Do Lean Individuals With Fatty Liver Disease Have Worse Outcomes?

Study finds that lean people with NAFLD had a higher risk for liver events, cancer and mortality.

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Lean people with nonalcoholic fatty liver disease (NAFLD) may be at greater risk for liver-related events, cancer, kidney disease and death compared to people with overweight and NAFLD, according to findings from a French study presented at the 2021 International Liver Congress.

Arising from the accumulation of fat in the liver, NAFLD and its more severe form, non-alcoholic steatohepatitis (NASH), are responsible for a growing proportion of advanced liver disease worldwide. As a result of inflammation, NAFLD can lead to the buildup of scar tissue (fibrosis), cirrhosis (advanced scarring) and even liver cancer. With no effective approved medical therapies, disease management is dependent on lifestyle changes, such as weight loss and exercise.

Oumarou Nabi, MD, MPH, PhD, of the Pierre Louis Institute of Epidemiology and Public Health at Sorbonne University in France, and colleagues studied the features of NAFLD among lean French adults.

To begin with, they included 127,291 participants from the CONSTANCES cohort, a representative sample of the adult French population, who were enrolled between 2012 and 2017. Next, they ruled out individuals with high alcohol intake, viral hepatitis and other liver-related diseases, short-listing 110,120 people. After excluding individuals for whom the fatty liver index could not be calculated, the researchers evaluated the final study population totaling 106,846 people.

Over a follow-up period of 30 months, the researchers assessed several outcomes, including liver cancer, cancer outside the liver, heart disease, kidney disease, liver transplantation and death.

Lean individuals with NAFLD were younger on average, more likely to be women, more likely to be current smokers or alcohol drinkers and had fewer metabolic risk factors. More than half (56%) showed no metabolic risk factors, such as diabetes, high blood pressure or elevated cholesterol. Lean people with NAFLD had higher levels of alanine aminotransferase (ALT), an enzyme indicating liver inflammation, and had more advanced fibrosis than people with overweight and NAFLD.

Across the study population, NAFLD was seen in 18% of all participants: 42% of those with

overweight or obesity and 5% of those who were lean.

Of those who were diagnosed with NAFLD, 16% were lean, 41% had overweight and 43% had obesity.

Lean people with NAFLD experienced worse liver events, such as advanced fibrosis, heart and kidney disease, liver cancer and even overall death in comparison with people with overweight and NAFLD.

After adjusting for numerous other variables, lean people with NAFLD were found to be at a higher risk for liver cancer and other liver-related conditions, chronic kidney disease and overall death in comparison to people without NAFLD. In a parallel analysis, people with overweight and NAFLD were at higher risk for liver events and heart disease. When compared to people with overweight and NAFLD, lean people with NAFLD were more likely to experience a liver event, cancer outside the liver, kidney disease and death.

The researchers found that alcohol and soft drink consumption as well as tobacco smoking worsened the risk for NAFLD in lean individuals compared to those with overweight. Conversely, coffee consumption and exercise lessened the risk for NAFLD in lean versus non-lean people.

“From a large French community-based cohort, this study confirms the significant prevalence of lean NAFLD and suggests that NAFLD is more severe in terms of advanced fibrosis, liver disease progression and overall mortality in lean compared to non-lean subjects, despite fewer metabolic risk factors,” wrote the researchers. “Differences in lifestyle, genetics and microbiota may explain those results.”

In contrast, a related study of nearly 5,000 people in the United States found that people with normal weight and NAFLD had a healthier metabolic profile and appeared to have a lower likelihood of liver disease progression than people with obesity and NAFLD, although they had a similar risk for heart disease and cancer. Lean Asians with NAFLD have also been found to be at lower risk for cirrhosis and cardiovascular disease.

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