Liver specific, systemic and genetic contributors to alcohol-related liver disease progression

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Abstract

Alcohol-related liver disease (ALD) impacts millions of patients worldwide each year and the numbers are increasing. Disease stages range from steatosis via steatohepatitis and fibrosis to cirrhosis, severe alcohol-associated hepatitis and liver cancer. ALD is usually diagnosed at an advanced stage of progression with no effective therapies. A major research goal is to improve diagnosis, prognosis and also treatments for early ALD. This however needs prioritization of this disease for financial investment in basic and clinical research to more deeply investigate mechanisms and identify biomarkers and therapeutic targets for early detection and intervention. Topics of interest are communication of the liver with other organs of the body, especially the gut microbiome, the individual genetic constitution, systemic and liver innate inflammation, including bacterial infections, as well as fate and number of hepatic stellate cells and the composition of the extracellular matrix in the liver. Additionally, mechanical forces and damaging stresses towards the sophisticated vessel system of the liver, including the especially equipped sinusoidal endothelium and the biliary tract, work together to mediate hepatocytic import and export of nutritional and toxic substances, adapting to chronic liver disease by morphological and functional changes. All the aforementioned parameters contribute to the outcome of alcohol use disorder and the risk to develop advanced disease stages including cirrhosis, severe alcoholic hepatitis and liver cancer. In the present collection, we summarize current knowledge on these alcohol-related liver disease parameters, excluding the aspect of inflammation, which is presented in the accompanying review article by Lotersztajn and colleagues.