STIFTUNG FÜR LEBERKRANKHEITEN

Universitätsklinik für Viszerale Chirurgie und Medizin
Hepatologie

Research Progress Report

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

Name of Grantee: Antonenko Antonina
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Summary / Brief outline of topic

Metabolic-dysfunction-associated steatotic liver disease (MASLD, previously known as non-alcoholic fatty liver disease (NAFLD)) is considered an important cause of chronic liver disease and a well-known risk factor for hepatocellular carcinoma (HCC)[1,2]. However, the incidence of HCC related to MASLD has wide differences across geographical areas and ethnicities[3]. Current guidelines from the European Association for the Study of the Liver (EASL) for Hepatocellular Carcinoma recommends the periodical screening for HCC at patients with cirrhosis regardless of its ethology, in patients with chronic HBV infection at high risk of HCC and in HCV infected, non-cirrhotic F3 patients. Regarding non-cirrhotic MASLD patients, mounting evidence also suggests that pre-cirrhotic MASLD might confer an increased risk of HCC, independent of cirrhosis[5], but data from prospective studies describing the incidence and the factors associated with relevant HCC risk, aimed to support HCC surveillance in this population, are still lacking[6]. It is also questioned whether hepatic MRI should be considered as an alternative to ultrasound in a selected population. The main aim of this scientific work is to determine the incidence of primary liver cancer in at risk MASLD population (Stage F3-F4). Among the secondary aims we are considering to determine the diagnostic performance of screening ultrasound to detect liver nodules in MASLD population and to determine the association between liver fibrosis and incidence of primary liver cancer in MASLD.

Activities

It is a multicenter, international prospective, observational study. The length of the study is for 5 years planed. The participating centers include Barcelona (Hospital Clinic) and Bern (Bern University Hospital). Patients are divided into two groups according to the liver fibrosis stage (F3 and F4). We started enrolling patients on August 1, 2022 after submitting and receiving ethical approval for an amendment allowing collecting additional data not included in the original application.

Results

Up to date we have included 58 patients with MASLD and advanced fibrosis in the study, which is a significant number given the short time elapsed. Among 58 patients: 19 patients - with histological diagnosis of NAFLD fibrosis stage F3, 17 patients – with a histological diagnosis of NAFLD fibrosis stage F4 and 22 patients with NAFLD cirrhosis without liver

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biopsy but cirrhosis diagnosed with the universally accepted clinical, analytical and ultrasound criteria. At the time of inclusion in the study, the average age of patients was 63.9 +-1.5 years. During follow up two patients died, and one patient with histologically diagnosed MASH-cirrhosis developed further autoimmune hepatitis and this patient was excluded from the study. On the initial liver ultrasound, we assessed whether or not the ultrasound images were adequate to evaluate the whole liver parenchyma. In these 58 cases ultrasound visualization in the majority of cases (36 cases – 62%) was limited due to the obesity and the presence of gas in the abdominal cavity (LIRADS score B). In 10.3% (6 cases) of all cases the ultrasound visualization was very difficult either due to the presence of a large number of nodules of unclear etiology or due to the peculiarity that the majority part of the liver was not visible (LIRADS score C). After the ultrasound visualization liver MRI was performed in 6 cases with LIRADS score C and in 13 patients with LIRADS B. 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 made only due to MRI that was performed after elevated AFP level (ultrasound did not show any lesions).
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 58 cases included into our study up to date the median Liver frailty index value was 3.92, which indicates pre-frailty.

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: Scholarship at Risk (SAR) Grant

Outlook / Next steps
In a next step we plan to prepare an abstract to the EASL Liver Cancer Summit 2025 about the incidence of primary liver cancer in Swiss cohort with advanced fibrosis due to metabolic-dysfunction-associated steatotic liver disease and to determine the diagnostic performance of screening ultrasound to detect liver nodules in NAFLD population.

Literature:
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Administration: Lilian Smith
Murtenstrasse 35, 3008 Bern, Tel. +41 31 632 32 88
lilian.smith@insel.ch
www.swissliver.ch