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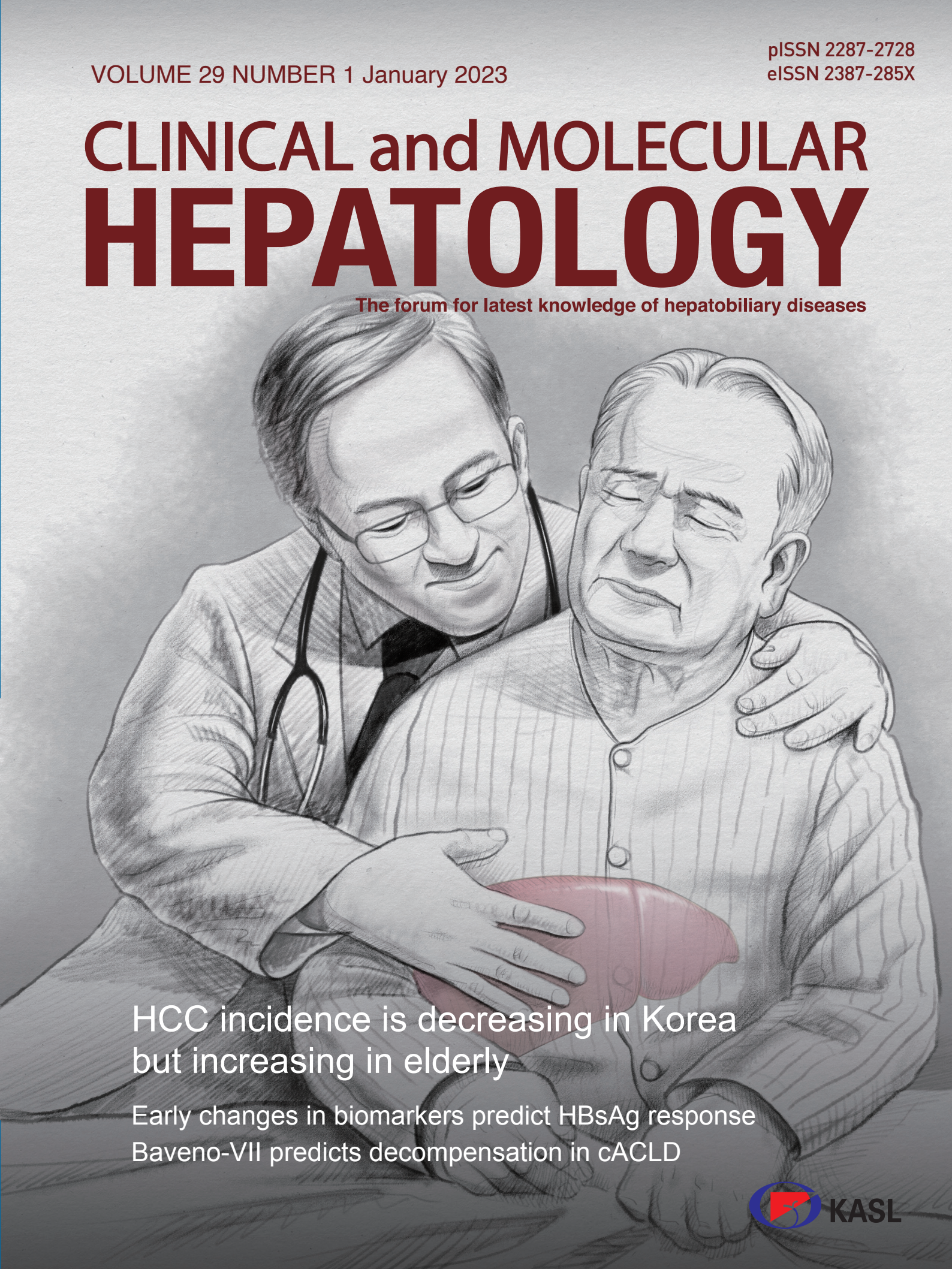

## HCC incidence is decreasing in Korea but increasing in elderly

Early changes in biomarkers predict HBsAg response

Baveno-VII predicts decompensation in cACLD

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## Correspondence

# Correspondence on Editorial regarding "Impact of nationwide hepatocellular carcinoma surveillance on the prognosis in patients with chronic liver disease"

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**Keywords:** Hepatocellular carcinoma; Chronic hepatitis; Liver cirrhosis; Early detection of cancer

Dear Editor,

We appreciate the interest and comments from Kim et al.[1] on our recently published paper on the impact of nationwide hepatocellular carcinoma (HCC) surveillance on the prognosis of patients with chronic liver disease.[2] In the article, the authors speculated on the current status of HCC surveillance and suggested a course of action.[1] We agree with the suggestions and would like to discuss several related issues in detail.

With the current era of antiviral treatment in chronic hepatitis B (CHB) or chronic hepatitis C (CHC), high-risk groups for HCC surveillance need to be redefined in a more detailed manner, especially considering the use of antiviral agents in chronic viral hepatitis. Based on the annual incidence of HCC and its cost-effectiveness, HCC surveillance is traditionally recommended for patients with CHB aged >40 years or with any type of cirrhosis.[3,4] However, the risk of HCC development in CHB has changed since the introduction of antiviral treatment. The risk of HCC development is decreased in CHB patients receiving nucleotide analogs as the use of potent antiviral treatment effectively suppresses hepatitis B virus replication.[5,6] However, the risk of HCC development remains higher in these patients than in those with inactive CHB.[7] As a result, HCC surveillance in CHB should be subdivided based on the phases of CHB (such as, immune-tolerant, immune-active phase with the use of antiviral treatment, and inactive phase).

Additionally, the reduced risk of advanced fibrosis or cirrhosis during or after antiviral therapy should be considered. Recent studies have reported that long-term use of antiviral agents could induce the regression of advanced fibrosis or cirrhosis in CHB.[8,9] It is well established that cirrhosis is a crucial factor in the development of HCC. In a certain percentage of patients, regression of advanced fibrosis or cirrhosis fol-

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lowing antiviral treatment has been reported.[8,9] Therefore, it is necessary to consider the regression of advanced fibrosis or cirrhosis as a risk factor for HCC development in CHB patients receiving antiviral treatment. Similarly, information regarding HCC surveillance in patients with CHC, who have achieved sustained virologic response (SVR) after direct-acting antivirals is unclear.[10] Therefore, it is necessary to define risk stratification for HCC surveillance in this group of patients. As mentioned earlier, the high-risk group for HCC surveillance is defined based on the annual incidence of HCC and cost-effectiveness.[3,4] Unfortunately, our study[2] lacked data on cost-effectiveness, such as incremental cost-effectiveness ratio or quality-adjusted life year. A recent meta-analysis has reported that biannual surveillance for HCC in CHC patients who achieved SVR is cost-effective for patients up to 70 years old with cirrhosis and up to 60 years old with advanced fibrosis.[11]

It is also unclear whether HCC surveillance is helpful for survival gain in patients with nonalcoholic fatty liver disease (NAFLD), particularly those without advanced fibrosis or cirrhosis.[12] NAFLD-associated HCC can frequently occur without advanced fibrosis or cirrhosis, even in patients with simple steatosis and without steatohepatitis.[12] Therefore, it is necessary to define a high-risk group for NAFLD-associated HCC by another method apart from advanced fibrosis or cirrhosis. A recent study showed that a genetic polymorphism might be a significant risk factor for NAFLD-associated HCC.[13] A polygenic risk score based on genetic polymorphisms associated with hepatic fat may also prove to be a useful tool to stratify high-risk groups for NAFLD-associated HCC, particularly in patients without advanced fibrosis or cirrhosis.

Screening is the next issue that needs to be addressed regarding HCC surveillance. Although ultrasonography is recommended as a screening tool, the diagnostic accuracy of this method for early-stage HCC is suboptimal in some patients. Furthermore, the diagnostic accuracy in obese patients is lower than that in non-obese patients.[14] Additionally, it is difficult to differentiate HCC from regenerative nodules or dysplastic nodules in patients with cirrhosis using this method.[15] Therefore, an alternative screening tool beyond ultrasonography is needed to increase the efficacy of HCC surveillance. Computed tomography (CT) or magnetic resonance imaging (MRI) has shown better performance in the detection of HCC in cirrhotic patients compared to ultrasonography.[3] However, it is necessary to clarify the role of CT or MRI as HCC surveillance tools based on their adverse effects and costs.

Taken together, it can be concluded that HCC surveillance in patients with chronic liver disease is crucial for detecting early-stage tumors and improving overall survival. However, changes are needed regarding the strategies being employed for HCC surveillance. The use of antiviral agents in viral hepatitis, dynamic changes in advanced fibrosis or cirrhosis, genetic factors for HCC development in non-cirrhotic patients, particularly in NAFLD, and screening tools other than ultrasonography should be considered to achieve better precision in HCC surveillance among patients with chronic liver disease.

## Authors' contribution

All authors contributed to the conception of the study and drafting of the manuscript. All authors contributed to the critical revision of this article. All the authors provided final approval for the version to be published.

## Conflicts of Interest

The authors have no conflicts to disclose.

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**Abbreviations:**

CHB, chronic hepatitis B; CHC, chronic hepatitis C; CT, computed tomography; HCC, hepatocellular carcinoma; MRI, magnetic resonance imaging; NAFLD, nonalcoholic fatty liver disease; SVR, sustained virologic response

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