FD ID: FD1987
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Project Title: Prediction of Liver Cancer Risk in American MASLD Patients Using Existing Longitudinal Data

Background/Rationale:

Our group, with ties to Sorbonne University (Paris, France), APHP Pitié-Salpétrière, and INSERM, has been actively involved in liver disease research for the past 40 years, contributing to the collective understanding through ~600 publications. A key development from our work is the FibroTest, also known as FibroSure, a diagnostic model that was created in collaboration with Sorbonne University. This tool, based on a combination of biochemical markers—alpha-2-macroglobulin, haptoglobin, apolipoprotein-A1, GGT, and bilirubin—aims to assess liver fibrosis non-invasively.

The application of FibroTest spans several liver conditions, including infections by HCV and HBV, MASLD, alcohol-induced liver disease, and other complex scenarios involving multiple causes. Acknowledged by professional bodies like the AGA (American Gastroenterological Association), AASLD (American Association for the Study of Liver Diseases) and WHO (World Health Organization), the test has been incorporated into clinical practice, leading to real-world data accumulation, which has been documented in numerous peer-reviewed articles. This contribution also extends to the evaluation of Steatosis and SteatoHepatitis, supporting the broader goal of improving liver disease diagnosis and management.

There exists a significant unmet need in the hepatology community for an easy-to-use blood test specifically designed for the stratification of liver cancer risk. Currently, despite the guidelines suggested by the AASLD, only a quarter of eligible patients adhere to the recommended liver cancer surveillance protocols. This low participation rate can be attributed to the suboptimal sensitivities of the existing diagnostic tools (ultrasonography 47% and Alpha-Fetoprotein (AFP) 63%).

The Liver Cancer Risk (LCR) score represents a novel prognostic tool for stratifying 5-year liver cancer risk, boasting a 99.4% negative predictive value (NPV). Its development and subsequent validation were chronicled in APT 2019 for HBV and HCV cohorts, J Hepatology Report 2021 for an external validation HCV cohort (n=3,755), and Gastro Hepatology Advances 2022 for an external validation HBV cohort (n=3,520). Building on the FibroTest biomarkers, LCR score incorporates AFP measurements, improving its predictive performance for hepatocellular carcinoma.

Specific Aims:

The primary aim of the study is to externally validate the Liver Cancer Risk (LCR) score in patients with metabolic dysfunction-associated steatotic liver disease (MASLD), leveraging follow-up data from American electronic health records (EHRs) available through the PCOR network.

Secondary objectives include further external validation of the LCR score within cohorts of patients affected by Hepatitis C Virus (HCV) and Hepatitis B Virus (HBV).

Intervention (if applicable): no intervention (only restrospective anonymous data collection)

Eligible anonymous patients for this study are those with existing data for the FibroTest/FibroSure components: gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT), total bilirubin, apolipoprotein-A1, haptoglobin, and alpha-2-macroglobulin, in addition to age and gender demographics. A contemporary Alpha-Foetoprotein (AFP) measurement within six months of the FibroTest is also required. Optional biomarkers include glycated hemoglobin (HbA1c) and adiponectin. The etiological spectrum includes HBV, HCV, MASLD, alcohol-induced liver disease, and other causes.

Follow-up data should detail mortality with cause and date, occurrence of liver and other cancers with dates, and the date of the last follow-up. There is no stipulated time limit between FibroTest assessment and the acquisition of follow-up data. However, patients with cancer occurrence before or within two years post-FibroTest will be excluded from the study.

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