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Columns: Topic Highlights

Prevention of hepatocellular carcinoma by correction of metabolic

Javier Ampuero, Manuel Romero-Gómez

#### Abstract

Hepatocellular carcinoma is the third leading cause of cancer-related deaths in the world. It is associated with an important mortality rate and the incidence is increasing. Patients showing metabolic syndrome seem to have higher incidence and mortality rates from hepatocellular carcinoma than healthy subjects, especially those with type 2 diabetes mellitus and obesity. Thus, metformin and statins, both to treat features of metabolic syndrome, have been proposed to decrease the risk of hepatocellular carcinoma. Otherwise, liver cancer is the result of a complex process which impairs several signaling cascades, such as RAS/RAF/MEK/ERK, PI3K/AKT/mTOR and Wnt/ $\beta$ -catenin signaling. Metformin (through 5'-adenosine monophosphate-activated protein kinase pathway activation) and statins (through 3-hydroxy-3-methylglutaryl coenzyme A inhibition) show anti-tumoral properties modifying several steps of RAS/RAF/MEK/ERK, PI3K/AKT/mTOR and Wnt/ $\beta$ -catenin signaling cascades. On the other hand, metformin and statins have been found to reduce the risk of hepatocellular carcinoma up to 50% and 60%, respectively. Furthermore, both drugs have shown a dose-dependent protective effect. However, information about chemopreventive role of metformin and statins is

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