



NAFLD/NASH IN LEAN INDIVIDUALS: WHAT SHOULD PATIENTS KNOW?

While obesity is strongly associated with NAFLD/NASH, people who are not overweight can also have NAFLD/NASH.

Read more below about how you can prevent, manage, and treat NAFLD/NASH if you are lean.



What is NAFLD/NASH?

Nonalcoholic fatty liver disease (NAFLD)

Nonalcoholic fatty liver disease (NAFLD) is a condition in which too much fat builds up in the liver. If left untreated, NAFLD can lead to serious liver problems.

Nonalcoholic Steatohepatitis (NASH)

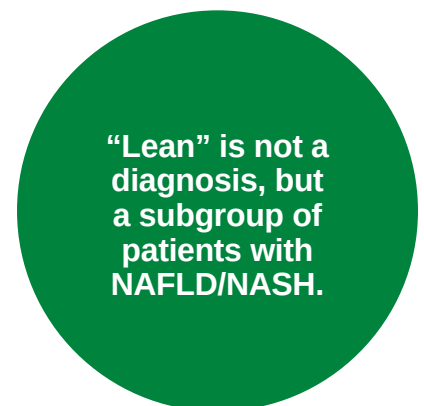
Nonalcoholic steatohepatitis (NASH) is caused when that extra fat turns into inflammation (swelling in the liver) and fibrosis (scarring) of the liver. If severe enough, NASH can lead to cirrhosis or liver cancer, potentially requiring a liver transplant, which presents a difficult situation. Livers for transplants usually come from deceased donors, or people who have recently passed away,¹ and the waiting period for these livers can be long, ranging from less than 30 days to five years in the United States alone.²

What is “lean NAFLD/NASH” or “non-obese NAFLD/NASH”?

The terms “lean NAFLD/NASH” or “non-obese NAFLD/NASH” are colloquial ways of referring to NAFLD/NASH that occurs in a patient who is not obese. These terms are not distinct diagnoses; rather, patients who are lean and have NAFLD/NASH are a subset of the larger NAFLD/NASH patient population.

In general, physicians and researchers define patients with NAFLD/NASH who are “lean” as those who have a body mass index (BMI) of $<25 \text{ kg/m}^2$.³ An exception to this definition is that Asian patients with a BMI of $<23 \text{ kg/m}^2$ are considered “lean”.^{4,5}

A note: The determination for who is “lean” is different for patients with type 2 diabetes (T2D) than patients with NAFLD/NASH. Patients with T2D are considered “lean” if they have a BMI of $<19 \text{ kg/m}^2$.⁶



How common is NAFLD or NASH in lean patients?

Though NAFLD and NASH are closely linked with obesity, the prevalence of NAFLD in non-obese patients is growing.⁷ Researchers estimate that 7-20% of the Western population and 5-26% of the Asian population are lean and have NAFLD.⁸

I am not obese or overweight. Am I at risk for NAFLD/NASH?

Though you may not be overweight or obese, you could still be at risk for NAFLD and the progression to NASH. For patients who are lean, risk factors for NAFLD include:^{9 10 11}

- High body fat
- High blood pressure
- Diabetes
- Body weight gain even within normal weight limits
- High fructose and cholesterol intake
- Genetic predisposition

The most common causes of NAFLD in patients who are lean are metabolic-related, such as insulin resistance and increased visceral adiposity (fat around your abdomen). Additional causes include genetic disorders (e.g. Wilson's disease), infectious-inflammatory disorders (e.g. hepatitis C), and certain drugs/medications (Amiodarone, Tamoxifen, and Diltiazem).¹²

High fructose and cholesterol intake are risk factors for NAFLD/NASH in lean patients.

How can I reduce my risk for NAFLD/NASH?

In general, the amount of fat in the liver can be reduced through nutrition, physical activity, maintaining a healthy weight, and adequate sleep.¹³ Focusing on these areas can help prevent and treat NAFLD/NASH for many patients.

Talk with your doctor to tailor a plan that works for you and addresses your specific needs and risk factors.



Is NAFLD/NASH less severe in patients who are not obese?

Not necessarily. A study in Japan, for instance, examined 762 patients with NAFLD — including patients who were non-obese, obese, and severely obese — and found that NAFLD was not milder in non-obese patients.¹⁴

What are the signs and symptoms of NAFLD/NASH in lean patients?

Research is ongoing in the area of NAFLD/NASH in lean patients, but data does not yet indicate that lean individuals with NAFLD have a different experience with symptoms than patients who are obese.¹⁵

NAFLD and NASH can cause few observable symptoms in the early stages. Once prominent damage to the liver has occurred, signs of NASH may become more obvious. Individuals with NASH may report:

- Fatigue (tiredness that does not resolve with rest)
- Changes to skin color (yellowing)
- Abdominal pain

NASH may cause cirrhosis, an advanced liver disease. If it develops, these symptoms may be observed:

- Jaundice (yellowing of the skin and whites of eyes)
- Itchy skin
- Swelling of the abdomen
- Dark urine

How is NAFLD/NASH diagnosed in lean patients?

Providers may use several tests to diagnose NAFLD/NASH. These tests include:

- 1 **General clinical history/exam**
- 2 **Blood tests**
- 3 **Imaging tests (e.g., ultrasound, MRI)**
- 4 **Liver biopsy**

What are the treatment options for lean patients with NAFLD/NASH?

Currently, only India has a medication approved specifically for NASH. Several medications, however, are being tested in clinical trials for approval. For lean patients who have NAFLD, it is important that providers look for and treat the specific cause or causes, when present.

It is possible to stop NAFLD/NASH in early stages from progressing to severe liver damage through lifestyle change by focusing on physical activity and nutrition. In fact, researchers have found that NAFLD can be reversed in 67% of non-obese patients after lifestyle intervention, with the majority of patients achieving NAFLD remission with modest weight loss of 3-10%.

Are clinical trials for me?

If you are at risk or diagnosed with NAFLD or NASH, you may consider participating in a clinical trial for a drug or device. Clinical trials are research studies that look at different, new ways to prevent,

detect, treat disease, or improve quality of life. For more information, check out the GLI resource, [NAFLD/NASH: How Can Patients Participate in Clinical Trials?](#)

Studies need volunteers with diverse characteristics and backgrounds to ensure that researchers understand the risks and outcomes for the different groups affected by a particular disease. Demographics that can affect risk, benefit, and outcomes for treatment include: race, ethnicity, age, gender, and physical sizes and abilities.¹⁶ Asian patients, in particular, are under-represented in most drug trials¹⁷ and may want to consider participation.

Studies need volunteers with diverse characteristics and backgrounds.



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