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Linking nonalcoholic fatty liver disease to hepatocellular carcinoma: from bedside to bench and back

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ABSTRACT

Aims and background. Nonalcoholic fatty liver disease (NAFLD) and hepatocellular carcinoma (HCC) are two major causes of liver disease worldwide. Epidemiological and clinical data have clearly demonstrated that NAFLD and its associated metabolic abnormalities are a risk factor for HCC. Traditionally, the mechanisms whereby NAFLD acts as a risk for HCC are believed to include replicative senescence of steatotic hepatocytes and compensatory hyperplasia of progenitor cells as a reaction to chronic hepatic injury. Recent years have witnessed significant advances in our understanding of the mechanisms underlying the link between NAFLD and HCC.

Methods. In the present review, we provide an update on the pathophysiological pathways linking NAFLD and its associated metabolic derangements to malignant hepatic transformation, with a special focus on insulin resistance, adipokines, inflammation, and angiogenesis. We will also discuss the potential therapeutic implications that such molecular links carry.

Results. Although treating NAFLD could reduce the risk of malignant hepatic transformation, no long-term studies focusing on this issue have been conducted thus far. Insulin resistance, inflammation as well as derangements in adipokines and angiogenic factors associated with NAFLD are closely intertwined with the risk of developing HCC.

Conclusions. Traditional therapeutic approaches in NAFLD including metformin and statins may theoretically reduce the risk of HCC by acting on common pathophysiological pathways shared by NAFLD and HCC.

Key words: nonalcoholic fatty liver disease, hepatocellular carcinoma, insulin resistance, adipokines.

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