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Editorial: Diabetes and its association with hepatocellular carcinoma in chronic hepatitis B

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The impact of metabolic syndrome and its complications, namely hepatic steatosis and diabetes, have appropriately become focal points of investigation within hepatology in the setting of the evolving obesity epidemic. Although there is a large body of research that has demonstrated an increased risk of hepatocellular carcinoma (HCC) in patients with diabetes, the specific disease characteristics that modify this relationship require further investigation. (1) This is particularly the case in patients with viral hepatitis, where studies have produced conflicting data in terms of the independent association of metabolic risk factors with HCC. (1–4)

In a recent issue, Fu *et al* provide further data to support the observation of increased risk of HCC for diabetic patients with CHB.(5) Using the Taiwanese National Health Insurance Research Database, they included a random sample of 2099 patients with CHB with new-onset diabetes and 2080 age, gender, and inception-point matched non-diabetic patients. After adjusting for possible contributing factors, diabetes was an independent predictor for HCC with a hazard ratio of 1.798.

This study has several strengths including a large sample-size, length of longitudinal follow-up, and accounting for multiple potential confounders for competing risk for developing HCC. Several unaddressed questions remain however, particularly those stemming from the lack of histology to address possible concomitant steatohepatitis. It is well known that

diabetes is an independent risk factor and driver of steatohepatitis, and untreated steatohepatitis, along with other metabolic dysregulations associated with diabetes, have been shown to increase the risk of HCC in the setting of hepatitis B infection.(6, 7) Additionally, further detail regarding duration of diabetes and control of diabetes on the risk of HCC should also be evaluated.(2, 3, 8, 9) Lastly, the impact of anti-diabetic regimen should be assessed as data has suggested decreased risk of HCC and liver related mortality in patients on metformin.(8, 10) In this study only 39% of diabetics were on treatment and the effect of diabetic treatment agents on HCC risk was not assessed.

Overall this study demonstrates the importance of addressing modifiable metabolic risk factors in patients with CHB. Lifestyle interventions to prevent obesity, diabetes and other features of the metabolic syndrome should be emphasized in the care of patients with CHB. Further studies are needed to clarify the attributable risk of HCC in diabetics (such as duration and severity of steatohepatitis), as well as optimal treatment of steatohepatitis, in order to minimize the risk of incident HCC in CHB.

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