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EDITORIAL

How much management is necessary? Sustaining the benefit of achieving a sustained virologic response to hepatitis C

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Described as a silent killer by the media, hepatitis C virus (HCV) infection can be present in the body for 20 years or more before causing serious complications. An estimated 130–150 million persons globally are infected with HCV, among which 350,000–500,000 deaths each year can be attributed to HCV, including HCV-related liver disease, cirrhosis, and hepatocellular carcinoma (HCC) [1]. With appropriate screening and treatment, many of these deaths can be prevented.

With the approval of direct-acting antivirals for clinical use in 2011, HCV treatment regimens have demonstrated increased efficacy, fewer side effects, and wider application due to fewer contraindications and greater availability of treatment options [2, 3]. Treatment success is more likely, with 50–90 % of persons treated eradicating the virus (as determined by undetectable RNA) and achieving a sustained virologic response (SVR).

In patients achieving SVR in response to treatment, the issue becomes how best to monitor and support patients who have cleared the virus. Current management strategies support routine screenings to monitor for HCC development at 6-month intervals among persons with advanced liver disease, i.e., staged at F3 or F4, or with certain risk factors such as male gender, advanced age, progression of liver fibrosis, and low platelet count [4, 5]. However, there is limited evidence on the duration of the protective benefit that achieving SVR has on the development of HCC.

In this issue of the Journal of Gastroenterology, Yamashita et al. [6] explore long-term outcomes experienced by HCV-infected persons who have achieved SVR, focusing on risks associated with the development of HCC and benefits of early HCC diagnosis to inform clinical management decisions regarding periodic HCC screenings. Yamashita and colleagues identify advanced age (≥50 years), AFP elevation (>8 ng/mL), and alcohol consumption (≥30 g/day) as predictors of HCC development among their study population, which aligns with the literature [4, 5]. This study also emphasizes that among persons who received periodic cancer screenings at least every 6 months, the 5-year survival rate was 93 % instead of 60 % among persons monitored less frequently than every 6 months. The most surprising finding from this study, however, is the large number of patients staged at F2 via liver biopsy who developed HCC following SVR. If supported through further study, this suggests that even moderate liver disease may be an important risk factor to consider when determining the management of patients.

This study comes at an important time in the research on hepatitis C. Yamashita and colleagues were able to clearly recognize the state of the evidence and push the agenda forward, drawing focus to the question of "what next?" By teasing out the long-term outcomes for persons who have achieved SVR, as well as the 5-year survival benefit from early detection of HCC, this study may help clinicians better evaluate different management strategies and influence future research on the topic.

Yamashita and colleagues demonstrate the ability to expand the observation period up to 20.5 years for retrospective research on persons who have achieved SVR. This encourages future researchers to examine the robustness and representativeness of Yamashita's finding that persons with moderate liver disease, specifically F2, should receive

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periodic screenings to detect HCC development. Additional study can also shed light on the rate of HCC development as compared to that found by Yamashita and colleagues (5.5 %) and that from a recent meta-analysis (1.6 %) [7], and help to investigate long-term outcomes in varying stages of fibrosis. Another topic for exploration that benefits from an expanded observation period is how aging and progression of liver disease interact, as younger patients may be less susceptible to the development of HCC even with moderate or advanced liver disease, whereas older persons ($\geq$60 years) may be more susceptible with less evidence of liver disease.

Advances in the efficacy and safety of treatment for HCV emphasize the importance of determining the most effective management strategies for maintaining the health of persons who achieve SVR. The contributions by Yamashita and colleagues should be considered along with other evidence when making management decisions about periodic follow-up screenings to support early identification of HCC, providing patients with the most options for greatest survival. In addition to the benefits increased research on HCV treatment has for the successful treatment of patients, the evidence on long-term outcomes following HCV eradication will improve the options available for patient management and promoting effective HCC screening and prevention.

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