Cirrhosis Caused by Fatty Liver Disease May Run in Families

Having a parent or sibling with NAFLD-related cirrhosis dramatically increases the risk.

June 27, 2017 By Liz Highleyman

People who have a close relative with liver cirrhosis related to non-alcoholic fatty liver disease have more than a 12-fold higher likelihood of developing advanced fibrosis or cirrhosis themselves, suggesting a genetic predisposition, according to research published recently in the Journal of Clinical Investigation and presented at the AASLD Liver Meeting last November.

Fatty liver disease, often associated with obesity and metabolic syndrome, is the leading cause of liver disease in the United States. Non-alcoholic fatty liver disease (NAFLD), and its more severe form, non-alcoholic steatohepatitis (NASH), refer to fat accumulation in the liver in people who do not drink heavily.

Over time, fatty liver disease can progress to liver fibrosis (accumulation of fibrous scar tissue) and cirrhosis (serious scarring that interferes with liver function), and it increases the risk of developing hepatocellular carcinoma, a type of liver cancer. Several pharmaceutical companies are testing new therapies for NAFLD and NASH, but currently, diet and weight loss are the mainstays of treatment.

Rohit Loomba, MD, of the University of California at San Diego, and colleagues with the Familial NAFLD Cirrhosis Research Consortium looked at the risk of advanced fibrosis and cirrhosis in family members of people with NAFLD-related cirrhosis.

While obesity is increasingly common in the United States, not everyone who is obese will develop NAFLD, and not everyone with NAFLD will progress to advanced fibrosis or cirrhosis, the researchers noted. A better understanding of family risk could help determine who might benefit from cirrhosis screening.

The researchers did a cross-sectional analysis (a study of data collected at specific point in time) of 26 patients with NAFLD-related cirrhosis and 39 of their first-degree relatives: parents, siblings or children. For comparison, they looked at a control group of 69 people without NAFLD or cirrhosis, representing the general population, who were paired with a twin, non-twin sibling, parent or child.

The presence of advanced fibrosis or cirrhosis was assessed using a noninvasive imaging method known as elastography, which measures liver stiffness. A higher liver stiffness measurement indicates more severe fibrosis.

The NAFLD-related cirrhosis patients had an average age of 63 years and a mean body mass index (BMI) of 31.7, considered to be moderately obese. Their relatives had a mean age of 48 and a mean BMI of 31.0. The control group was younger and leaner, with an average age of about 44 and a mean BMI of 25.0. Nearly three quarters of the NAFLD patients but only about 2 percent of the control group had type 2 diabetes.

Loomba's team found that 74 percent of close relatives of people with NAFLD-related cirrhosis had NAFLD themselves, compared with about 9 percent of relatives of the non-NAFLD control group. The prevalence of advanced fibrosis or cirrhosis was substantially higher in relatives of patients with NAFLD-related cirrhosis than in relatives of people without NAFLD or cirrhosis (17.9 percent versus 1.4 percent).

Overall, first-degree relatives of people with NAFLD-related cirrhosis were 14.9 times more likely to have advanced fibrosis or cirrhosis than relatives of people without NAFLD or cirrhosis. After adjusting for age, sex, ethnicity, BMI and diabetes status, family members of people with NAFLD still had a 12.5 times greater risk—a difference that was both statistically and clinically significant, according to the researchers.

"Risk of cirrhosis is significantly higher if you have a family history of NASH cirrhosis in first-degree relatives, so we should consider screening for cirrhosis in this population," Loomba said in a press release issued at the Liver Meeting.

"These data may impact and potentially change clinical practice in increasing awareness of advanced fibrosis in NAFLD in high-risk populations such as those with a first-degree relative with NAFLD cirrhosis," the researchers wrote. "The clinical implications of this study are potentially significant, as earlier detection of cirrhosis would perhaps lead to earlier initiation of hepatocellular carcinoma screening and surveillance. Once a small suspected hepatocellular carcinoma is recognized via these screening programs, more timely referrals for liver transplant could be done, and this possibly may improve survival."

However, the researchers noted that NAFLD risk is probably multifactorial, including environmental, lifestyle and behavioral factors as well as genetics.
