Focus | Gastrointestinal Imaging

eISSN 2005-8330
https://doi.org/10.3348/kjr.2023.0168
Korean J Radiol 2023;24(7):660-667

Korean Journal of Radiology
KJR

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Prognosis Prediction of Hepatocellular Carcinoma Based on Magnetic Resonance Imaging Features

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Take-home points

- Current staging systems for hepatocellular carcinoma (HCC) are centered on treatment decisions and based on prognosis determined by a combination of imaging, laboratory, and clinical parameters; imaging provides preoperative anatomic delineation of the tumor extent.
- Magnetic resonance imaging (MRI) imaging additionally provides multiparametric information on the cellular composition of certain variants of HCC that have prognoses ranging from better to worse compared to not otherwise specific HCC.
- Hepatobiliary MRI findings of microvascular invasion and non-hypervascular hypointense nodules are promising for assessing the prognosis of tumor recurrence and patient survival.
- Standardization of imaging-based classification systems could improve both the diagnosis and prognosis assessment of HCC but requires further validation.

Keywords: Hepatocellular carcinoma; MRI; Prognosis; Recurrence; Survival

Received: February 18, 2023 **Revised:** April 2, 2023
Accepted: April 17, 2023
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Clinical Staging Systems for Hepatocellular Carcinoma Prognostication and the Role of Imaging

Due to the close association between hepatocellular carcinoma (HCC) and liver cirrhosis, the prognosis of patients with HCC is dependent not only on the biological behavior and extent of the tumor itself but also on the degree of underlying liver dysfunction and cirrhosis-associated complications, such as portal hypertension, ascites, and life-threatening hemorrhage from gastroesophageal varices [1]. As such, it is not surprising that patients treated with transplantation have a lower mortality rate than those treated with surgical resection alone, since transplantation not only removes the tumor but also regains liver function [2]. In terms of treatment, surgical resection and liver transplantation play major roles, with an expected overall survival (OS) above 60% at 5 years in well-selected candidates [3]. However, the risk of recurrence after resection can be as high as 70% at 5 years, even after curative liver resection. Most recurrences are intrahepatic and occur within 2 years of resection [4]. Locoregional ablation, systemic chemotherapy, and immunotherapy are other accepted treatment options for advanced HCC. Prognostication is important for clinicians when selecting treatment options and counseling patients with HCC. The Barcelona Clinic Liver Cancer (BCLC) and Hong Kong Liver Cancer (HKLC) staging systems are commonly used. Both staging systems provide recommendations based on tumor stage and degree of liver impairment using a combination of performance status, biochemical markers, and radiological features [5]. Tumor-specific factors, such as size, gross morphological type, presence of capsule and satellite

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nodules, cellular differentiation, vascular invasion, and TNM stage, have been shown to be important risk factors that determine the prognosis of patients with HCC [6]. Imaging plays an important role in the pretreatment evaluation of tumor size, number of lesions, vascular invasion, and presence of extrahepatic disease in staging systems. It is crucial to note that tumor-specific imaging features that portend a poor prognosis (such as subtype or microvascular invasion [MVI]) are not included in BCLC and HKLC. This is also the case with other staging systems, such as the Cancer of the Liver Italian Program (CLIP) score and the Okuda staging system [7].

Imaging-Based Staging Systems for HCC Prognostication

Consensus guidelines for the imaging diagnosis of HCC are restricted to patients with a high pre-test probability of developing HCC, such as those with cirrhosis or chronic viral hepatitis. Most guidelines, except the Liver Imaging Reporting and Data System (LI-RADS) and the Korean Liver Cancer Association-National Cancer Center Korea Practice Guidelines (KLCA-NCC), are binary in terms of the purpose of diagnosing rather than prognosticating HCC. For example, lesions without the characteristic imaging features of HCC would still require biopsy as part of the diagnostic algorithm [8,9]. LI-RADS and KLCA-NCC accommodate lesions with intermediate probabilities of HCC; observations that are greater than 2 cm in size and demonstrate arterial phase hyper-enhancement (APHE) with no washout appearance are classified as LR-4 on LI-RADS. The KLCA-NCC guidelines employ a similar framework with nodules diagnosed as "probable HCC," which corresponds to the concept of LR-4 in LI-RADS [9]. The management strategies after the multidisciplinary team discussion included close-interval follow-up, biopsy, or definitive treatment. According to a recent meta-analysis, lesions classified as "probable HCC" by KLCA-NCC have a pooled sensitivity of 74% and 80% for being HCC and (overall) malignancy, respectively [10].

Correlation of HCC Pathological Subtypes with Imaging and Prognosis

The 2019 5th edition of the World Health Organization (WHO) Classification of Digestive System Tumors has made image-based diagnosis more complex, stating that as much as 35% of HCCs can be categorized into eight subtypes based on their molecular properties. However, because the WHO classification is based on histopathology, not all imaging variants are specified in the latest version. Notably, some subtypes can have a worse and others a better prognosis compared to not otherwise specific HCCs (NOS-HCC) [11]. However, some recent studies have attempted to evaluate the imaging appearance according to the WHO HCC subtypes. For example, substantial necrosis is associated with Macrotrabecular-Massive (MTM)-HCC, whereas steatohepatitis HCC tumors exhibit prominent fat deposition.

Although LI-RADS was developed to incorporate the imaging features of contrast-enhanced ultrasound, computed tomography (CT), and MRI [8], a significant component of LI-RADS is dedicated to MRI features, given its greater discriminatory ability for ancillary features. Table 1 lists the known characteristics associated with the pertinent MRI and histopathologic features and prognosis of these subtypes. Fat content could denote certain variants, notably steatohepatitic or clear-cell type HCC, which are associated with a better prognosis. Another feature is a targetoid appearance, which can be due to rim-like APHE, delayed central enhancement, targetoid diffusion restriction, or targetoid appearance in the hepatobiliary phase. Observations with a targetoid appearance are classified as LR-M, indicating the presence of malignant features but not specific for HCC. The differential diagnoses for LR-M observations included atypical HCCs, intrahepatic cholangiocarcinoma (CCA), combined HCC-CCA (cHCC-CCA), or metastases [12]. Occasionally, benign entities, such as sclerosing hemangiomas, can be mistakenly classified as LR-M [12]. Several studies have reported higher aggressiveness and a poorer prognosis with shorter disease-free survival (DFS) and OS in HCCs that demonstrate rim APHE or LR-M [13,14]. Sarcomatoid (Fig. 1) and MTM-HCC often display a rim-APHE or LR-M appearance and have a poorer prognosis than NOS-HCC.

In 7%–20% of HCC cases, numerous nodules may appear "infiltrative" on imaging (Fig. 2) rather than as discrete nodules or masses. Microscopically, infiltrative HCC is characterized by the spread of minute tumor nodules throughout the affected liver. Therefore, the term "infiltrative" is a misnomer, with some authors believing that it represents innumerable intrahepatic metastases [15]. The American Joint Committee on Cancer (AJCC) staging system does not consider this pattern a distinct indicator of tumor aggressiveness [16], whereas the WHO does not classify it as a distinct subtype. Infiltrative

 https://doi.org/10.3348/kjr.2023.0168

Table 1. Variant Subtypes of HCC with Characteristic, Associated Prognosis, Relevant Histopathologic and Key Imaging Features Compared to NOS-HCC

Characteristic	Prognosis*	Variant	Relevant Histopathologic Features	Key Imaging Features
Fat-containing	Similar	Steatohepatitic	Intracytoplasmic fat ballooning, peri-cellular fibrosis and inflammation	Signal drop-out on opposed phase imaging
	Better	Clear cell	Criterion of > 80% of tumor with clear cell morphology	Atypical enhancement relative to degree of clear cell change, signal drop-out on opposed phase imaging
Uptake of hepatobiliary contrast	Better	Beta-catenin (CTNNB1)	Lower serum AFP compared to NOS-HCC	APHE with washout appearance and smooth hypointense rim unlike FNH
Progressively enhancing	Unclear	Scirrhous	Criterion of dense fibrous stroma in > 50% of tumor	Rim-like APHE, progressive enhancement similar to CCA
Calcification	Better (Similar to NOS-HCC in non-cirrhotic livers)	Fibrolamellar	Well-differentiated with abundant eosinophilic cytoplasm, on a background of thick, fibrous, lamellar bands	Large size, heterogeneous APHE, central T2 hypointense, non-enhancing scar, calcification
Targetoid/rim-like APHE/ hypoenhancing	Worse	Macrotrabecular-massive	Criterion of macrotrabecular (> 6 cells thick) architecture in > 50% of tumor	Central necrosis, intratumoral artery, peritumoral APHE
		Sarcomatoid HCC	Considered as undifferentiated primary hepatic tumor	Targetoid appearance on DWI and/or hepatobiliary phase, rim-like APHE with central necrosis
		Infiltrative HCC	Often associated with tumour in vein	Geographic, ill-defined appearance. Enhancement pattern confounded by tumour thrombus.
Non-specific	Similar	Chromophobe	Smooth, clear (chromophobic) cytoplasm, focal nuclear anaplasia	Possible APHE and washout, thick pseudocapsule
	Worse	Neutrophil-rich	Marked infiltration by neutrophils	Possible APHE and washout
	Better	Lymphocyte-rich	Predominance of cytotoxic CD8+ lymphocytes	Possible APHE and washout

*In comparison with not otherwise specific hepatocellular carcinoma (NOS-HCC). APHE = arterial phase hyper-enhancement, AFP = alpha-fetoprotein, FNH = focal nodular hyperplasia, DWI = diffusion-weighted imaging, CCA = cholangiocarcinoma

HCC has a worse prognosis than conventional HCC because of frequent vascular invasion and aggressive biological behavior [17]. In addition, the Japan Society of Hepatology (JSH) consensus statements indicated that the macroscopic classification of HCC provides insights into the tumor's biological aggressiveness. Specifically, simple nodular-type HCCs that exhibit extra-nodular growth and confluent multinodular-type HCCs have a higher likelihood of intrahepatic metastasis and recurrence than small nodular-type HCCs with indistinct margins or simple nodular-type HCCs. Therefore, special consideration is required when administering locoregional treatments for these HCC subtypes as opposed to others [18].

Conversely, some HCC variants portend a better prognosis than NOS-HCC. In the beta-catenin (CTNNB1) subtype (Fig. 3), OATP1B3 receptors are upregulated, which is histopathologically associated with pseudo-glandular proliferation and a higher grade of differentiation [19]. On gadoxetic acid-enhanced MRI, this subtype shows a high enhancement ratio on hepatobiliary phase images [19]. Clinically, it possesses less aggressive biological behavior and reduced levels of alpha-fetoprotein (AFP) and AFP-L3 fractions compared with NOS-HCC [20]. On MRI, the washout appearance in the portal venous phase remains useful for

https://doi.org/10.3348/kjr.2023.0168

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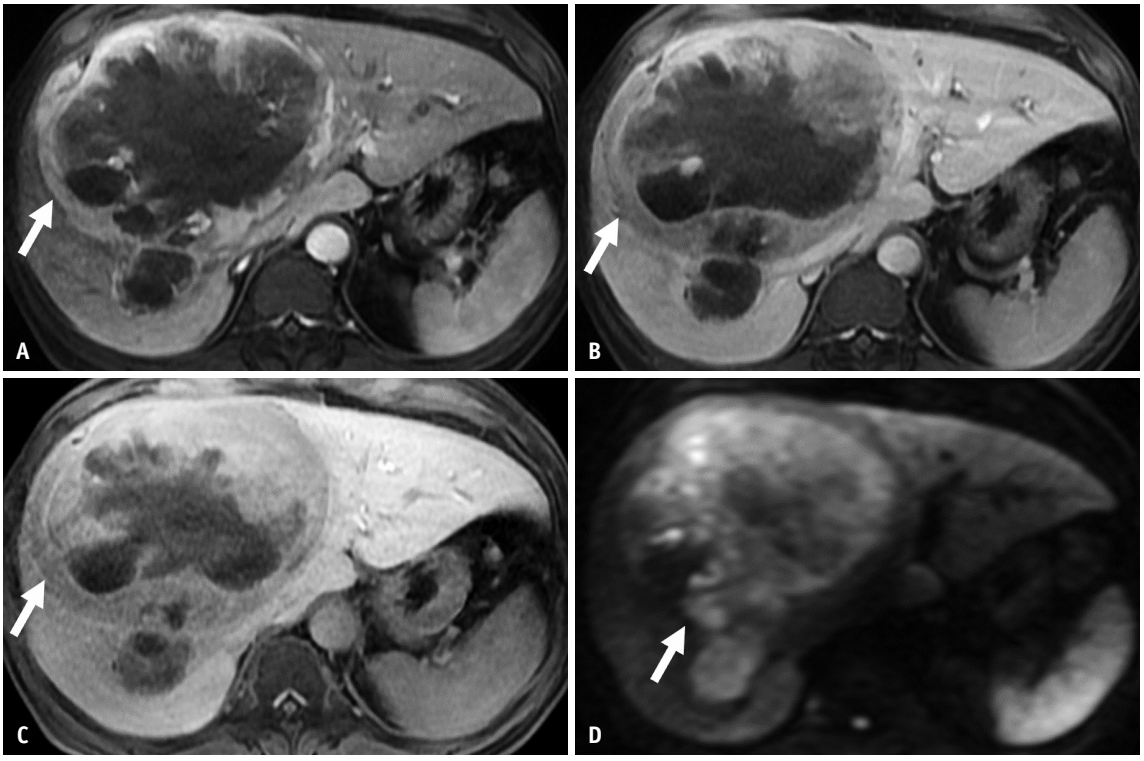

Fig. 1. Gadoxetate-enhanced magnetic resonance imaging of sarcomatoid hepatocellular carcinoma in the central portion of the liver. The tumor (arrows) shows **(A)** rim arterial phase hyper-enhancement, with **(B)** washout in the portovenous phase, **(C)** targetoid hypointensity in the hepatobiliary phase, and corresponding **(D)** heterogeneous hyperintensity on diffusion-weighted imaging. Sarcomatoid tumors are currently considered undifferentiated primary hepatic tumors under the World Health Organization classification.

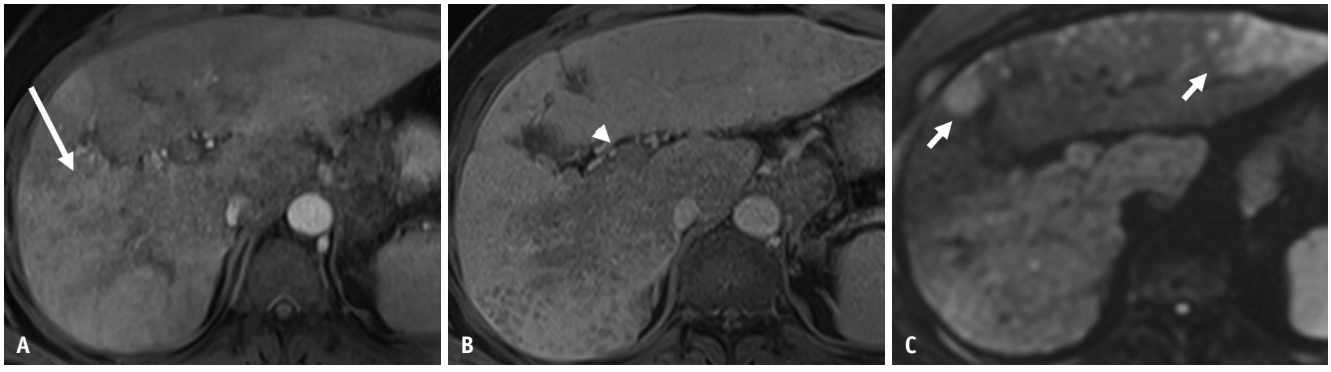

Fig. 2. Magnetic resonance imaging of infiltrative hepatocellular carcinoma (HCC) in both hepatic lobes using an extracellular contrast agent (gadoterate meglumine). The tumor shows **(A)** diffuse faint arterial phase hyper-enhancement in a geographic distribution predominantly in the right lobe (arrow), which **(B)** persists into the portal venous phase and extends into the main portal vein as a tumor thrombus (arrowhead), with **(C)** corresponding hyperintensity on diffusion-weighted imaging with confluent nodules in the anterior liver (arrows). Portal vein thrombosis and its ensuing vascular changes may partly explain why infiltrative HCCs often do not demonstrate overt features of enhancement.

differentiating these HCCs from other OATP1B3-upregulated lesions such as focal nodular hyperplasia [21]. Although not ascribed to a specific variant, it is noteworthy that HCCs with intact capsules have a better prognosis than HCCs of similar grade and size but without (intact) capsules. The presence of a fibrous capsule is a common pathological feature of progressed HCC and is depicted in portal venous or delayed phases by an enhancing rim, postulated to represent the retention of extracellular contrast agent within prominent peritumoral sinusoids and/or fibrosis [22].

Imaging Features of MVI

In addition to the features described above, discontinuous

https://doi.org/10.3348/kjr.2023.0168

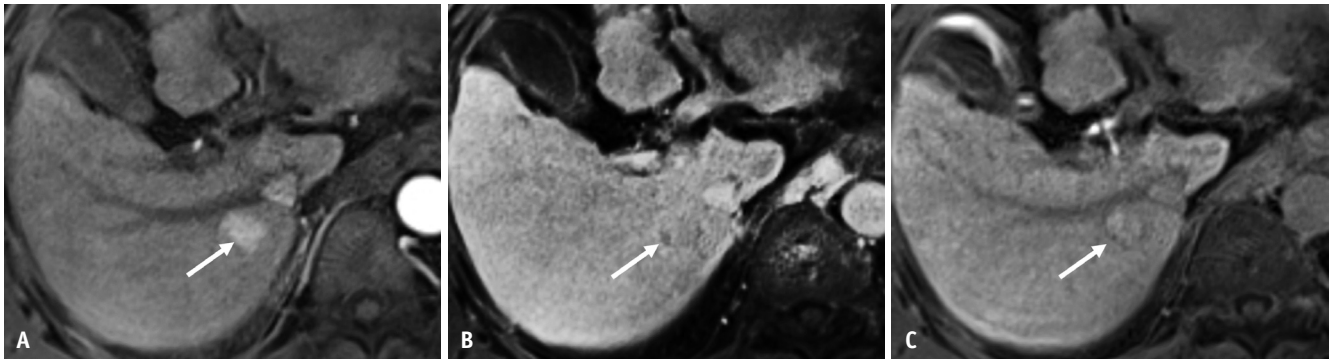

Fig. 3. Gadoxetate-enhanced magnetic resonance imaging of beta-catenin subtype hepatocellular carcinoma (HCC) in the posterior right hepatic lobe. The tumor (arrows) shows **(A)** heterogeneous non-rim arterial phase hyper-enhancement in the arterial phase, with corresponding **(B)** subtle washout in the portal venous phase, but **(C)** accumulation of gadoxetate in the hepatobiliary phase. The presence of washout and a smooth hypointense rim in the hepatobiliary phase are key to differentiating HCC from focal nodular hyperplasia.

capsules, corona enhancement, restricted diffusion, and lower tumor signals on hepatobiliary phase imaging have been correlated with poor tumor grade [23,24]. These have been associated with pathological findings of tumor MVI, which portends a poorer prognosis, higher rates of recurrence, lower DFS and OS, and post-resection and post-transplant recurrences [25]. In earlier studies, Vauthey et al. [26] showed that ethnic origin, cirrhosis, necrosis, and grade did not affect survival, and using multivariable analysis, only vascular invasion predicted the outcome. In a recent study, MVI was independently associated with a 35% increased risk of disease recurrence and a 66% increased risk of death [27]. However, the impact of MVI on the prognosis of small HCCs (less than 2 cm) remains unclear [28].

Tumor size, non-smooth tumor margins, peritumoral enhancement, and portal vein invasion are accurate predictors of MVI [29]. In the meta-analysis of ten studies by Hu et al. [30], the authors found a significant association between MVI and peritumoral enhancement (odds ratio [OR] 4.04) and peritumoral hypointensity on hepatobiliary phase (HBP) (OR 10.62); both features demonstrated high specificity (0.90–0.94) but low sensitivity (0.29–0.40) for MVI. More recent publications have suggested that peritumoral hypointensity on HBP images has higher ORs than peritumoral APHE [31]. Although there are positive imaging findings for the detection of MVI, certain factors need to be considered. In addition to the relatively low sensitivity of preoperative imaging, identifying relevant features can be subjective, with significant interobserver variability. Min et al. [32] found only fair to moderate agreement between observers, even among more experienced radiologists, for the imaging features of MVI, regardless of whether the features were interpreted in isolation or in combination. Adopting standardized terminology or lexicons for imaging features may enhance radiologists' consensus and facilitate interactions with referring physicians [33].

There has been immense interest in the literature regarding the use of adjunct techniques in MRI for preoperative prediction, such as magnetic resonance elastography [34] and dynamic contrast-enhanced MRI for MVI [35] and intravoxel incoherent motion diffusion-weighted imaging for HCC tumor grade [36]. Integration of these features has the potential to improve prognostic stratification in patients with HCC. In addition, various solutions have been proposed to reduce inter-observer variability. Preliminary studies appear promising, albeit limited by small sample sizes. These solutions include texture analysis, radiomics, clinicopathological scoring systems, and a combination of imaging and clinicopathological data. Xiong et al. [37] developed a prediction model based on preoperative AFP, tumor diameter, and TNM stage with an area under the receiver operating characteristic curve of 0.80 and good practicability. Texture analysis of tumor nodules could improve the diagnosis of MVI over visual analysis by human readers [38] and harbors the potential for deep learning algorithm development. Unfortunately, owing to the numerous types of image features, most studies have used different classification features and weights to predict MVI. A consensus on the optimal scoring system, followed by large-scale validation, is necessary for its adoption in mainstream practice.

Imaging Features of Non-Hypervascular Hypointense Nodules

Concurrently, the use of hepatobiliary contrast agents has

https://doi.org/10.3348/kjr.2023.0168

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led to the development of non-hypervascular hypointense nodules (NHHN). On MRI, they do not show APHE but appear as discrete nodules. NHHN are typically observed in cirrhotic livers and represent part of the spectrum of hepatocarcinogenesis. They are indicative of higher liver stiffness and a higher risk of HCC development, either de novo or elsewhere in the liver [39]. When correlated with histopathology, NHHNs represented progressed HCCs in 44% of patients, early HCCs in 20%, high-grade dysplastic nodules in 28%, and low-grade dysplastic nodules or regenerative nodules in 8% [40]. The presence of NHHN can be used to stratify patients into high-risk categories and requires closer surveillance. Approximately 50% of NHHN will develop into progressed HCC within 5 years [41]. Lee et al. [42] showed that the 5-year recurrence-free survival was lower in patients with concomitant NHHN than in those without NHHN who underwent resection (34% vs. 65%) and radiofrequency ablation (25% vs. 51%), irrespective of Milan's criteria.

Because NHHN is a precursor rather than a malignant lesion, its presence is neither a transplant criterion nor an indication for treatment [43]. However, because the presence of NHHN is associated with an increased risk of intrahepatic distant recurrence, there is value in its preoperative identification [44] and stratification of higher-risk patients for more aggressive post-operative surveillance [45]. Greater hypointensity of NHHN has been linked to a higher risk of HCC development as a manifestation of the loss of normal OATP1B3 receptors in progressively dysplastic lesions [46]. While the cost-effectiveness of hepatobiliary MRI for patients suspected of having HCC is comparable to that of CT in some countries [47], given the high cost of hepatobiliary MRI, further studies on its use for surveillance in patients with NHHN are warranted.

CONCLUSION

In summary, multimodal data (imaging, clinical, and laboratory) were used to predict the prognosis of patients with HCC. MRI has the advantage of being noninvasive and serves well in defining the anatomical extent of tumors. While we know that liver impairment coexists with HCC and reduces OS, the use of MRI for the assessment of liver function per se is still evolving and has not been covered in this review. Beyond anatomical imaging, MRI can depict certain HCC variants that portend better or comparable prognoses to NOS-HCC, such as CTNNB1 and clear cell or steatohepatitis subtypes. HCCs that show LR-M features such as rim APHE or targetoid appearance could represent infiltrative, MTM, or sarcomatoid subtypes with a worse prognosis. Recent studies suggest that hepatobiliary MRI may indicate MVI and NHHN, which are markers of poor prognosis. Standardization of imaging-based classification systems that comprise these additional features of HCC could improve prognostication but requires further validation.

Conflicts of Interest

Jeong Min Lee, a contributing editor of the *Korean Journal of Radiology*, was not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

Author Contributions

Conceptualization: Cher Heng Tan. Data curation: Cher Heng Tan, Hsien Min Low. Project administration: Cher Heng Tan. Resources: Cher Heng Tan. Software: Cher Heng Tan. Supervision: Cher Heng Tan, Jeong Min Lee. Visualization: Cher Heng Tan. Writing—original draft: Cher Heng Tan, Hsien Min Low. Writing—review & editing: all authors.

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Funding Statement

None

REFERENCES

1. Pinter M, Trauner M, Peck-Radosavljevic M, Sieghart W. Cancer and liver cirrhosis: implications on prognosis and management. *ESMO Open* 2016;1:e000042
2. Golabi P, Fazel S, Otgonsuren M, Sayiner M, Locklear CT, Younossi ZM. Mortality assessment of patients with hepatocellular carcinoma according to underlying disease and treatment modalities. *Medicine (Baltimore)* 2017;96:e5904
3. Marrero JA, Kulik LM, Sirlin CB, Zhu AX, Finn RS, Abecassis MM, et al. Diagnosis, staging, and management of hepatocellular carcinoma: 2018 practice cuidance by the American Association for the Study of Liver Diseases. *Hepatology* 2018;68:723-750

4. Tabrizian P, Jibara G, Shrager B, Schwartz M, Roayaie S. Recurrence of hepatocellular cancer after resection: patterns, treatments, and prognosis. *Ann Surg* 2015;261:947-955
5. de Freitas LBR, Longo L, Santos D, Grivicich I, Álvares-da-Silva MR. Hepatocellular carcinoma staging systems: Hong Kong liver cancer vs Barcelona clinic liver cancer in a Western population. *World J Hepatol* 2019;11:678-688
6. Renne SL, Sarcognato S, Sacchi D, Guido M, Roncalli M, Terracciano L, et al. Hepatocellular carcinoma: a clinical and pathological overview. *Pathologica* 2021;113:203-217
7. Bednarsch J, Czigany Z, Heise D, Joechle K, Luedde T, Heij L, et al. Prognostic evaluation of HCC patients undergoing surgical resection: an analysis of 8 different staging systems. *Langenbecks Arch Surg* 2021;406:75-86
8. Moura Cunha G, Chernyak V, Fowler KJ, Sirlin CB. Up-to-date role of CT/MRI LI-RADS in hepatocellular carcinoma. *J Hepatocell Carcinoma* 2021;8:513-527
9. Korean Liver Cancer Association (KLCA) and National Cancer Center (NCC) Korea. 2022 KLCA-NCC Korea Practice Guidelines for the management of hepatocellular carcinoma. *Korean J Radiol* 2022;23:1126-1240
10. van der Pol CB, Lim CS, Sirlin CB, McGrath TA, Salameh JP, Bashir MR, et al. Accuracy of the liver imaging reporting and data system in computed tomography and magnetic resonance image analysis of hepatocellular carcinoma or overall malignancy-a systematic review. *Gastroenterology* 2019;156:976-986
11. Loy LM, Low HM, Choi JY, Rhee H, Wong CF, Tan CH. Variant hepatocellular carcinoma subtypes according to the 2019 WHO classification: an imaging-focused review. *AJR Am J Roentgenol* 2022;219:212-223
12. Chiow SM, Khoo HW, Low JK, Tan CH, Low HM. Imaging mimickers of cholangiocarcinoma: a pictorial review. *Abdom Radiol (NY)* 2022;47:981-997
13. Kierans AS, Makkar J, Guniganti P, Cornman-Homonoff J, Lee MJ, Pittman M, et al. Validation of Liver Imaging Reporting and Data System 2017 (LI-RADS) criteria for imaging diagnosis of hepatocellular carcinoma. *J Magn Reson Imaging* 2019;49:e205-e215
14. An C, Kim DW, Park YN, Chung YE, Rhee H, Kim MJ. Single hepatocellular carcinoma: preoperative MR imaging to predict early recurrence after curative resection. *Radiology* 2015;276:433-443
15. Reynolds AR, Furlan A, Fetzer DT, Sasatomi E, Borhani AA, Heller MT, et al. Infiltrative hepatocellular carcinoma: what radiologists need to know. *Radiographics* 2015;35:371-386
16. Chun YS, Pawlik TM, Vauthey JN. 8th Edition of the AJCC cancer staging manual: pancreas and hepatobiliary cancers. *Ann Surg Oncol* 2018;25:845-847
17. Kneuertz PJ, Demirjian A, Firoozmand A, Corona-Villalobos C, Bhagat N, Herman J, et al. Diffuse infiltrative hepatocellular carcinoma: assessment of presentation, treatment, and outcomes. *Ann Surg Oncol* 2012;19:2897-2907
18. Kudo M, Kawamura Y, Hasegawa K, Tateishi R, Kariyama K, Shiina S, et al. Management of hepatocellular carcinoma in Japan: JSH consensus statements and recommendations 2021 Update. *Liver Cancer* 2021;10:181-223
19. Kitao A, Matsui O, Yoneda N, Kozaka K, Kobayashi S, Sanada J, et al. Hepatocellular carcinoma with β-Catenin mutation: imaging and pathologic characteristics. *Radiology* 2015;275:708-717
20. Kitao A, Matsui O, Yoneda N, Kozaka K, Kobayashi S, Koda W, et al. Gadoxetic acid-enhanced MR imaging for hepatocellular carcinoma: molecular and genetic background. *Eur Radiol* 2020;30:3438-3447
21. Kim JW, Lee CH, Kim SB, Park BN, Park YS, Lee J, et al. Washout appearance in Gd-EOB-DTPA-enhanced MR imaging: a differentiating feature between hepatocellular carcinoma with paradoxical uptake on the hepatobiliary phase and focal nodular hyperplasia-like nodules. *J Magn Reson Imaging* 2017;45:1599-1608
22. Cho ES, Choi JY. MRI features of hepatocellular carcinoma related to biologic behavior. *Korean J Radiol* 2015;16:449-464
23. Li X, Zhang K, Shi Y, Wang F, Meng X. Correlations between the minimum and mean apparent diffusion coefficient values of hepatocellular carcinoma and tumor grade. *J Magn Reson Imaging* 2016;44:1442-1447
24. Zhang L, Yu X, Wei W, Pan X, Lu L, Xia J, et al. Prediction of HCC microvascular invasion with gadobenate-enhanced MRI: correlation with pathology. *Eur Radiol* 2020;30:5327-5336
25. Rodríguez-Perálvarez M, Luong TV, Andreana L, Meyer T, Dhillon AP, Burroughs AK. A systematic review of microvascular invasion in hepatocellular carcinoma: diagnostic and prognostic variability. *Ann Surg Oncol* 2013;20:325-339
26. Vauthey JN, Klimstra D, Franceschi D, Tao Y, Fortner J, Blumgart L, et al. Factors affecting long-term outcome after hepatic resection for hepatocellular carcinoma. *Am J Surg* 1995;169:28-34; discussion 34-35
27. Endo Y, Alaimo L, Lima HA, Moazzam Z, Ratti F, Marques HP, et al. A novel online calculator to predict risk of microvascular invasion in the preoperative setting for hepatocellular carcinoma patients undergoing curative-intent surgery. *Ann Surg Oncol* 2023;30:725-733
28. Shindoh J, Andreou A, Aloia TA, Zimmitti G, Lauwers GY, Laurent A, et al. Microvascular invasion does not predict long-term survival in hepatocellular carcinoma up to 2 cm: reappraisal of the staging system for solitary tumors. *Ann Surg Oncol* 2013;20:1223-1229
29. Renzulli M, Brocchi S, Cucchetti A, Mazzotti F, Mosconi C, Sportoletti C, et al. Can current preoperative imaging be used to detect microvascular invasion of hepatocellular Carcinoma? *Radiology* 2016;279:432-442
30. Hu HT, Shen SL, Wang Z, Shan QY, Huang XW, Zheng Q, et al. Peritumoral tissue on preoperative imaging reveals microvascular invasion in hepatocellular carcinoma: a systematic review and meta-analysis. *Abdom Radiol (NY)* 2018;43:3324-3330
31. Hong SB, Choi SH, Kim SY, Shim JH, Lee SS, Byun JH, et al. MRI features for predicting microvascular invasion of hepatocellular carcinoma: a systematic review and meta-

https://doi.org/10.3348/kjr.2023.0168

analysis. *Liver Cancer* 2021;10:94-106
32. Min JH, Lee MW, Park HS, Lee DH, Park HJ, Lim S, et al. Interobserver variability and diagnostic performance of gadoxetic acid-enhanced MRI for predicting microvascular invasion in hepatocellular carcinoma. *Radiology* 2020;297:573-581
33. Chernyak V, Tang A, Do RKG, Kamaya A, Kono Y, Santillan CS, et al. Liver imaging: it is time to adopt standardized terminology. *Eur Radiol* 2022;32:6291-6301
34. Zhang L, Li M, Zhu J, Zhang Y, Xiao Y, Dong M, et al. The value of quantitative MR elastography-based stiffness for assessing the microvascular invasion grade in hepatocellular carcinoma. *Eur Radiol* 2023;33:4103-4114
35. Feng ST, Jia Y, Liao B, Huang B, Zhou Q, Li X, et al. Preoperative prediction of microvascular invasion in hepatocellular cancer: a radiomics model using Gd-EOB-DTPA-enhanced MRI. *Eur Radiol* 2019;29:4648-4659
36. Zhou Y, Zheng J, Yang C, Peng J, Liu N, Yang L, et al. Application of intravoxel incoherent motion diffusion-weighted imaging in hepatocellular carcinoma. *World J Gastroenterol* 2022;28:3334-3345
37. Xiong Y, Cao P, Lei X, Tang W, Ding C, Qi S, et al. Accurate prediction of microvascular invasion occurrence and effective prognostic estimation for patients with hepatocellular carcinoma after radical surgical treatment. *World J Surg Oncol* 2022;20:328
38. Sim JZT, Hui TCH, Chuah TK, Low HM, Tan CH, Shelat VG. Efficacy of texture analysis of pre-operative magnetic resonance imaging in predicting microvascular invasion in hepatocellular carcinoma. *World J Clin Oncol* 2022;13:918-928
39. Hwang JA, Kang TW, Kim YK, Kim SH, Paik YH, Ha SY, et al. Association between non-hypervascular hypointense nodules on gadoxetic acid-enhanced MRI and liver stiffness or hepatocellular carcinoma. *Eur J Radiol* 2017;95:362-369
40. Joo I, Kim SY, Kang TW, Kim YK, Park BJ, Lee YJ, et al. Radiologic-pathologic correlation of hepatobiliary phase hypointense nodules without arterial phase hyperenhancement at gadoxetic acid–enhanced MRI: a multicenter study. *Radiology* 2020;296:335-345
41. Park HJ, Lee TY, Kim SY, Kim MJ, Singal AG, Lee SJ, et al. Hypervascular transformation of hepatobiliary phase hypointense nodules without arterial phase hyperenhancement on gadoxetic acid–enhanced MRI: long-term follow-up in a surveillance cohort. *Eur Radiol* 2022;32:5064-5074
42. Lee S, Kim KW, Jeong WK, Kim MJ, Choi GH, Choi JS, et al. Gadoxetic acid-enhanced MRI as a predictor of recurrence of HCC after liver transplantation. *Eur Radiol* 2020;30:987-995
43. Takeishi K, Yoshizumi T, Itoh S, Yugawa K, Yoshiya S, Toshima T, et al. Surgical indications for hepatocellular carcinoma with non-hypervascular hypointense nodules detected by Gd-EOB-DTPA-Enhanced MRI. *Ann Surg Oncol* 2020;27:3344-3353
44. Cha DI, Jang KM, Kim SH, Kim YK, Kim H, Ahn SH. Preoperative prediction for early recurrence can be as accurate as postoperative assessment in single hepatocellular carcinoma patients. *Korean J Radiol* 2020;21:402-412
45. Kim TH, Woo S, Han S, Suh CH, Lee DH, Lee JM. Hepatobiliary phase hypointense nodule without arterial phase hyperenhancement: are they at risk of HCC recurrence after ablation or surgery? A systematic review and meta-analysis. *Eur Radiol* 2020;30:1624-1633
46. Wang F, Numata K, Chuma M, Nihonmatsu H, Moriya S, Nozaki A, et al. The value of hepatobiliary phase in EOB-MRI in predicting hypervascularization outcome of non-hypervascular hypointense lesions in high-risk patients for hepatocellular carcinoma. *Abdom Radiol (NY)* 2021;46:2527-2539
47. Lee JM, Kim MJ, Phongkitkarun S, Sobhonslidsuk A, Holtorf AP, Rinde H, et al. Health economic evaluation of Gd-EOB-DTPA MRI vs ECCM-MRI and multi-detector computed tomography in patients with suspected hepatocellular carcinoma in Thailand and South Korea. *J Med Econ* 2016;19:759-768

 https://doi.org/10.3348/kjr.2023.0168