Abstrakt

Nonalcoholic fatty liver disease (NAFLD) occurs frequently not only in the general population, but also in liver transplant (LT) recipients. The data about prevalence, evolution, causes and significance of steatosis in patients after LT are limited.

In a large retrospective study in LT recipients with histological evaluation of steatosis, we found high prevalence of steatosis (56,4 %) and steatohepatitis (10,4 %), the prevalence of steatosis increased after LT. Pretransplant predictors of steatosis included alcoholic cirrhosis and high BMI, whereas increased alkaline phosphatase and mycophenolate mofetil given initially were protective. Posttransplant predictors of steatosis included BMI, serum triglycerides, alcohol consumption and presence of type 2 diabetes mellitus, whereas increased serum creatinine was protective. Presence of significant steatosis/steatohepatitis was not associated with increased grade of fibrosis. There was no difference between the occurrence of steatosis in surviving and lost grafts. Survival of patients with/without significant steatosis was similar with a trend to higher long-term mortality of patients with significant steatosis.

In the evaluation of the impact of *TM6SF2* rs58542926 and *PNPLA3* rs738409 genotypes of the donor and recipient on pathophysiology of steatosis after LT, we found that *TM6SF2* c.499A and *PNPLA3* c.444G alleles of the donor (hepatic expression), but not of the recipient (extrahepatic expression) predicted increased liver fat content after LT and their effect was additive. The effect of the donor *TM6SF2* c.499A and *PNPLA3* c.444G alleles increased with higher BMI of the recipient.

In a subsequent prospective study, we confirmed that posttransplant NAFLD and its progression to NASH and fibrotic form is affected by posttransplant insulin resistance (IR), which has a close relationship to changes of BMI. We did not prove the effect of immunosuppression on posttransplant IR.

Key words: Steatosis, NAFLD, NASH, liver transplantation, PNPLA3, TM6SF2, insulin resistance, immunosuppression