Editorial
J Liver Cancer 2023;23(1):124-126
pISSN 2288-8128 • eISSN 2383-5001
https://doi.org/10.17998/jlc.2023.3.7

Impact of the updated KLCA-NCC criteria for diagnosis of "probable HCC" in liver MRI: comparisons between KLCA v2022 and v2018

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See Article "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" on Pages 157-165.

In 2022, the Korean Liver Cancer Association-National Cancer Center (KLCA-NCC) released updated guidelines for hepatocellular carcinoma (HCC).[1] The KLCA-NCC v2018 implemented ordinal diagnoses of HCC, definite HCC, probable HCC, and indeterminate nodules instead of the previous binary classification.[2] The KLCA-NCC v2018 also expanded the timepoint of "washout" from the transitional phase to the hepatobiliary phase on magnetic resonance imaging (MRI) with a hepatobiliary agent (HBA-MRI) and adopted exclusion criteria to improve sensitivity and maintain specificity. The latest KLCA-NCC v2022 includes several changes to the non-invasive diagnostic flow and HCC criteria on computed tomography and MRI, in addition to the inclusion of a new first-line imaging modality (Kupffer cell-specific contrast-enhanced ultrasound).[3] Regarding the diagnostic flow, probable HCC can be diagnosed based on the first line examination, instead of mandating a second line examination. This is because additional examination may be difficult to perform for clinical reasons, or the benefit of the second screening is unclear. Another change in diagnostic criteria has been made for "probable HCC." The diagnostic criteria for "definite HCC" remain the same as those in the KLCA-NCC v2018; however, the criteria for probable HCC have been modified. In the KLCA-NCC v2018, two ancillary features were adopted. One is ancillary features suggestive of malignancy (mild to moderate T2 hyperintensity, diffusion restriction, threshold growth) and the other is ancillary features specific to HCC (enhancing or non-enhancing capsules, presence of intralesional fat or hemorrhage, nodule-in-nodule appearance, mosaic architecture). To be classified as "probable HCC", at least one ancillary feature from each category was required. The KLCA-NCC v2022 applies different criteria for "probable HCC" depending on the presence of arterial phase hyperenhancement (APHE). For observations with APHE that do not meet the criteria of "definite HCC", at least one ancillary feature is required to be "probable HCC", regardless of its category. For observations without APHE, the diagnostic criteria remain the same as those in the KLCA-NCC v2018. This change was made based on studies reporting a high probability of HCC or HCC progression in LR-3 or LR-4 observations with APHE compared to those without APHE.[3-5]

In this issue of *Journal of Liver Cancer*, Yoon et al.[6] reported the diagnostic performance of the KLCA-NCC v2022 on liver MRI, compared with the KLCA-NCC v2018. The authors evaluated the imaging features of 535 observations in 415 treatment-naïve patients at risk of developing HCC, and 190 observations were found on MRI using an extracellular agent (ECA-MRI) in 152 patients and 345 observations were found on HBA-MRI in 263 patients. The mean observation size was 28.5 mm, and 77% (412/535) were diagnosed as

Received Mar. 7, 2023 **Accepted** Mar. 7, 2023

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HCC. There were no significant differences in sensitivity and specificity between KLCA-NCC v2018 and v2022 because the criteria for "definite HCC" remained the same in each modality. However, when the authors expanded the criteria of test positive as both "definite HCC" and "probable HCC", the sensitivity of KLCA-NCC v2022 significantly increased on ECA-MRI compared with that of KLCA-NCC v2018 (85.3% vs. 78.3%, P=0.002) without significant difference of specificity (93.6% for each). However, KLCA-NCC v2022 and KLCA-NCC v2018 did not show significant differences in sensitivity (83.6% vs. 83.3%) or specificity on HBA-MRI (90.8% vs. 92.1%, P>0.999 for both).

This study is one of the earliest to investigate the impact of the latest KLCA-NCC guidelines on HCC diagnosis. Since the KLCA-NCC v2022 did not change the diagnostic criteria for "definite HCC", it is not surprising that both KLCA-NCC v2022 and v2018 did not show a significant difference in diagnostic performance between ECA-MRI and HBA-MRI. However, the number of "probable HCCs" is expected to increase according to KLCA-NCC v2022 by relaxing the diagnostic criteria. Indeed, this study showed that the increase in number of "probable HCC" cases was so substantial that the sensitivity of ECA-MRI increased. Based on the study results, we assume that a substantial number of HCCs with APHE and without "washout" failed to present ancillary features of both categories, and only applying one category is appropriate enough to reach the diagnosis of "probable HCC." Furthermore, applying the modified criteria did not decrease the specificity compared to KLCA-NCC v2018. This supports the rationale of KLCA-NCC v2022 based on a higher probability of HCC in observations with APHE than in observations without APHE. Because we recommend different follow-up strategies for "probable HCC" and "indeterminate nodules", precise triage is clinically relevant. With the updated criteria, we can sensitively make actionable calls for observations without a significant increase in false positives and the modified criteria seem to work well.

On the contrary, no significant difference in "probable HCC" diagnostic performance was observed between the KLCA-NCC v2022 and v2018 on HBA-MRI. It is probably because most observations with APHE show portal venous phase washout or hypointensity on transitional/hepatobiliary phase and fall into the "definite HCC" category, regardless of ancillary features. Therefore, a limited number of observations with APHE do not meet the "definite HCC" criteria, such as HCCs showing hepatobiliary hyperintensity on HBA-MRI.[7] The incidence of such atypical HCC is known to be low, which explains the similar sensitivity of the two versions on HBA-MRI (83.3% of v2018 and 83.6% of v2022).

I would like to mention a few study limitations. First, it was a retrospective study, and we do not know the clinical flow in which some patients underwent ECA-MRI and other HBA-MRI and its potential bias. Furthermore, "probable HCC" is not a representative metric for measuring the diagnostic performance of non-invasive HCC diagnostic criteria. Finally, the presence of multiple lesions in a single patient was not statistically corrected for diagnostic performance, which lowered the reliability of the results.

In conclusion, Yoon et al.[6] investigated the impact of the KLCA-NCC v2022 modified "probable HCC" criteria on both ECA and HBA-MRI. A significant number of observations were reclassified as "probable HCC" on ECA-MRI, resulting in improved sensitivity and similar specificity, as both "definite HCC" and "probable HCC" were considered positive. The study results support the idea that updated KLCA-NCC v2022 has improved diagnostic outcomes.

Conflict of Interest

Jeong Hee Yoon currently serves on the Editorial Board of J Liver Cancer. She was not involved in the review process of this article. Otherwise, the author has no conflicts of interest to disclose.

Ethics Statement

This editorial is fully based on the articles which were already published and did not involve additional patient participants. Therefore, IRB approval is not necessary.

Funding Statement

None.

Data Availability

Data sharing not applicable to this article as no datasets were generated or analyzed.

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Author Contribution

Conceptualization, Data curation, Investigation, Writing original draft, Editing, Approval of final manuscript: JHY

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