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Performance of HCC diagnosis in the KLCA-NCC guidelines: a closer look at MRI contrast agents and HCC imaging hallmarks

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We were glad to read the study entitled, “Diagnostic performance of the 2022 KLCA-NCC criteria for hepatocellular carcinoma on magnetic resonance imaging with extracellular contrast and hepatobiliary agents: comparison with the 2018 KLCA-NCC criteria” by Yoon et al.¹ Unlike the definite hepatocellular carcinoma (HCC) category, the probable HCC category has been revised in the 2022 Korean Liver Cancer Association-National Cancer Center (KLCA-NCC) criteria.² Yoon et al.¹ highlighted that in using extracellular contrast agent (ECA)-magnetic resonance imaging (MRI), the 2022 KLCA-NCC offers a high sensitivity in HCC diagnosis compared to that of the 2018 KLCA-NCC, particularly, in the definite and probable HCC categories. Moreover, their results reaffirmed that hepatobiliary agent (HBA)-MRI outperformed ECA-MRI in terms of sensitivity without sacrificing specificity across the 2018 and 2022 KLCA-NCC criteria. This aligns with our understanding, especially in the Korean medical environment, as HBA-MRI is predominantly used for liver cancer diagnosis, and there is a premium for high sensitivity. With this foundation, we wish to provide further insights into this topic.

Highlighting that the diagnostic ability for HCC may be influenced by the type of contrast medium as well as the specific diagnostic criteria is essential. Specifically, the washout definition or type of major features used can substantially influence the diagnostic performance for HCC. The main conclusion is that for the definite HCC category, HBA-MRI provides better sensitivity than ECA-MRI, in accordance with the intention of the KLCA-NCC versions. This is largely attributable to the expanded washout definition, which inherently favors HBA-MRI. Nevertheless, these findings need to be approached with caution; early contrast uptake

into hepatocytes, even in the portal venous phase, may exaggerate washout on HBA-MRI,^{3,4} albeit not being associated with the study results. Furthermore, the enhancing capsule, a major feature in Liver Imaging Reporting and Data System (LI-RADS) that is better visualized in ECA-MRI than in HBA-MRI, is used only as an ancillary feature favoring HCC in the KLCA-NCC guidelines.⁵ Thus, in interpreting the results of Yoon et al.,¹ we should consider the expanded washout and undervaluing of enhancing capsules in the KLCA-NCC guidelines, as opposed to solely focusing on the intrinsic differences between the two MRI contrast agents. Consequently, the conclusions of this study should be interpreted as specifically applicable to the KLCA-NCC criteria used in clinical scenarios, emphasizing early HCC detection and treatment.

Subsequently, we are slightly concerned about the interpretation of HCC hallmark visualization based on MRI contrast agents because the details of the imaging features are missing. As highlighted in the editorial by Yoon,⁶ the similar diagnostic performance of the ver. 2018 and ver. 2022 KLCA-NCC on HBA-MRI is likely attributed to the fact that most observations with arterial phase hyperenhancement (APHE) and washout (portal venous phase washout or hypointensity on transitional/hepatobiliary phase) can be classified as definite HCC, irrespective of the ancillary features. To confirm this, a more detailed depiction of imaging features is essential. Furthermore, application of ancillary features in the updated 2022 KLCA-NCC diagnostic flow for probable HCC differs according to the presence of APHE. In comparing the 2018 and 2022 KLCA-NCC using ECA-MRI, what combinations of APHE and ancillary features of both categories were included in probable HCC? We empirically presume that in ECA-MRI,

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observations showing APHE and mild-to-moderate T2 hyperintensity and/or restricted diffusion (with no other ancillary features favoring HCC in particular) would be responsible for a significant increase in the probable HCC category with ver. 2022, but not with ver. 2018. The observation of APHE, no washout, and ancillary features favoring malignancy in general may include other HCC mimickers, such as inflammatory lesions or other tumors like combined hepatocellular cholangiocarcinoma, angiomyolipoma, and neuroendocrine tumors. Further, in Yoon's study,⁶ non-surgical candidates were excluded from the final cohort, thus enriching the cohort for HCC. Although there was no significant sacrifice in specificity with ver. 2022 along with expanded washout, relaxing the criteria for probable HCC may inevitably inflate specificity. The difference in the upgraded number of probable HCC by using ver. 2022 between the two contrast agents used in the two patient cohorts might imply an introduced potential bias in Yoon's study.⁶ This issue should be re-evaluated because the motivation of revised version 2020 is not to increase probable HCC categorization with ECA-MRI but not with HBA-MRI. Therefore, caution should be exercised when applying probable HCC in ver. 2022 KLCA-NCC, especially in using ancillary features favoring malignancy in general, because non-HCC lesions can be misdiagnosed as HCC.

Notably, there is an inherent selection bias that should be emphasized. As previously mentioned, the study cohort is biased toward a large number of HCCs and a relatively small number of other malignancies or cirrhosis-related benign nodules. Further, specificity may have been overestimated. Additionally, the study may not have discerned subtle differences in specificity. Without individual comparisons, the reliability of the results may have been compromised. These factors should be considered when interpreting the results.

Yoon et al.¹ provided insights into the evolving landscape of HCC diagnosis using MRI contrast agents within the KLCA-NCC guidelines. As with all studies, the clinical context and guideline specifics play a pivotal role in the interpretations. We appreciate their dedicated efforts and look forward to continued dialogue on this critical subject, fostering a more profound understanding and eventually refining the diagnostic approaches.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

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