Editorial

Severity of microvascular invasion does matter in hepatocellular carcinoma prognosis

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Vascular invasion has a significant impact on the prognosis of patients with hepatocellular carcinoma (HCC)(1,2). HCC staging schemes, such as the tumor-node-metastasis system from the American Joint Committee on Cancer and the Barcelona Clinic Liver Cancer (BCLC) classification, incorporate macrovascular invasion as a critical prognostic feature(3–5).

Microvascular invasion (MVI) is also a potent prognostic factor in HCC. Unlike macrovascular invasion, which is apparent in cross-sectional images, MVI status could be determined through histologic examination of biopsy or surgically removed tissue specimens. The MVI classification method and nomograms made it possible to estimate tumor recurrence risk and overall survival in HCC patients with greater accuracy after R0 liver resection(6). MVI is characterized by a wide variety of histological features, and it remains unclear whether the degree of MVI is associated with patient outcomes and whether imaging can predict the presence of MVI(7,8).

A recent study published in Clinical Molecular Hepatology by Hwang et al., demonstrated that the presence of severe MVI, defined as ≥5 microvessels, or the presence of microvessels with ≥50 invaded tumor cells was significantly associated with decreased survival, while mild MVI had no prognostic impact(9). There was a trend towards worse recurrence-free survival (RFS) for moderate MVI, although there was no discernible difference in overall survival between patients with and without MVI. The degree of MVI was found to be helpful in identifying a subgroup of HCC patients who have a higher risk of recurrences beyond Milan criteria, making them less likely to respond to curative therapies when they do occur(10).

In contrast to previous research, the current study did not show any prognostic value of muscularized MVI. This finding may be partially explained by the low incidence rate of muscularized MVI (8%), as the authors indicated. Roayaie et al.(11) and Feng et al. (6) have examined the distance between MVI and the primary tumor, as well as the degree of filling of the tumor's small blood veins as a prognostic factor in HCC. Of note, there is a drawback to utilizing the distance to categorize MVI on standard microscope slides as distinct regions of...
healthy liver tissue on the same slide are required for an accurate measurement of the distance. The current study revealed that a major predictor of prognosis is the number of HCC tumor cells that have invaded several small blood arteries.

Predicting MVI on imaging prior to surgical resection can be particularly helpful for presurgical prognostication. Previous studies have revealed distinct MRI characteristics such as non-smooth tumor margin(12), large size (13,14), arterial peritumoral enhancement(15), rim arterial enhancement(16), diffusion limitation, non-peripheral washout(17), non-enhancing capsule, tumor hypointensity or peritumoral hypointensity on hepatobiliary phase (HBP)(12,15), and multifocality, may predict microvascular invasion MVI in HCC. (12,18) However, these predictive radiologic findings varied between the studies. This study found that both non-smooth tumor margins and satellite nodules are independent predictors of severe MVI, although the accuracy of imaging features to predict MVI was not high enough, with AUCs lower than 0.70.

Nevertheless, the authors indicated that a non-smooth tumor margin may be useful for excluding the presence of severe MVI, as it showed a high sensitivity (88.2%) and negative predictive value (90.7%) for detecting severe MVI. The presence of satellite nodules may be used cautiously to predict the presence of severe MVI due to high specificity (88.9%).

Due to the retrospective nature of this investigation, there is a chance that the liver tumor specimen processing methodology was inconsistent throughout the study period. Furthermore, the number of slides examined from each tumor may affect the probability of MVI detection. For instance, extensive inspections are performed on small tumors, but larger tumors may present technical difficulties, potentially leading to an undervaluation of MVI. Another limitation is that, multiple cross-sections of the same vessel or its branches were included when counting invaded microvessels, which could inflate MVI counts, particularly in cases with extensive invasion. A more objective approach may have avoided potential inaccuracies in determining the degree of MVI given the difficulty of precisely counting MVI and cancer cells in narrow blood vessels.
Finally, this study was conducted in a cohort of HCC patients with a predominant etiology of HBV and preserved liver function. Therefore, prognostic significance of MVI categorization and radiologic features indicative of MVI should be further validated in future studies to confirm their predictive values in independent cohorts of HCC patients with different liver disease etiology and degrees of liver dysfunction.

Investigating the possibility of using artificial intelligence to analyze histology slides and improve the accuracy and efficacy of MVI identification will further enhance the current understanding of the prognostic impact of MVI extent on prognosis in HCC. AI-guided radiomic analysis may also identify accurate imaging biomarkers predicting high-risk MVI in HCC, ultimately improving in the HCC care continuum, including prognostication of HCC.
References


