Reply to: “Severity of microvascular invasion does matter in hepatocellular carcinoma prognosis”

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Running title: Classification of microvascular invasion of HCC
List of abbreviations: AJCC = American Joint Committee on Cancer, AUC = area under the curve, FIGO = International Federation of Gynecology and Obstetrics, HCC = hepatocellular carcinoma, LVSI = lymphovascular space invasion, MRI = magnetic resonance imaging, MVI = microvascular invasion

Author Contributions


Conflict of interest statement

The authors have no relevant financial or non-financial interests to disclose.
Dear Editor,

We would like to thank Dr. Attia et al. for their interest in our study entitled “Classification of microvascular invasion of hepatocellular carcinoma: correlation with prognosis and magnetic resonance imaging”, and for their insightful comments¹.

As highlighted in the editorial, we found that the presence of severe microvascular invasion (MVI) – defined as invasion of ≥5 microvessels and the presence of microvessels with ≥50 invaded tumor cells – in hepatocellular carcinoma (HCC) was significantly associated with decreased overall survival, while MVI with one or none of the two features (“mild MVI”) was associated with a prognosis similar to that of HCC with no MVI. As liver pathologists, we sometimes encounter surgically resected HCC specimens for which we can only find rare MVI containing a few isolated floating tumor cells after a diligent hunt under the microscope, and this led us to wonder if such findings had enough clinical impact to increase the tumor stage. We thus hypothesized that MVI that is extensive and composed of well-formed intravascular tumor cell clusters would have more clinical significance.

Interestingly, stratification of the degree of lymphovascular space invasion (LVSI) is used in tumor staging in the case of endometrioid carcinomas of the uterus. Several reports have demonstrated the presence of “focal” LVSI in low-grade endometrioid endometrial carcinomas were similar to those with no LVSI in terms of patient outcome, and this has been adopted in the updated 2023 International Federation of Gynecology and Obstetrics (FIGO) staging of endometrial cancer: the presence of “no or focal (<5 vessels)” versus “substantial (≥5 vessels)” LVSI is now one of the determinants in staging (stage I versus stage IIB) ²,³. According to the current edition of the American Joint Committee on Cancer (AJCC) Staging manual, MVI is the determinant for assigning solitary HCCs of >2cm as pT1b versus pT2, while pT1a is assigned for solitary HCCs ≤2cm regardless of MVI status as MVI has not been shown to have an impact on clinical outcome for small tumors. It would be worth exploring whether applying the severity/extent of MVI to the current AJCC staging system – similarly to the FIGO staging for endometrial cancer – would have better prognostic implications. Our results would need to be validated in larger independent patient cohorts.
Considering the prognostic importance of MVI, predicting MVI using imaging studies before treatment is a key aspect of managing HCC patients. Previous research has identified several magnetic resonance imaging (MRI) features associated with MVI, such as non-smooth tumor margins, peritumoral arterial enhancement, and peritumoral hypointensity on the hepatobiliary phase of gadoxetic acid-enhanced liver MRI. In our study, we also observed that non-smooth tumor margins and the presence of satellite nodules were significantly associated with severe MVI. However, the reported imaging findings associated with MVI have varied across different studies. The diagnostic performance of imaging studies in predicting MVI is limited, with area under the curve (AUC) values ranging from 0.58 to 0.74. Additionally, inter-observer agreement on imaging findings related to MVI has been modest, with kappa values ranging from 0.44 to 0.61. Therefore, predicting MVI using imaging studies remains challenging. In this context, employing artificial intelligence techniques, such as deep learning, may have the potential to enhance diagnostic performance for MVI prediction and reduce variability among readers.
References


