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# Technique may identify patients with fast-progressing fibrosis in nonalcoholic fatty liver disease

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Combining multiple non-invasive measures, researchers at University of California San Diego School of Medicine describe a novel method to quantify the progression of nonalcoholic fatty liver disease (NAFLD) to its more dangerous and deadly states—advanced fibrosis and cirrhosis.

The findings are published in the Oct 5 online issue of *Hepatology*.

Roughly one-quarter of all Americans—an estimated 100 million adults and children—have NAFLD, which occurs when fat accumulates in liver cells due to causes other than excessive alcohol use. The precise cause is not known, but obesity, diabetes, diet and genetics play substantial roles.

Most people with NAFLD exhibit few or no symptoms, but the condition can progress to nonalcoholic steatohepatitis (NASH), a more extreme form of the disease, which in turn can result in cirrhosis or liver cancer. One driver of the disease is excessive production of collagen, an extracellular structural protein that in over-abundance can lead to harmful scarring and dysfunction in affected tissues; in this case, the liver.

"Progression of the condition, from NAFLD to NASH or from mild fibrosis (thickening and scarring of tissue) to cirrhosis, varies greatly from patient to patient," said Rohit Loomba, MD, professor of medicine at UC San Diego School of Medicine and director of the Nonalcoholic

Fatty Liver Disease Research Center at UC San Diego Health. "Having a diagnostic technique that can effectively predict individual clinical fibrotic disease progression quickly—which patients are more likely to develop serious liver health problems—would obviously be extremely valuable."

The current gold standard for monitoring fibrosis progression are repeat liver biopsies, but these are problematic for several reasons. They are invasive. There is a related health risk, including the chance of death. And sampling may miss or not fully capture a liver's full fibrotic state.

In recent years, non-invasive scanning technologies, such as magnetic resonance imaging (MRI), have been used to measure liver stiffness (an indicator of fibrosis), but they assess only disease status in the moment and cannot provide a more kinetic assessment of metabolic process of the rate of scarring.

"As a result, patients with fast-progressing fibrotic disease are typically identified only when they are in the late stages of the condition," said Loomba, when treatments and effectiveness are more limited.

In their study, Loomba and colleagues asked 21 patients with suspected NAFLD to ingest "heavy water," (a form of water that contains deuterium, a "heavier" form of hydrogen) two to three times daily for three to five weeks prior to a liver biopsy. The heavy water was used to label and measure collagen growth. Additionally, blood samples from study participants were measured for collagen synthesis rates and MRIs taken to assess liver stiffness. They found that all of these assessment tools—some used for the first time to provide direct, immediate measurements—correlated with established risks for fibrotic disease progression.

"If confirmed in larger, longer studies, these findings have potential

implications for charting the prospective course of disease and managing patients' treatment accordingly," said Loomba.

**More information:** *Hepatology*, DOI: 10.1002/hep.28860/full

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