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LUDWIG BOLTZMANN INSTITUTE Rare and Undiagnosed Diseases

MEDICAL UNIVERSITY OF VIENNA

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A simple online calculator detects liver cirrhosis patients at high risk for clinical complications

Researchers at CeMM, the Medical University of Vienna (MedUni Vienna), and the Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD) joined efforts to use their expertise in machine learning and management of patients with cirrhosis to develop a non-invasive algorithm that can help clinicians to identify patients with cirrhosis at highest risk for severe complications. Cirrhosis develops in response to repeated injury to the liver, such as fatty liver disease or viral hepatitis. Initially, cirrhosis is mostly asymptomatic, thus, early identification of risk factors for severe complications represents an unmet clinical need.

(Vienna, October 04, 2022) There are two clinical stages of liver cirrhosis: compensated and decompensated. Patients with compensated liver cirrhosis have very few or even no symptoms. However, patients may progress decompensated cirrhosis, which occurs with severe complications such as internal (variceal) bleeding or by an accumulation of fluid in the abdomen (ascites) and may even lead to death. Unfortunately, the risk of decompensation in patients with compensated cirrhosis currently requires an invasive procedure. i.e., the measurement of the hepatic venous pressure gradient (HVPG). An elevated HVPG ≥10 mmHg is associated with a higher probability of complications. Patients with an even higher HVPG of ≥16 mmHg are at imminent risk for hepatic decompensation.

In a study by first authors Jiri Reinis from Stefan Kubicek's group at CeMM and Oleksandr Petrenko from Thomas Reiberger's group at MedUni Vienna, CeMM, and LBI-RUD, machine learning models were trained on blood test parameters obtained from patients with compensated cirrhosis to detect elevated levels of portal vein pressure, thereby identifying those at risk for developing clinical complications. The study was now prominently published in the Journal of Hepatology.

Best clinical parameters for prediction

The key data sources used in the project were derived from the ongoing Vienna Cirrhosis Study, conducted at the Division of Gastroenterology and Hepatology of the MedUni Vienna at the Vienna General Hospital. For this study, HVPG measurements were performed in 163 compensated cirrhosis patients in whom blood samples were simultaneously obtained in order to

determine a range of 124 biomarkers. Out of the entire set of clinical variables, three and five optimal parameters for the detection of high-risk patients were computationally determined. In the VICIS patient cohort, the model performed excellently for the identification of patients with HVPG values of ≥10 mmHg and ≥16 mmHg, respectively.

Validation of the dataset

To assess the diagnostic power of the non-invasive models to predict complications, the researchers tested their non-invasive machine learning model on a combined cohort of 1,232 patients with compensated cirrhosis from 8 European clinical centers. The novel approach was confirmed to be of excellent diagnostic value in the overall cohort and importantly is based on 3 or 5 widely available laboratory parameters only, is non-invasive, and does not require dedicated and expensive equipment.

Project leader Thomas Reiberger explains “While an HVPG measurement is still required for reliable identification of patients with clinically significant or severe portal hypertension, the novel approach could be applied for prioritization for treatment to prevent decompensation or for selection of patients for clinical trials. Due to its simplicity, the proposed methodology could be eventually employed during routine check-ups at little additional cost.”

Online calculator

Finally, the researchers developed an online calculator to allow clinicians to calculate the risk of decompensation for their patients with compensated cirrhosis, available at https://liver.at/vlsg/HVPG-Calculator/

The Study “Assessment of portal hypertension severity using machine learning models in patients with compensated cirrhosis” was published in the Journal of Hepatology on September 22, 2022, DOI: 10.1016/j.jhep.2022.09.012

Photo: Thomas Reiberger, Benedikt Simbrunner, Oleksandr Petrenko, Jiří Reiniš, Stefan Kubicek (from left to right), © Anna Yuwen, CeMM

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Research Association.

Thomas Reiberger joined the LBI-RUD and CeMM in November 2018 as an Adjunct PI. After obtaining his MD at the Medical University of Vienna, he did a first postdoc at the Department of Pathophysiology at the Medical University of Vienna focusing on ex-situ liver perfusion and liver cell biology. During his residency for Internal Medicine, he pursued a career as a physician-scientist while conducting translational clinical studies on portal hypertension and fibrosis. In addition to his clinical activity, he established the Experimental (HEPEX) and Clinical Hepatic Hemodynamic Laboratory. After another postdoctoral fellowship in the United States from 2012 to 2015, Thomas Reiberger joined the Faculty at the Division of Gastroenterology and Hepatology at the Medical University of Vienna. Thomas Reiberger is also the director of the Cirrhosis Outpatient Clinic and the Vienna Hepatic Hemodynamic Laboratory at the Vienna General Hospital. In his role as the coordinator of the Rare Liver Disease (RALID) Center of the European Reference Network (ERN) RARE-LIVER at the Vienna Medical University Campus, he complements the mission of the LBI-RUD with translational research on rare liver diseases.

The **CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences** is an international, independent, and interdisciplinary research institution for molecular medicine under the scientific direction of Giulio Superti-Furga. CeMM is oriented towards medical needs and integrates basic research and clinical expertise to develop innovative diagnostic and therapeutic approaches for precision medicine. Research focuses on cancer, inflammation, metabolic and immune disorders, and rare diseases. The Institute's research building is located on the campus of the Medical University and the Vienna General Hospital.
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The **Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD)** was founded in April 2016 in a joint effort of Ludwig Boltzmann Gesellschaft, CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, Medical University of Vienna, and St. Anna Children's Cancer Research Institute. The three founding partner institutions, and CeRUD Vienna Center for Rare and Undiagnosed Diseases, constitute LBI-RUD's most important collaboration partners. Research at LBI-RUD focuses on the deciphering of rare immunological, hematopoietic, nervous, dermal, gastro-intestinal, and hepatic diseases. Those studies provide unique insights into human biology and are the basis for the development of tailored therapeutic concepts in the sense of the personalized medicine of the future. The mission of LBI-RUD is – together with its partner institutions – to sustainably develop and maintain research infrastructure integrating scientific, societal, ethical, and economical aspects of rare diseases. rare-diseases.at

Medical University of Vienna (MedUni Vienna) is one of the most traditional medical education and research facilities in Europe. With almost 8,000 students, it is currently the largest medical training center in the German-speaking countries. With 6,000 employees, 30 departments and two clinical institutes, 12 medical theory centers and numerous highly specialized laboratories, it is also one of Europe's leading research establishments in the biomedical sector. meduniwien.ac.at

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