Letter to the Editor

Microvascular Invasion as a Prognostic Predictor in Hepatocellular Carcinoma: How Accurate Is It?

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Dear Editor

We read the paper “Microvascular Invasion and a Size Cutoff Value of 2 cm Predict Long-Term Oncological Outcome in Multiple Hepatocellular Carcinoma: Reappraisal of the American Joint Committee on Cancer Staging System and Validation Using the Surveillance, Epidemiology, and End-Results Database” by Dr. Shindoh et al., published in a recent issue of *Liver Cancer* [1], with enormous interest. Two large surgical cohorts (1,175 patients in the training set and 5,249 patients in the validation set) were analyzed to investigate the prognostic significance of microvascular invasion (MVI) and its ability to improve the performance of AJCC system in hepatocellular carcinoma (HCC). Although their findings are interesting, a few concerns may deserve further discussion.

Independent studies indicated that MVI was a major risk factor for tumor recurrence in patients with HCC undergoing surgical treatment [2, 3]. Although MVI is an important prognostic predictor for HCC, the confirmation of MVI can only be demonstrated from the serially slice-cut resected specimen postoperatively. This is especially crucial when the prevalence rate of MVI was reported to reach 40.5% for tumors ≤ 2 cm and 49.6% for tumors 2.1–4 cm in diameter, respectively, in a surgical series of 322 patients [2]. Notably, the reported prevalence rate of MVI in Shindoh et al.’s series [1] could be profoundly underestimated (only 25.8% for median tumor diameter of 2.2 cm in the training cohort and 26.8% for median tumor diameter of 5.0 cm in the validation cohort). Underestimation of MVI could significantly compromise its prognostic ability in terms of outcome prediction. Consistent with this speculation is that in Shindoh et al.’s series [1], a new staging model based on MVI had only a

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slightly better performance than the AJCC 8th edition in both the training cohort (c-statistics, 0.648 vs. 0.629) and the validation cohort (c-statistics, 0.646 vs. 0.645) with marginal prediction benefits.

The potentially high frequency of MVI in small HCC is further supported by a classical study that looked at the explant livers in HCC patients undergoing liver transplantation [4]. Tiny satellite nodules or tumor nests (<0.5 cm) were frequently identified in the explants through serially examining the slice-cut specimen, thus greatly limiting the ability of imaging detection tools in these cases. In summary, MVI acts as a distinct tumor behavior and may serve as a unique prognostic marker for HCC. For patients who receive curative resection, identification of MVI should be best demonstrated from multiple, serially slice-cut resected pathological specimens. To avoid possible underestimation of MVI, a thorough examination of surgical specimen is mandatory and considered the standard way of confirmation. Accurate information on MVI is expected to play an important role in refining the currently used staging system for HCC.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

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