Research may speed identification of patients who need liver transplants

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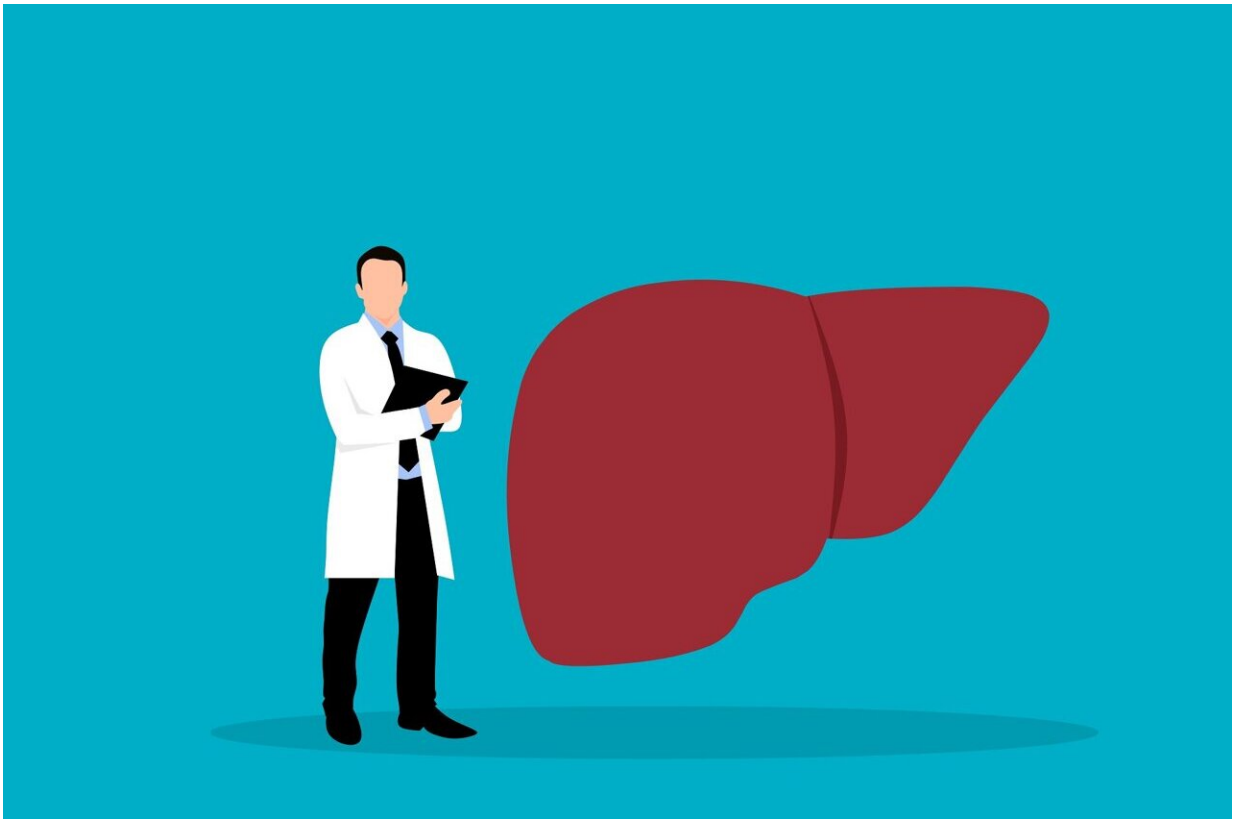

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Research findings from Rutgers, the University of Michigan, the University of Texas Southwestern, and the Medical University of South Carolina could save lives by enabling faster and more accurate

identification of hospitalized patients who need liver transplants or are likely to recover.

Retrospective analysis of blood samples and medical records from 270 patients admitted to the hospital with acute liver failure (ALF) found that concentrations of a short-lived but abundant serum protein called carbamoyl phosphate synthetase 1 (CPS1) helped predict which patients survive or die without a transplant.

"We still need to validate these results in more patients to further confirm that CPS1 levels predict ALF from causes other than acetaminophen (Tylenol), but this has the potential to be a highly valuable prognostic and clinical management tool for acetaminophen and other causes of liver failure," said Bishr Omary, senior vice chancellor for academic affairs and research at Rutgers Biomedical and Health Sciences and senior author of the study just published in the journal *Clinical Gastroenterology and Hepatology*.

About 3,000 Americans suffer acute liver failure each year, according to the *New England Journal of Medicine*. Acetaminophen is the most common cause, but other causes include prescription medications, herbal supplements, autoimmunity and viruses such as hepatitis A and B.

Most patients with acetaminophen-associated ALF recover without a transplant, but the need for transplant organs far exceeds the supply. Of transplant livers, 214 of 9,528 went to patients with acute liver failure last year.

"Any prognostic tool that helps distinguish patients likely to recover from those likely to die from their ALF—while transplant candidates are still healthy enough to survive the surgery—would thus be extremely valuable," said Robert Fontana, professor of internal medicine and director of the Transplant Hepatology Fellowship Program at the

University of Michigan, a co-author of this study and a leading investigator in the study of ALF and drug-induced liver injury.

The same team of researchers has systemically established CPS1's potential as such a tool. Their previous work has shown that the protein only reaches the blood when acute hepatotoxicants damage CPS1-rich liver cells.

Previous studies also show that the protein has a short half-life. If the liver starts recovering and cell death slows down or stops—a strong indication that a patient will survive without a transplant—blood-borne CPS1 decreases within hours.

In the latest study, researchers reviewed records and samples from 103 patients with acetaminophen-induced liver failure and 167 with liver failure from other causes. Patients from the first group who received liver transplants or died within 21 days of hospitalization had, on average, about twice as much CPS1 in the blood as those who spontaneously recovered. Patients from the second group who died or received transplants also had higher CPS1 levels than those who recovered, about a third higher, but the researchers calculated an 11 percent chance that this was a coincidence.

Notably, an increase of CPS1 when comparing day three with day one of hospitalization, but not other liver enzymes that normally indicate injury, was found in a higher percentage of patients with acetaminophen-induced ALF who died or required liver transplantation.

A follow-up study on more patients will seek to confirm the findings in a separate patient cohort and determine with greater certainty if there is a connection between CPS1 and ALF outcomes from causes unrelated to acetaminophen. The follow-up study also will seek to confirm another major finding of the new paper: Adding CPS1 measurements to existing

tools for predicting outcomes for liver-failure patients improves their accuracy, particularly in the first days after liver failure occurs, or as part of a daily assessment of CPS1 level during hospitalization.

"Enhanced diagnostics, like CPS1, that allow earlier decision-making regarding the need for liver transplantation and that improve the predictability of outcome would clearly improve the care of patients with ALF," said Lu Chen, a visiting scholar at the Rutgers Center for Advanced Biotechnology and Medicine who was one of the paper's primary authors.

More information: Raymond Kwan et al, The role of CPS1 as a prognostic biomarker in patients with acetaminophen-induced acute liver failure, *Clinical Gastroenterology and Hepatology* (2023). DOI: 10.1016/j.cgh.2023.03.002

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