## STIFTUNG FÜR LEBERKRANKHEITEN

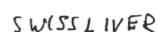
Universitätsklinik für Viszerale Chirurgie und Medizin Hepatologie

#### Stiftungsratspräsidentin:

- Prof. Dr. med. Dr. phil. nat. Annalisa Berzigotti

#### Stiftungsrat:

- Sébastien Baumann, Rechtsanwalt, Stiftungsrat
- Prof. Dr. med. Dr. phil. nat. Jaime Bosch, Stiftungsrat
- Prof. Dr. med. Jean-François Dufour, Stiftungsrat
- Prof. Dr. med. Dr. phil. nat. Nikolai Naoumov, FAASLD, Stiftungsrat
- Dr. med. Michael Schenk, Stiftungsrat



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**Research Progress Report** 

Project 1: Surveillance of primary liver cancer in non-alcoholic fatty liver disease (NAFLD)

Project 2: The Role of Spleen Stiffness Measurement in Ruling Out High-Risk Varices in Patients with Porto-Sinusoidal Vascular Disorder

Name of Grantee: Antonenko Antonina

Date: 27.04.2025

# Summary / Brief outline of topic

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), previously referred to as Non-Alcoholic Fatty Liver Disease (NAFLD), is a significant cause of chronic liver disease and a well-established risk factor for hepatocellular carcinoma (HCC). However, the incidence of HCC related to MASLD varies widely across different geographical regions and ethnic groups. SURPASS is a multicenter, international prospective, observational study designed to explore these variations. The study is planned to span 5 years, with participating centers including Hospital Clinic in Barcelona and Bern University Hospital in Switzerland. Patients in the study are classified into two groups based on their liver fibrosis stage: F3 (advanced fibrosis) and F4 (cirrhosis). Enrollment began on August 1, 2022, following the submission and approval of an amendment that allows for the collection of additional data not included in the original application. As of 2024, we have successfully recruited 10 additional eligible patients and provided follow-up assessments for previously enrolled participants.

### Results

As of the latest update, we have successfully enrolled 69 patients with MASLD and advanced fibrosis into the study. Among these 69 patients: 21 patients have a histological diagnosis of MASLD fibrosis stage F3; 17 patients have a histological diagnosis of MASLD fibrosis stage F4, 31 patients have MASLD cirrhosis, diagnosed without liver biopsy but based on universally accepted clinical, analytical, and ultrasound criteria. At the time of inclusion, the average age of the patients was 65.9 ± 3.5 years. During the follow-up period, two patients passed away, and one patient, who had been histologically diagnosed with MASH-cirrhosis, developed further autoimmune hepatitis and was subsequently excluded from the study. In the initial liver ultrasound, we assessed whether the ultrasound images were adequate to evaluate the entire liver parenchyma. Follow-up imaging included MRI in 18 patients (26.1%) and CT scans in 7 patients (10.1%). Additionally, 4 patients underwent MRI twice, as the quality of their initial ultrasound images was insufficient for effective HCC screening.

After performing the MRI hepatocellular carcinoma was confirmed in 4 patients (6.98%) with liver cirrhosis. One case of cancer was diagnosed during the 3rd follow-up (1.5 year), in 2 cases it was diagnosed during 2nd follow-up (1 year), in 1 case during 1st follow up. In one patient diagnosis was

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made only due to MRI that was performed after elevated AFP level (ultrasound did not show any lesions). In two patients, nodules detected on ultrasound were later characterized as LI-RADS 3 lesions on MRI.

For all patients, that are suitable for inclusion in the SURPASS study we measured the liver frailty index, that includes balance, hand grip strength and 5 time chair stands. This tool was specifically developed in patients with cirrhosis to objectively measure physiological reserve. Among those 69 cases included into our study up to date the median Liver frailty index value was 3.98, which indicates pre-frailty.

### **Activities**

In 2024, in collaboration with our colleagues from the VALDIG group, we also participated in a project focused on analyzing spleen stiffness measurements (SSM) in patients with porto-sinusoidal vascular disorders (PSVD) and the presence of high-risk varices (HRV) as identified by endoscopy. The study included a total of 309 patients with PSVD. Using multivariable logistic regression analysis, it was found that SSM-VCTE >40 kPa and serum bilirubin ≥1 mg/dL were independently associated with the presence of HRV. A combination of SSM-VCTE ≤40 kPa and bilirubin <1 mg/dL demonstrated a sensitivity of 96% to rule out HRV, potentially allowing for 38% of screening endoscopies to be avoided, with only 4% of HRV cases missed and a negative predictive value (NPV) of 95%. In a validation cohort of 155 patients, this combined approach could spare 21% of screening endoscopies, with 4% of HRV missed and an NPV of 94%.

# **Discussion**

The incidence of primary liver cancer in the at-risk MASLD population (stage F3-F4) in our study cohort is 6.98%, which is undoubtedly a high percentage. Periodical screening for HCC at patients with cirrhosis and advanced fibrosis (F3) is very important for timely diagnosis of liver cancer and prescription of therapy. Taking into account that ultrasound visualization is often limited due to obesity, gas and presence of regenerate nodules annually performing MRI investigation of benefit.

# **Achievements (Grants / Prizes / Publications) Publications:**

1) Performance of spleen stiffness measurement to rule out high-risk varices in patients with porto-sinusoidal vascular disorder Pierre-Emmanuel Rautou; on behalf of the ERN RARE-LIVER; a study of VALDIG, an EASL consortium Authors' affiliations, Hepatology 81 (2), 2024

### **Grants:**

2) Scholarship at Risk (SAR) Grant 2022; 2023

## **Outlook / Next steps**

- 1) To complete the SURPASS study as per protocol by August 2026 and to publish the results in a peer-reviewed journal.
- 2) Following the publication of results demonstrating the utility of spleen stiffness measurements in ruling out high-risk varices in patients with PSVD, we decided to evaluate the prognostic performance of liver stiffness measurement (LSM) and spleen stiffness measurement (SSM) using vibration-controlled transient elastography (VCTE) in this patient population.

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