markers of fibrosis:

- Hyaluronic acid (HA): Extracellular matrix (ECM) component
- Procollagen III N-terminal peptide (PIIINP): ECM component
- Tissue inhibitor of metalloproteinase 1 (TIMP-1): Inhibits breakdown of collagen III

As the prevalence of metabolic disease continues to increase, more accurately assessing risk of NASH disease progression can go a long way toward ensuring more patients have better health outcomes.

Improve clinical outcomes through early identification and intervention

To learn more about the ELF Score from Quest Diagnostics, visit **QuestDiagnostics.com/NAFLD.**

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