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Article type : Letter to the Editor Author response to Letter to the Editor: "Chronological change in alpha-fetoprotein levels in hepatocellular carcinoma after eradication of hepatitis C virus" _____ Authors: Vincent L. Chen, Neehar D. Parikh Affiliation: Division of Gastroenterology and Hepatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI 48109, USA **Correspondence**: Vincent L. Chen, M.D., M.S. 1500 East Medical Center Drive, Taubman Center SPC 3912 Ann Arbor, MI 48109 Email: vichen@med.umich.edu Phone: 734-936-8643 Fax: 734-936-7392 Keywords: sustained virologic response, direct-acting antiviral, chronic hepatitis C, surveillance

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Abbreviations:

AFP, alpha-fetoprotein. DAA, direct-acting antiviral. HCC, hepatocellular carcinoma. HCV, hepatitis C virus. SVR, sustained virologic response.

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Letter to the editor:

We thank Dr. Fukumoto and colleagues for their letter related to our manuscript.^{1,2} There are few data on sensitivity of alpha-fetoprotein (AFP) for hepatocellular carcinoma (HCC) detection in patients with cirrhosis who achieved sustained virologic response (SVR) after direct-acting antiviral (DAA) therapy for hepatitis C virus (HCV) infection.³ Our study was not able to directly address whether including AFP in HCC surveillance in this population is associated with improved outcomes, for two reasons. First, in our cohort, AFP was infrequently used for HCC surveillance (at least in conjunction with imaging, as we did not consider AFP-only surveillance) with median proportion of time covered by both AFP and ultrasound of 0%. Second, only a small proportion of patients had received DAA therapy as the study period was largely in the pre-DAA era.

With the caveat that data are limited in patients with HCV and SVR, we believe that the balance of evidence favors inclusion of AFP in HCC surveillance. In a recent meta-analysis, AFP plus ultrasound demonstrated higher sensitivity than ultrasound alone for early-stage HCC detection (63% vs. 45%).⁴ Longitudinal AFP measurement may further increase sensitivity for HCC detection.⁵ Further studies are required to establish sensitivity and specificity of ultrasound with or without AFP in patients with HCV cirrhosis after SVR with DAA therapy, to determine the benefits of incorporating AFP into HCC surveillance in this population.

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