Medical Xpress

When liver cirrhosis is deadly

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When the body can no longer compensate the gradual failure of the liver caused by liver cirrhosis, there is a high risk of acute decompensated liver cirrhosis. In some patients this develops quickly into an often deadly acute-on-chronic liver failure, in which other organs such as the kidneys or brain fail. A study by an international team of researchers

headed by Professor Jonel Trebicka from the Frankfurt University Hospital and funded by the foundation EF Clif, has discovered which patients are particularly at risk. With their findings, the scientists have laid the foundation for the development of preventive therapy to prevent acute-on-chronic liver failure.

The liver has many functions: it stores nutrients and vitamins, produces dextrose, coagulation factors and hormones, and breaks down toxins, drugs and alcohol. Chronic alcohol abuse, viruses or other diseases can damage the liver and lead to chronic liver disease. Without treatment, chronic liver disease leads to liver cirrhosis in the final stages, in which liver tissue turns into connective tissue, making the liver increasingly unable to carry out its functions. The result: the blood's clotting ability is impaired, toxic metabolic products are fortified, the liver is not adequately supplied with blood and blood pressure rises in the portal veins that supply the liver.

The body tries to compensate for the reduced liver function. For example, new veins develop as alternative circulation from the esophagus, stomach and intestines which expand into varicose veins. When the disease progresses to the point that this kind of compensation is no longer possible—physicians speak of acute decompensated liver cirrhosis—the situation becomes life-threatening: tissue fluid (ascites) collects in the abdominal cavity, leading to bacterial infections and internal bleeding, for example in the esophagus. Difficulty concentrating, mood swings and sleepiness are signs of a poisoning of the brain (hepatic encephalopathy) that can result in a hepatic coma.

A European clinical study headed by Professor Jonel Trebicka, and carried out under the umbrella of the European Foundation for the Study of Chronic Liver Failure, has for the first time identified three clinical course variations in patients admitted to the hospital with acute decompensated cirrhosis.

1. The first clinical course is characterized by high blood inflammation values, indicating inflammatory reactions throughout the body. Within three months after admission to the hospital, a number of body organs fail: the acute decompensation becomes "acute-on-chronic liver failure" (ACLF). The physicians therefore call this variation Pre-ACLF. More than half of patients die from it; only a third survive after a year.
2. Patients with the second clinical course do not develop ACLF and have moderate inflammation values. They suffer, however, from significant hypertension in the portal vein. Approximately 20 percent die within the following three months, another 15 percent over the course of the following year. The physicians named this variation "instable decompensated liver cirrhosis".
3. The patients with the third clinical course exhibit neither high inflammation values nor frequent complications. They do not develop ACLF in the first three months. Within a year, however, one in ten dies. The physicians call this variation "stable decompensated liver cirrhosis."

Lead investigator Professor Jonel Trebicka, gastroenterologist and hepatologist at Medical Clinic I of University Hospital Frankfurt explains: "We are now working intensively on the development of new diagnostic options, especially for the group of pre-ACLF patients, in order to identify this group before admission to the hospital so that preventive measures can be implemented early on. The development of preventive therapies for the often deadly ACLF is one of our most important research goals in this context."

Study co-author Professor Stefan Zeuzem, Dean of the Faculty of Medicine and Director of Medical Clinic I at Frankfurt University Hospital explains: "Liver diseases are one of the main focal points of Medical Clinic I and we offer numerous specialized outpatient departments for patients with acute and chronic liver diseases. So on the

one hand we were able to observe patients for the study. On the other hand, the research findings on improving ACLF prevention and therapies will rapidly benefit all of our patients."

The research findings are part of a European-wide study called PREDICT. The study observes the clinical course of acute decompensated liver cirrhosis in order to find early indications for the development of acute-on-chronic liver failures (ACLF). The study was funded by the European Foundation for the Study of Chronic Liver Failure. 136 scientists from 47 centers and institutions in 14 European countries are participating in PREDICT.

More information: Jonel Trebicka et al. The PREDICT study uncovers three clinical courses of acutely decompensated cirrhosis that have distinct pathophysiology, *Journal of Hepatology* (2020). DOI: 10.1016/j.jhep.2020.06.013

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