Abstract

Liver cirrhosis represents the end stage of most chronic liver diseases. The course of the disease and its complications can be significantly influenced by host genetic factors and the severity of portal hypertension (PH).

The aim of the study was to describe the role of genetic factors influencing the progression and complications of liver disease and to determine the role of non-invasive assessment of the stage of liver fibrosis and severity of PH and their correlation with portosystemic gradient (HVPG) measurements. We first focused on the role of allelic variants in TLR4 signalling pathway genes in the risk of occurrence of severe bacterial infections in patients with advanced liver cirrhosis, liver transplant (LT) candidates. We found that the *TNFA* c.-238G/A promoter variant significantly reduced the risk of bacterial infections and was associated with a decreased mortality rate. We further investigated the role of the variant G allele in *PNPLA3* gene in the progression of chronic liver failure and the need for LT in patients with liver cirrhosis due to HCV infection. As a result, we found that the carriage of the variant G allele led to a faster progression of chronic liver failure and the need for LT at a younger age. Third, we investigated whether the efficacy of triple combination treatment of HCV infection with pegylated interferon-alpha, ribavirin and a first generation protease inhibitor depends on the pre-treatment interferon-sensitive genes expression profile. We demonstrated that the only factor that predicted cure was the expression of *USP18* both before and in the early phase of antiviral treatment. We further investigated the non-invasive assessment of liver stiffness (LS) by 2D shear-wave elastography (SWE) in patients with advanced liver cirrhosis and its correlation with the degree of PH assessed as HVPG measurement. We demonstrated a strong correlation between LS using 2D-SWE and HVPG across a wide range of values. When assessing serum markers of PH, osteopontin was the most accurate indicator of its severity. Finally, we sought to elucidate the contribution of static and dynamic components of the LS measurement in the previously described cohort of patients. We found that LS in patients with advanced liver cirrhosis is determined primarily by the HVPG value, whereas the contribution of collagen content in the liver is relatively low.

Keywords: Liver cirrhosis, portal hypertension, bacterial infection, genetic factors, *PNPLA3*, liver stiffness, HCV infection.