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Imaging features related with prognosis of hepatocellular carcinoma

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Abstract

We discuss various imaging features that have been reported to be associated with the prognosis of hepatocellular carcinoma (HCC) but not included in the current staging systems: findings related with microvascular invasion, tumor encapsulation, intratumoral fat, presence of satellite nodules, peritumoral hypointensity on hepatobiliary phase images of gadoxetic-acid enhanced MRI, restricted diffusion, and irregular rim-like hyperenhancement. Current evidence suggests that larger (> 2 cm) tumor size, presence of satellite nodules, presence of irregular rim-like hyperenhancement of a tumor, peritumoral parenchymal enhancement in the arterial phase, and peritumoral hypointensity observed on hepatobiliary phase images are independent imaging features to portend a worse prognosis in patients with hepatocellular carcinoma.

Key words: Prognosis—Hepatocellular carcinoma—Magnetic resonance imaging—Computed tomography

The goal of medical imaging studies such as computed tomography (CT) or magnetic resonance imaging (MRI) is to assist in providing a patient with the best care by accurately assessing the patient's disease status. In this respect, relating the prognosis or clinical outcome to imaging features may be as important as making a correct diagnosis by imaging.

When we encounter a hepatic mass in a patient at risk of developing primary hepatic malignancy, we may try to decide whether it is hepatocellular carcinoma (HCC) or another malignancy, whether it is well or poorly differentiated, and whether it shows vascular invasion or not, because we consider these factors important for planning treatment and predicting prognosis. However, one of the problems with this approach is that primary liver cancer has a diverse spectrum [1], and distinguishing between different types of hepatic carcinoma is often difficult. The criteria for classification of hepatic carcinomas advocated by experts have been continuously evolving even in the pathology literature [2–4]. In addition, we observe substantial disagreement among pathologists themselves in both grading histologic differentiation and evaluating vascular invasion [5, 6]. Although biopsy is frequently used to define histologic or molecular characteristics when imaging features are inconclusive, biopsy results can differ significantly from the results of pathologic examination after surgery [7]. Therefore, if we could directly utilize imaging findings to predict prognosis, this would be a good non-invasive alternative for individualized management of a patient.

Various imaging features have been reported to be associated with the prognosis of HCC. Among them, tumor size, number, and the presence or absence of vascular invasion are included in existing staging systems [8–12]. However, there are other potentially useful imaging features that are not included in the staging systems (Fig. 1). In this article, we will discuss imaging features that may be useful for predicting the prognosis of HCC. We hope that the awareness of those prognostic imaging features can be useful for radiologists to help communicate with hepatologists and surgeons in the multidisciplinary discussion for better planning the management and treatment.

Imaging features related with vascular invasion

Vascular invasion is one of the most important radiologic and histologic features associated with the prognosis of HCC [13]. Identification of gross vascular invasion is usually not difficult. However, microvascular invasion (MVI) is generally considered difficult to determine on imaging studies [14]. In fact, reliable determination of the presence or absence of MVI is difficult even on histologic examination, because of wide

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Imaging feature	Schematic drawing	Explanation
Better prognostic features		
Intralesional fat		Focal or diffuse fat signal (i.e. intensity drop between in- and opposed-phases) within the tumor.
Capsule appearance		Smooth, uniform, sharp border around the tumor with progressive enhancement.
Hyper- or iso-intensity in the hepatobiliary phase		Intensity in the hepatobiliary phase unequivocally higher than or the same as, in whole or in part, the liver
Worse prognostic features		
Irregular rim-like enhancement in the arterial phase		Irregularly shaped rim-like peripheral hyperenhancement with central hypoenhancing areas in the arterial phase.
Peritumoral parenchymal enhancement in the arterial phase		Focal areas of arterial phase hyperenhancement in the liver parenchyma abutting the tumor.
Satellite nodule		Small (<2 cm) tumor nodules close (<2 cm) to the main tumor.
Peritumoral hypointensity in the hepatobiliary phase		Focal areas of hypointensity in the liver parenchyma abutting the tumor on hepatobiliary phase images.

Fig. 1. Description and schematic drawings of prognostic imaging features of hepatocellular carcinoma.

interobserver variability and difficulty in examining the entire tumor [5].

Nonetheless, several imaging features have been proposed as predictors of MVI, including multifocality [15], large tumor size and elevation of tumor markers [16–18], non-capsulation or irregular tumor margin [19–21], peritumoral hemodynamic alteration (i.e., peritumoral parenchymal enhancement) [22, 23], peritumoral parenchymal hypointensity in the hepatobiliary phase of gadoxetate-enhanced MRI [24], low apparent diffusion coefficients (ADCs) or high mean kurtosis value on diffusion-weighted imaging (DWI) [25–27], and expression of certain radiogenomic biomarkers [28]. Conversely, isointensity or hyperintensity of the tumor on gadoxetate-enhanced MRI has been associated with a low probability of MVI [29].

Radiogenomic venous invasion (RVI), a CT biomarker, is considered present when internal arteries and

tumor-liver differences are observed in the absence of a hypodense halo [30]. Positive RVI showed accuracy, sensitivity, and specificity of 89%, 76%, and 94% for the prediction of MVI, respectively, and was also associated with shorter overall survival and recurrence-free survival (Fig. 2) [30]. Recently, three worrisome features – non-smooth margin, peritumoral enhancement, and two-trait predictor of venous invasion (a modified version of RVI; positive if internal arteries are present in the absence of a hypodense halo)–have been shown to predict histologic MVI on CT or MRI with positive predictive values greater than 95% [31].

However, it is still difficult to predict MVI in small tumors, as imaging predictors such as internal arteries and hypodense halo are not frequently observed in the case of small tumors. In a study, one-third of small (1–2 cm) HCCs had MVI [32]. According to the results of that study, while all small HCCs with MVI displayed a typical dynamic pattern (arterial hyperenhancement and washout appearance), T2 hyperintensity, and diffusion restriction, those without MVI tended to show atypical imaging features, such as isointensity on T2-weighted images, often without diffusion restriction or arterial hyperenhancement [32]. Thus, the presence of typical imaging features not only suggests a diagnosis of HCC but may also suggest a higher probability of MVI in small HCCs. However, this result also implies that HCC without MVI tends to show atypical imaging features and thus is difficult to diagnose by imaging alone in the first place.

Size threshold may have a similar prognostic significance to that of MVI in early-stage HCC. An et al. [33] devised a staging system based on MRI that used a size threshold of 2 cm (instead of vascular invasion) to differentiate between tumor stages 1 and 2 (T1: single tumor < 2 cm; T2: single tumor ≥ 2 cm). They compared it with the 7th American Joint Committee on Cancer (AJCC) staging system and showed that the pre-operative MRI staging system could predict the prognosis of HCC after surgical resection as accurately as the 7th AJCC TNM staging system [33]. In another recent study of 1109 patients with solitary HCC ≤ 2 cm, MVI did not have a significant impact on long-term survival [34]. In accordance with the results of these studies, the 8th AJCC staging system divides T1 disease into two subcategories: T1a, for patients with solitary HCC ≤ 2 cm irrespective of MVI, and T1b, for patients with solitary HCC > 2 cm without MVI. Patients with solitary HCC > 2 cm with MVI are classified into the T2 category, along with those with multiple HCCs ≤ 5 in the 8th AJCC staging system [35].

Imaging features related with prognosis

Several imaging features that are not incorporated in staging systems also have been reported to be associated with the prognosis of HCC. These include gross tumor type, encapsulation, intratumoral fat, dynamic enhancement pattern, and findings on DWI, perfusion MRI, or hepatobiliary phase images [19, 36–47].

Tumor encapsulation, defined as the presence of a fibrous sheath around the tumor on gross inspection, has been suggested as a good prognostic indicator (Fig. 3) [19, 41, 45, 48]. A study showed that disease-free and overall survival rates were significantly higher for encapsulated tumors, especially in HCCs > 5 cm [45]. The presence of intratumoral fat was also suggested as a favorable prognostic factor; in a study, fatty change observed on MRI in HCC was associated with less

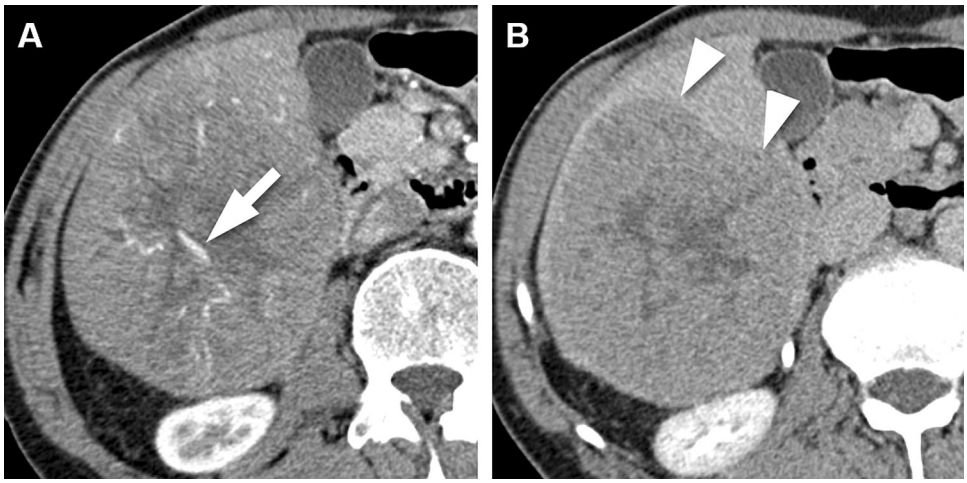

Fig. 2. Hepatocellular carcinoma with positive radiogenomic venous invasion in a 65-year-old man. An 11-cm mass in right liver displays internal arteries in the arterial phase of dynamic contrast-enhanced CT (arrows) (**A**) and tumor-liver difference (focal or circumferential sharp transition in attenuation between the tumor and the adjacent liver parenchyma) in the absence of a hypodense halo in the delayed phase (arrowheads) (**B**).

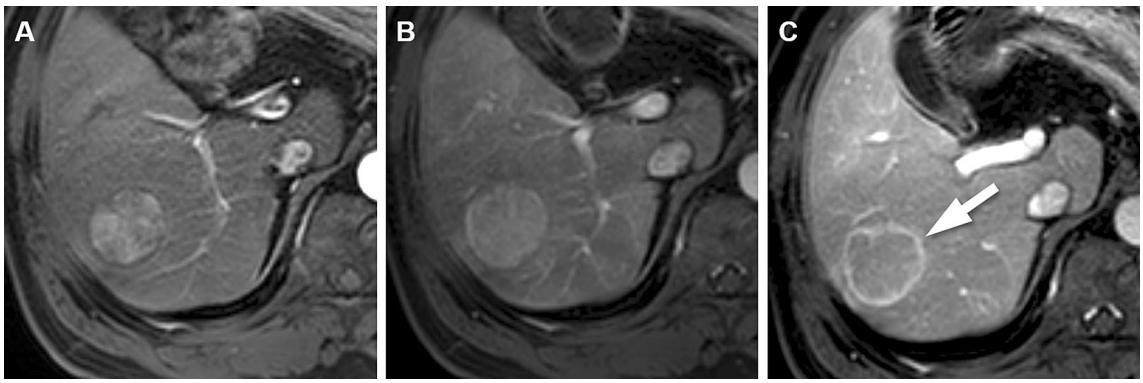

Fig. 3. Hepatocellular carcinoma with capsule appearance in a 72-year-old man. On arterial phase of extracellular contrast material-enhanced MRI **(A)**, a well-demarcated 2.2 cm mass in S6 of liver shows diffuse hyperenhancement. A peripheral rim of smooth hyperenhancement surrounding the tumor appears and becomes thicker and more prominent from early portal phase (**B**) to late dynamic phase (**C**), which is defined as a capsule appearance (arrow).

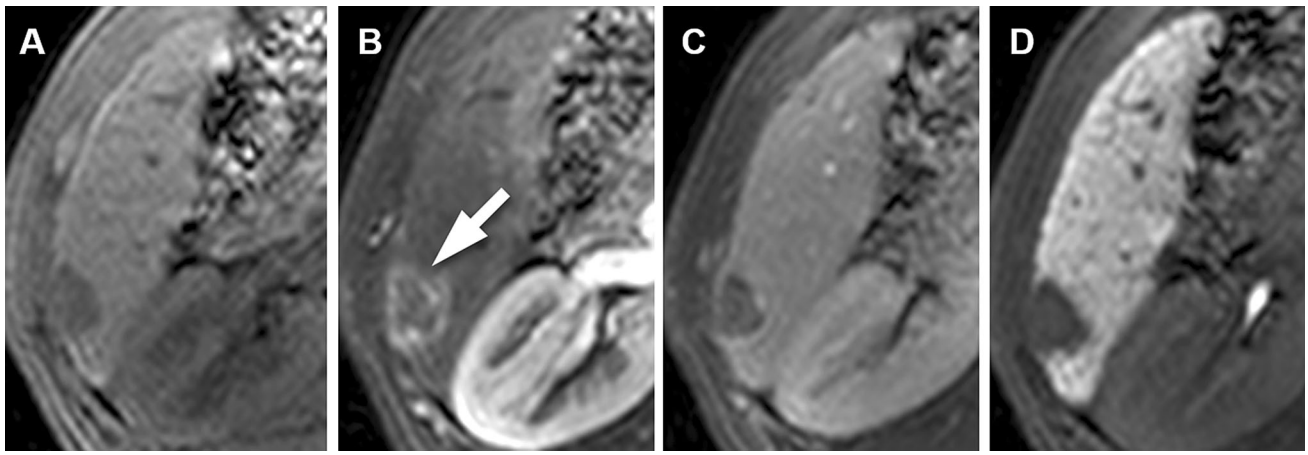

Fig. 4. Hepatocellular carcinoma with irregular rim-like enhancement in a 46-year-old man. Precontrast (**A**), arterial (**B**), portal (**C**), and hepatobiliary (**D**) phase images of gadoxetate-enhanced MRI, a 2.4-cm mass in right inferior liver shows irregular rim-like peripheral enhancement with central hypointense areas in the arterial phase (arrow).

common metastasis and longer time to progression [44]. On gadoxetate-enhanced MRI, it was shown that tumor hyperintensity produced by uptake of hepatocyte-specific contrast material in the hepatobiliary phase may indicate better differentiation, less frequent portal vein invasion, less expression of tumor markers in serum and tumors, lower recurrence rate, and better survival [29, 40, 47].

On the other hand, irregular rim-like arterial phase hyperenhancement and an irregular (or non-smooth) tumor margin have been suggested as indicators of aggressive behavior and a worse prognosis for HCC (Fig. 4) [38, 39, 49, 50]. In an MRI study, rapidly progressive HCC, defined as a lesion < 3 cm showing an increase in tumor size > 3 cm within one year or > 2 cm in 6 months, frequently manifested a rim-like enhancement pattern on initial MRI [39]. Similarly, in a CT study, a rim-like enhancement pattern was associated with a higher recurrence rate after radiofrequency ablation [38]. Histologically, irregular rim-like enhancement seems to be related to higher expression of various characteristics of tumor hypoxia and stem/progenitor cell features, including cytokeratin-19 and carbonic anhydrase [51–53].

According to studies examining quantitative prognostic features, lower values of mean or minimum ADC on DWI are associated with poor differentiation and a higher rate of early recurrence [42]. HCCs with higher peak values on perfusion MRI showed better responses to systemic therapy and longer survival [36].

Efforts to identify the independent prognostic imaging features

Since many imaging features have been identified as potential prognostic markers, it is imperative to identify independently valid prognostic predictors. To address

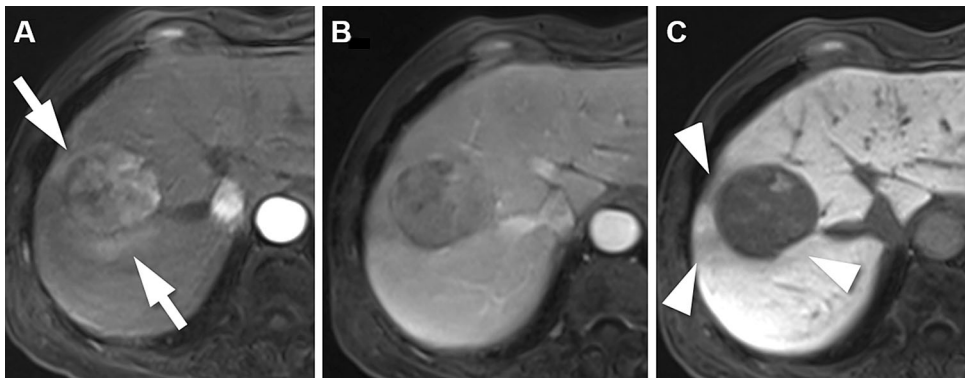

Fig. 5. Hepatocellular carcinoma with peritumoral arterial phase hyperenhancement in a 64-year-old woman. In the arterial phase of gadoxetate-enhanced MRI (**A**), a 4.5-cm mass in right liver shows diffuse hyperenhancement along with peritumoral parenchymal enhancement (arrows). In the portal phase (**B**), the peritumoral enhancement fades into isoenhancement. Note the multifocal areas of hypointensity in the surrounding liver in the hepatobiliary phase (arrowheads) (**C**).

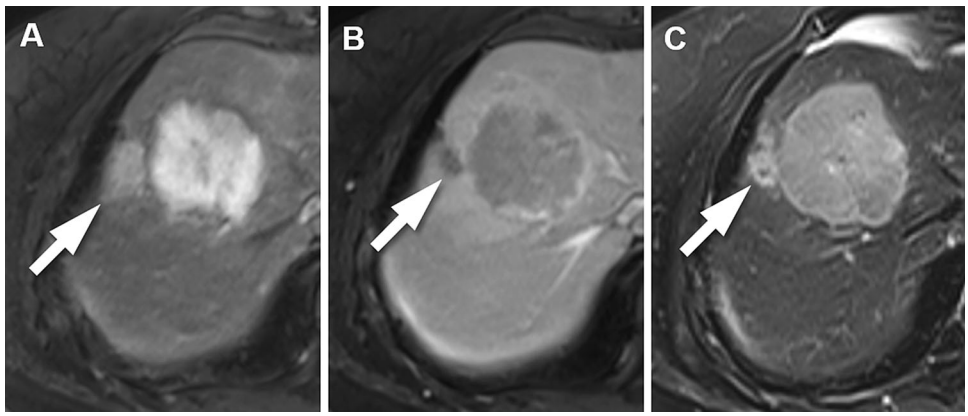

Fig. 6. Hepatocellular carcinoma with a satellite nodule in a 68-year-old woman. A 5.4-cm hepatic mass shows arterial phase hyperenhancement (**A**) and washout appearance (**B**) on dynamic gadoxetate-enhanced images, and intermediate hyperintensity on T2-weighted image (**C**). Another 1.2-cm nodule is noted close to the main tumor (arrows), which shows the same dynamic enhancement pattern and T2 intensity.

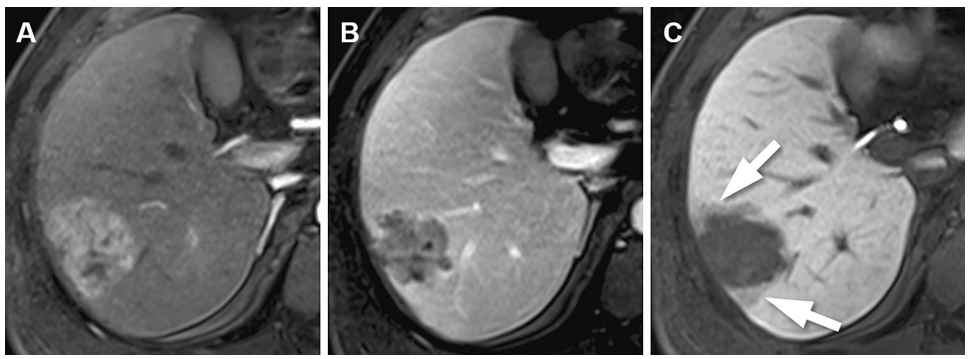

Fig. 7. Hepatocellular carcinoma with peritumoral hypointensity in the hepatobiliary phase in a 53-year-old man. Gadoxetate-enhanced MRI reveals a 4-cm mass with diffuse arterial phase hyperenhancement (**A**) and washout appearance (**B**) in right liver. On hepatobiliary phase image (**C**), irregular peritumoral hepatobiliary hypointensity is seen in the adjacent liver (arrows).

this question, a study investigated various qualitative and quantitative MRI features to determine their relative significance in predicting prognosis after surgical resection of HCC [54]. According to that study, a nomogram based on arterial phase rim-like enhancement, arterial phase peritumoral parenchymal enhancement, the pres-

ence of satellite nodules, and tumor size was useful for predicting early recurrence after curative resection of single HCC (Figs. 4, 5, 6). Similarly, Lee et al. [55] reported that the presence of two or more of the three imaging features indicating MVI (namely arterial peritumoral enhancement, non-smooth tumor margin, and peritumoral hypointensity on hepatobiliary phase images) could be used as a pre-operative imaging biomarker for predicting microvascular invasion with a specificity > 90%, and was associated with early recurrence after curative resection of single HCC (Fig. 7). In comparison, in a study conducted on patients who underwent radiofrequency ablation, irregular tumor margin, and peritumoral hypointensity on hepatobiliary phase images were identified as factors related to an increased rate of local tumor progression after the ablation [49]. Similar imaging criteria defined on pre-operative hepatobiliary MRI (either satellite nodule or peritumoral hypointensity on hepatobiliary phase images) were demonstrated to be useful for identifying a higher risk of tumor recurrence in patients who underwent transplantation, either within or outside the Milan criteria [56].

Caveats for the interpretation of prognostic imaging features

However, there are several caveats with respect to the interpretation of these imaging features associated with poor outcome after surgical or locally ablative treatments. First, irregular rim-like enhancement is commonly associated with irregular or non-smooth tumor margins. It is plausible that one of these two imaging findings might be equivalent to the other. Therefore, further studies may be warranted to determine whether these two findings should be considered together or separately evaluated. Similarly, arterial peritumoral hyperenhancement is frequently accompanied by peritumoral hypointensity in the hepatobiliary phase (Fig. 5). Therefore, it should also be determined whether combining these two findings could improve the ability to predict the presence of MVI or the prognosis. Second, irregular rim-like enhancement should be differentiated from the capsular appearance that is typically seen in late dynamic phases but may begin to appear in earlier phases (Figs. 3 and 4). Another imaging feature that should be distinguished from rim-like enhancement is corona enhancement, which is a phenomenon attributed to early drainage of contrast material from a hypervascular tumor surrounding sinusoids or portal venules [57, 58]. As the corona enhancement results from perfusion alteration rather than morphologic alteration, it usually fades to isointense in the portal venous or delayed phase. In contrast, rim-like tumor enhancement represents tumor vascularity confined within the tumor periphery, and usually persists or becomes hypointense in the delayed phase, showing an appearance of peripheral wash-out (Fig. 3).

Conclusions

In summary, current evidence suggests that larger (> 2 cm) tumor size, presence of satellite nodules, presence of irregular rim-like hyperenhancement of a tumor, peritumoral parenchymal enhancement in the arterial phase, and peritumoral hypointensity observed on hepatobiliary phase images are independent imaging features that portend a worse prognosis in HCC patients.

Compliance with ethical standards

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Conflict of interest Chansik An and Myeong-Jin Kim declared that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Sia D, Villanueva A, Friedman SL, Llovet JM (2017) Liver cancer cell of origin, molecular class, and effects on patient prognosis. Gastroenterology 152:745–761
2. Kim H, Park YN (2014) Hepatocellular carcinomas expressing 'stemness'-related markers: clinicopathological characteristics. Dig Dis 32:778–785
3. Walther Z, Jain D (2011) Molecular pathology of hepatic neoplasms: classification and clinical significance. Patholog Res Int 2011:403929
4. Elizabeth M, Brunt VP, Sempoux Christine, Theise ND (2015) Biphenotypic (hepatobiliary) primary liver carcinomas: the work in progress. Hepat Oncol 2:330–336
5. Fan L, Mac MT, Frishberg DP, et al. (2010) Interobserver and intraobserver variability in evaluating vascular invasion in hepatocellular carcinoma. J Gastroenterol Hepatol 25:1556–1561
6. Pirisi M, Leutner M, Pinato DJ, et al. (2010) Reliability and reproducibility of the edmondson grading of hepatocellular carcinoma using paired core biopsy and surgical resection specimens. Arch Pathol Lab Med 134:1818–1822
7. Pawlik TM, Gleisner AL, Anders RA, et al. (2007) Preoperative assessment of hepatocellular carcinoma tumor grade using needle biopsy: implications for transplant eligibility. Ann Surg 245:435–442
8. Bruix J, Sherman M, American Association for the Study of Liver Diseases (2011) Management of hepatocellular carcinoma: an update. Hepatology 53:1020–1022
9. European Association For The Study Of The Liver, European Organisation For Research And Treatment Of Cancer (2012) EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. J Hepatol 56:908–943
10. Kudo M, Matsui O, Izumi N, et al. (2014) Surveillance and diagnostic algorithm for hepatocellular carcinoma proposed by the Liver Cancer Study Group of Japan: 2014 update. Oncology 87(Suppl 1):7–21
11. Lee JM, Park JW, Choi BI (2014) 2014 KLCSG-NCC Korea Practice Guidelines for the management of hepatocellular carcinoma: HCC diagnostic algorithm. Dig Dis 32:764–777
12. Omata M, Lesmana LA, Tateishi R, et al. (2010) Asian Pacific Association for the Study of the Liver consensus recommendations on hepatocellular carcinoma. Hepatol Int 4:439–474
13. Bruix J, Reig M, Sherman M (2016) Evidence-based diagnosis, staging, and treatment of patients with hepatocellular carcinoma. Gastroenterology 150:835–853
14. Griffin N, Addley H, Sala E, et al. (2012) Vascular invasion in hepatocellular carcinoma: is there a correlation with MRI? Br J Radiol 85:736–744
15. Chandarana H, Robinson E, Hajdu CH, et al. (2011) Microvascular invasion in hepatocellular carcinoma: is it predictable with pretransplant MRI? AJR Am J Roentgenol 196:1083–1089

16. Eguchi S, Takatsuki M, Hidaka M, et al. (2010) Predictor for histological microvascular invasion of hepatocellular carcinoma: a lesson from 229 consecutive cases of curative liver resection. World J Surg 34:1034–1038
17. Kaibori M, Ishizaki M, Matsui K, Kwon AH (2010) Predictors of microvascular invasion before hepatectomy for hepatocellular carcinoma. J Surg Oncol 102:462–468
18. McHugh PP, Gilbert J, Vera S, et al. (2010) Alpha-fetoprotein and tumour size are associated with microvascular invasion in explanted livers of patients undergoing transplantation with hepatocellular carcinoma. HPB (Oxford) 12:56–61
19. Ariizumi S, Kitagawa K, Kotera Y, et al. (2011) A non-smooth tumor margin in the hepatobiliary phase of gadoxetic acid disodium (Gd-EOB-DTPA)-enhanced magnetic resonance imaging predicts microscopic portal vein invasion, intrahepatic metastasis, and early recurrence after hepatectomy in patients with hepatocellular carcinoma. J Hepatobiliary Pancreat Sci 18:575–585
20. Chou CT, Chen RC, Lin WC, et al. (2014) Prediction of microvascular invasion of hepatocellular carcinoma: preoperative CT and histopathologic correlation. AJR Am J Roentgenol 203:W253–W259
21. Lim JH, Choi D, Park CK, Lee WJ, Lim HK (2006) Encapsulated hepatocellular carcinoma: CT-pathologic correlations. Eur Radiol 16:2326–2333
22. Kim H, Park MS, Choi JY, et al. (2009) Can microvessel invasion of hepatocellular carcinoma be predicted by pre-operative MRI? Eur Radiol 19:1744–1751
23. Nishie A, Yoshimitsu K, Asayama Y, et al. (2008) Radiologic detectability of minute portal venous invasion in hepatocellular carcinoma. AJR Am J Roentgenol 190:81–87
24. Kim KA, Kim MJ, Jeon HM, et al. (2012) Prediction of microvascular invasion of hepatocellular carcinoma: usefulness of peritumoral hypointensity seen on gadoxetate disodium-enhanced hepatobiliary phase images. J Magn Reson Imaging 35:629–634
25. Suh YJ, Kim MJ, Choi JY, Park MS, Kim KW (2012) Preoperative prediction of the microvascular invasion of hepatocellular carcinoma with diffusion-weighted imaging. Liver Transpl 18:1171–1178
26. Xu P, Zeng M, Liu K, et al. (2014) Microvascular invasion in small hepatocellular carcinoma: is it predictable with preoperative diffusion-weighted imaging? J Gastroenterol Hepatol 29:330–336
27. Wang WT, Yang L, Yang ZX, et al. (2018) Assessment of microvascular invasion of hepatocellular carcinoma with diffusion kurtosis imaging. Radiology 286:571–580
28. Segal E, Sirlin CB, Ooi C, et al. (2007) Decoding global gene expression programs in liver cancer by noninvasive imaging. Nat Biotechnol 25:675–680
29. Kim JY, Kim MJ, Kim KA, Jeong HT, Park YN (2012) Hyperintense HCC on hepatobiliary phase images of gadoxetic acid-enhanced MRI: correlation with clinical and pathological features. Eur J Radiol 81:3877–3882
30. Banerjee S, Wang DS, Kim HJ, et al. (2015) A computed tomography radiogenomic biomarker predicts microvascular invasion and clinical outcomes in hepatocellular carcinoma. Hepatology 62:792–800
31. Renzulli M, Brocchi S, Cucchetti A, et al. (2016) Can current preoperative imaging be used to detect microvascular invasion of hepatocellular carcinoma? Radiology 279:432–442
32. Kim MJ, Lee M, Choi JY, Park YN (2012) Imaging features of small hepatocellular carcinomas with microvascular invasion on gadoxetic acid-enhanced MR imaging. Eur J Radiol 81:2507–2512
33. An C, Choi GH, Lee HS, Kim MJ (2012) Assessment of preoperative magnetic resonance imaging staging in patients with hepatocellular carcinoma undergoing resection compared with the seventh American Joint Committee on Cancer System. Invest Radiol 47:634–641
34. Shindoh J, Andreou A, Aloia TA, et al. (2013) 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 20:1223–1229
35. American Joint Committee on Cancer (2017) *AJCC cancer staging manual*, 8th edn. New York: Springer
36. Chen BB, Hsu CY, Yu CW, et al. (2016) Dynamic contrast-enhanced MR imaging of advanced hepatocellular carcinoma: comparison with the liver parenchyma and correlation with the survival of patients receiving systemic therapy. Radiology 281:454–464
37. Gao SY, Tang L, Cui Y, et al. (2016) Tumor angiogenesis-related parameters in multi-phase enhanced CT correlated with outcomes of hepatocellular carcinoma patients after radical hepatectomy. Eur J Surg Oncol 42:538–544
38. Kawamura Y, Ikeda K, Seko Y, et al. (2011) Heterogeneous type 4 enhancement of hepatocellular carcinoma on dynamic CT is associated with tumor recurrence after radiofrequency ablation. AJR Am J Roentgenol 197:W665–W673
39. Kierans AS, Leonardou P, Hayashi P, et al. (2010) MRI findings of rapidly progressive hepatocellular carcinoma. Magn Reson Imaging 28:790–796
40. Kitao A, Matsui O, Yoneda N, et al. (2012) Hypervascular hepatocellular carcinoma: correlation between biologic features and signal intensity on gadoxetic acid-enhanced MR images. Radiology 265:780–789
41. Murakata A, Tanaka S, Mogushi K, et al. (2011) Gene expression signature of the gross morphology in hepatocellular carcinoma. Ann Surg 253:94–100
42. Nakanishi M, Chuma M, Hige S, et al. (2012) Relationship between diffusion-weighted magnetic resonance imaging and histological tumor grading of hepatocellular carcinoma. Ann Surg Oncol 19:1302–1309
43. Shimizu R, Tamai H, Mori Y, et al. (2016) The arterial tumor enhancement pattern on contrast-enhanced computed tomography is associated with primary cancer death after radiofrequency ablation for small hepatocellular carcinoma. Hepatol Int 10:328–339
44. Siripongsakun S, Lee JK, Raman SS, et al. (2012) MRI detection of intratumoral fat in hepatocellular carcinoma: potential biomarker for a more favorable prognosis. AJR Am J Roentgenol 199:1018–1025
45. Wu TH, Yu MC, Chen TC, et al. (2012) Encapsulation is a significant prognostic factor for better outcome in large hepatocellular carcinoma. J Surg Oncol 105:85–90
46. Xu L, Peng ZW, Chen MS, et al. (2015) Prognostic nomogram for patients with unresectable hepatocellular carcinoma after transcatheter arterial chemoembolization. J Hepatol 63:122–130
47. Yamashita T, Kitao A, Matsui O, et al. (2014) Gd-EOB-DTPA-enhanced magnetic resonance imaging and alpha-fetoprotein predict prognosis of early-stage hepatocellular carcinoma. Hepatology 60:1674–1685
48. Ng IO, Lai EC, Ng MM, Fan ST (1992) Tumor encapsulation in hepatocellular carcinoma. A pathologic study of 189 cases. Cancer 70:45–49
49. Kang TW, Rhim H, Lee J, et al. (2016) Magnetic resonance imaging with gadoxetic acid for local tumour progression after radiofrequency ablation in patients with hepatocellular carcinoma. Eur Radiol 26:3437–3446
50. Kim BK, Kim KA, An C, et al. (2015) Prognostic role of magnetic resonance imaging vs. computed tomography for hepatocellular carcinoma undergoing chemoembolization. Liver Int 35:1722–1730
51. Jeong HT, Kim MJ, Kim YE, et al. (2012) MRI features of hepatocellular carcinoma expressing progenitor cell markers. Liver Int 32:430–440
52. Choi SY, Kim SH, Park CK, et al. (2018) Imaging features of gadoxetic acid-enhanced and diffusion-weighted MR imaging for identifying cytokeratin 19-positive hepatocellular carcinoma: a retrospective observational study. Radiology 286:897–908
53. Rhee H, An C, Kim H-Y, et al. (2018) Hepatocellular carcinoma with irregular rim-like arterial phase hyperenhancement: more aggressive pathologic features. Liver Cancer . https://doi.org/10.1159/000488540
54. An C, Kim DW, Park YN, et al. (2015) Single hepatocellular carcinoma: preoperative MR imaging to predict early recurrence after curative resection. Radiology 276:433–443
55. Lee S, Kim SH, Lee JE, Sinn DH, Park CK (2017) Preoperative gadoxetic acid-enhanced MRI for predicting microvascular invasion in patients with single hepatocellular carcinoma. J Hepatol 67:526–534
56. Kim AY, Sinn DH, Jeong WK, et al. (2018) Hepatobiliary MRI as novel selection criteria in liver transplantation for hepatocellular carcinoma. J Hepatol . https://doi.org/10.1016/j.jhep.2018.01.024

57. Li M, Xin Y, Fu S, et al. (2016) Corona enhancement and mosaic architecture for prognosis and selection between of liver resection versus transcatheter arterial chemoembolization in single hepatocellular carcinomas > 5 cm without extrahepatic metastases: an imaging-based retrospective study. Medicine 95:e2458

58. Sakon M, Nagano H, Nakamori S, et al. (2002) Intrahepatic recurrences of hepatocellular carcinoma after hepatectomy: analysis based on tumor hemodynamics. Arch Surg 137:94–99