Conflict of interest
The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors’ contributions
T.-I. Huo and P.-H. Liu performed the research. C.-Y. Hsu and T.-I. Huo designed the study and wrote the paper. All authors approved the final version of the manuscript.

Supplementary data
Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jhep.2017.11.041.

References

Reply to: “Detecting microvascular invasion in HCC with contrast-enhanced MRI: Is it a good idea?”

To the Editor:
We thank Teh-Ia Huo et al. for their interest in our recent study about preoperative gadoxetic acid-enhanced MRI for predicting microvascular invasion (MVI) in patients with single hepatocellular carcinoma (HCC), and we appreciate their comments.

The meta-analysis and systemic review by Rodriguez-Peralvarez et al. reported that the MVI rates of HCCs after surgical resection ranged from 22.3% to 52.0%. The studies, which accounted for more than 50% MVI rates of HCCs, were performed in patients with an average tumor size of 5 cm or greater. On the basis of multicenter international data of 1,073 patients who underwent HCC resection, Pawlik et al. reported the MVI rates of 25% and 40% in patients with HCCs of ≤3 cm and 3.1–5 cm in size, respectively. The single-center study by Tsai et al. which authors mentioned in the Letter to the Editor, presented MVI rates of 40.5% for tumors ≤2 cm in size and 49.6% for tumors 2.1–4 cm in diameter, respectively. However, that study included patients with not only single HCC, but also two or more HCCs. The MVI rate in our study (32.0%, 63/197) was similar to that in a recent study (37.3%, 87/233) in a surgical series of solitary HCCs of ≤5 cm in size.

The previous study by Rizzi et al. that used pretransplant imaging modalities such as ultrasonography, computed tomography, and hepatic angiography, which authors mentioned in the Letter to the Editor, reported a low sensitivity in detecting multicentric lesions. However, at present, MRI with hepatobiliary agents is the most sensitive method for diagnosis of HCC and the addition of diffusion-weighted (DW) image incrementally increases the detection rates of HCCs. Recent advances in MRI techniques and liver-specific contrast agents have enabled the identification of very small HCCs (even less than 1 cm in diameter).

We agree that MVI is difficult to directly visualize in HCC, even with the latest state-of-the-art MRI techniques such as 3-Tesla MRI with hepatobiliary agents, including DW imaging. In addition, in our study, eight (4.1%) of 197 patients with HCC had a microscopic satellite nodule that was not visible on preoperative MRI and seven (87.5%) of them had HCC with MVI. As the authors mentioned, MVI is a crucial prognostic factor of HCC, but is confirmed only by precise histopathological evaluation of resected specimens in patients who undergo surgical treatment. Surgery remains the most efficient treatment for patients with HCC. However, less than 30% of patients with HCC are candidates for surgery, including liver transplantation, mainly because of the multiplicity of HCC, which often occurs on a background of chronic liver disease.

In patients with HCC for whom locoregional therapy such as ablation as an alternative to curative therapy is planned instead of surgical resection, HCC with MVI cannot be predicted before the treatment without support of imaging studies. We think that the state-of-the-art MRI is one of the best methods for predicting MVI before the treatment of HCC. Thus, the effort for predicting MVI noninvasively before the management of HCC using this state-of-the-art MRI in surgical or nonsurgical candidates is highly important to reduce early recurrence.

On the basis of our study results, that a combination of two or more MRI findings among arterial peritumoral enhancement, non-smooth tumor margin, and peritumoral hypointensity on
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hepatobiliary phase can be used as a preoperative imaging biomarker for predicting MVI with a specificity of >90%, we believe that use of the state-of-the-art MRI for predicting MVI of HCC before surgical or nonsurgical management of HCCs would be helpful. This imaging will enable clinicians to determine the optimal treatment strategy for eradicating MVI, reducing early recurrence by enabling a sufficient resection margin in patients for whom surgery is planned, and by changing from ablation to surgical treatment or having sufficient ablative margin in patients for whom ablation is planned as an alternative to curative treatment.

In summary, although our study results may not be sufficient to justify the use of state-of-the-art MRI to predict MVI of HCC in clinical practice, we believe that the effort to predict MVI using this state-of-the-art MRI is a good idea.

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Authors’ contributions
Both authors (S.L. and S.H.K.) contributed to the writing and final approval of the reply letter.

Supplementary data

References

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Reply to: “Reply to: ‘Response to DAA therapy in the NHS England Early Access Programme for rare HCV subtypes from low and middle income countries’”

To the Editor:
We thank Zeuzem et al. for their response to our recently published findings.1,2 Their data provide a valuable addition to reports describing virological outcomes for patients infected with “rare” subtypes who have received sofosbuvir (SOF)-based therapy but have not been well represented in previous large-scale clinical trials. We agree with the authors that assessing treatment outcome in cohorts infected with poorly characterized or uncharacterized subtypes would ideally be determined from patients who have achieved both sustained virological response (SVR) and have had a treatment relapse. However, well-defined cohorts do not exist in most low- and middle-income countries (LMICs) where such subtypes are typically found, and consequently the necessary evidence base has been lacking.

We wish to comment further on the implications for treatment of patients in LMICs as part of the World Health Organization’s global elimination plan. Recently, we published a study illustrating the lack of HCV sequence data in LMICs, particularly those in Africa, South America and Central America.3 We agree