Received:
24 December 2017

Revised:
19 April 2018

Accepted:
21 May 2018

<https://doi.org/10.1259/bjr.20180017>

Cite this article as:

Ni T, Shang X-S, Wang W-T, Hu X-X, Zeng M-S, Rao S-X. Different MR features for differentiation of intrahepatic mass-forming cholangiocarcinoma from hepatocellular carcinoma according to tumor size. *Br J Radiol* 2018; **91**: 20180017.

FULL PAPER

Different MR features for differentiation of intrahepatic mass-forming cholangiocarcinoma from hepatocellular carcinoma according to tumor size

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Objective: To identify reliable magnetic resonance (MR) features for distinguishing mass-forming type of intrahepatic cholangiocarcinoma (IMCC) from hepatocellular carcinoma (HCC) based on tumor size.

Methods: This retrospective study included 395 patients with pathologically confirmed IMCCs ($n = 180$) and HCCs ($n = 215$) who underwent pre-operative contrast-enhanced MRI including diffusion-weighted imaging (DWI). MR features were evaluated and clinical data were also recorded. All the characteristics were compared in small (≤ 3 cm) and large tumor (> 3 cm) groups by univariate analysis and subsequently calculated by multivariable logistic regression analysis.

Results: Multivariable analysis revealed that rim arterial phase hyperenhancement [odds ratios (ORs) = 13.16], biliary dilation (OR = 23.42) and CA19-9 (OR = 21.45) were significant predictors of large IMCCs ($n = 138$), and washout appearance (OR = 0.036), enhancing capsule

appearance (OR = 0.039), fat in mass (OR = 0.057), chronic liver disease (OR = 0.088) and alpha fetoprotein (OR = 0.019) were more frequently found in large HCCs ($n = 143$). For small IMCCs ($n = 42$) and HCCs ($n = 72$), rim arterial phase hyperenhancement (OR = 9.68), target appearance at DWI (OR = 12.51), alpha fetoprotein (OR = 0.12) and sex (OR = 0.20) were independent predictors in multivariate analysis.

Conclusion: Valuable MR features and clinical factors varied for differential diagnosis of IMCCs and HCCs according to tumor size.

Advances in knowledge: MR features for differential diagnosis of large IMCC and HCC (> 3 cm) are in keeping with that recommended by LI-RADS. However, for small IMCCs and HCCs (≤ 3 cm), only rim enhancement on arterial phase and target appearance at DWI are reliable predictors.

INTRODUCTION

Intrahepatic cholangiocarcinoma (ICC) and hepatocellular carcinoma (HCC) are two primary liver malignancies. In recent years, their incidence has been increasing, and they gradually become the leading cause of death in patients with chronic liver disease.^{1,2} According to the morphology and growth characteristics, the Liver Cancer Study Group of Japan has classified ICCs into three types: mass-forming, periductal-infiltrative, and intraductal-growing types. Among them, the mass-forming type of intrahepatic cholangiocarcinoma (IMCC) is the most common type and its prognosis is generally unfavorable.³ There have been some criteria available for characterizing HCC and distinct MRI features of IMCC and HCC, recommended by the European Association for the Study of the Liver and American Association for the Study Liver Diseases, which have been widely accepted by many countries.⁴⁻⁸ In March 2011, the

American College of Radiology launched a Liver Imaging Reporting and Data System (LI-RADS) for interpreting and reporting of CT and MRI examinations of the liver in patients at high risk for HCC, which has been updated in 2014 and 2017.^{4,9} In all versions of the LI-RADS, they listed some main imaging features favoring non-HCC malignancy which was largely related to ICC because this was the most common non-HCC liver tumor.

However, accurately distinguishing IMCC and HCC is still one of the challenging issues of liver imaging because we often encounter some of them showing similar enhancement pattern in clinical practice. Recent studies have demonstrated that different size of IMCC in patients with cirrhosis showed different enhancement patterns at CT¹⁰ or MRI.¹¹ It was especially difficult to accurately identify small IMCC up to 3 cm from HCC. However, Sheng¹² reported

that dynamic enhancement patterns and signals in T_2 weighted images could differentiate small IMCC from atypical small HCC with cirrhosis and chronic viral hepatitis. In these above studies, they did not systematically assess the MR features based on LI-RADS. Misdiagnosis of IMCC and HCC may lead to inappropriate treatments. In addition to surgical resection, liver transplantation is another effective approach for HCC patients with decompensated cirrhosis,^{13,14} however, it is highly controversial for IMCC due to the high recurrence rate.¹⁵

Therefore, our aim was to determine the different MRI features for distinguishing IMCC from HCC in different tumor size based on LI-RADS.

METHODS AND MATERIALS

Patients

This retrospective study was conducted according to the ethical guidelines of the 1975 Declaration of Helsinki. The ethics review committee of Zhongshan Hospital of Fudan University granted approval of this study (approval number Y2015-228) on 2 June 2015, and informed consent was obtained from each patient included in the study. From January 2009 to October 2015, we found 950 consecutive patients who had been pathologically confirmed IMCC in Zhongshan Hospital of Fudan University by searching “hepatocellular carcinoma” and “intrahepatic cholangiocarcinoma” in the final diagnosis from medical records. The inclusion criteria were (1) patients with pathologically proven IMCC within 2 weeks after MRI; (2) patients who underwent pre-operative routine enhanced MRI scan; (3) patients who had not undergone locoregional therapy such as transarterial chemoembolization and radiofrequency ablation prior to MRI examination. The exclusion criteria were: lesions $\geq 50\%$ of

hemorrhage, necrosis. In addition, periductal-infiltrating, hilar, metastatic cholangiocarcinoma were excluded in this study.

Finally, 180 patients with IMCC were included in our study. We also selected 215 consecutive patients who had surgically confirmed HCC and met the inclusion criteria from January to September 2015. Detailed selection process of patients is presented in Figure 1.

MRI examinations

MR scans were performed on two 1.5 T MRs (Avanto; Siemens, Erlangen, Germany and Aera; Siemens, Erlangen, Germany). The standard MR protocol included axial T_2 weighted fat-suppressed two-dimensional turbo spin echo, in-phase and out-of-phase axial T_1 weighted imaging, diffusion-weighted imaging (DWI) and volumetric interpolated breath-hold examination (VIBE) for pre- and post-contrast enhancement. For contrast-enhanced MRI, gadopentate dimeglumine (Magnevist, Bayer Schering Pharma AG, Berlin, Germany, 0.1 mmol kg^{-1}) was rapidly injected manually (at a rate of approximately 2 ml s^{-1}) by one investigator through a 20-gauge intravenous catheter placed in a cubital or cephalic vein. Immediately afterward, a 20 ml saline flush was injected at the same rate. Arterial phase, portal venous phase and equilibrium phase images were obtained at 20–30 s, 70–80 s, and 180 s after contrast medium injection, respectively. MRI sequences are summarized in Table 1.

Image analysis

All MRI images were reviewed in consensus on a picture archiving and communication system by two board-certified abdominal radiologists (SXR and MSZ). If there was a discrepancy in reading between two radiologists, a third abdominal

Figure 1. Flowchart of the patients enrolled in the study. RFA; radio frequency ablation; TACE, transarterial chemoembolization.

Table 1. MRI acquisition parameters

Sequence	Area 1.5 T				Avanto 1.5 T			
	T2WI	T1WI (IP and OP)	DWI	T1WI with VIBE	T2WI	T1WI (IP and OP)	DWI	T1WI with VIBE
Repetition time (ms)	3500	230	3200	4.38	3300	112	2400–2600	5.04
Echo time (ms)	84	2.38/4.76	56	1.93	70	2.05/5.04	66	2.31
Flip angle (degrees)	140	70	/	12	150	70	/	10
Field of view (mm)	360 × 360	330 × 330 ~ 380 × 380	380 ~ 400 × 300 ~ 324	380 ~ 400 × 300 ~ 324	330 × 330 ~ 380 × 380	330 × 330 ~ 380 × 380	330 × 330 ~ 380 × 380	330 × 330 ~ 380 × 380
Matrix size	194 × 256	180 × 256	84 × 128	2116 × 288	207 × 384	144 × 256	112 × 128	250 × 512
Slice thickness (mm)	8	7	5.5	5	7	7	7	4–5
Slice gap (mm)	2	2	2	0	2.1	2.1	2.1	0

IP, in-phase; OP, out-of-phase; VIBE, volumetric interpolated breath-hold examination.

radiologist (YD) reviewed and reached a consensus. The readers were blinded to the final detailed pathological diagnosis to avoid bias.

According to the LI-RADS, the MRI features evaluated were as follows: (a) tumor size (largest outer-edge-to-outer-edge dimension of the largest lesion); (b) rim arterial phase hyper-enhancement (arterial phase enhancement in the periphery of the lesion); (c) peripheral washout appearance (peripheral rim enhancement decreased in portal venous phase or delayed phase); (d) target appearance at DWI [a central hypointense area and a peripheral hyperintense rim ($b = 500 \text{ s mm}^{-2}$)]; (e) liver surface retraction; (f) biliary dilation; (g) washout appearance (non-peripheral visually assessed temporal reduction in enhancement in whole or in part relative to composite liver tissue in portal venous phase or delayed phase resulting in hypoenhancement); (h) enhancing capsule appearance(smooth, uniform, sharp border around most or all of a lesion, unequivocally thicker or more conspicuous than fibrotic tissue around background nodules, and visible as enhancing rim in the portal venous phase or delayed phase); (i) nonenhancing capsule appearance(capsule appearance not visible as an enhancing rim); (j) fat in mass (a signal loss in whole or in part on out-of-phase compared to in-phase gradient echo images, relative to adjacent liver); (k) nodule-in-nodule architecture (presence of smaller inner nodule within and having different imaging features than larger outer nodule); (l) blood products in mass (intralesional or perilesional hemorrhage in the absence of biopsy, trauma or intervention).

Laboratory examinations analysis

Another abdominal radiologist (TN) recorded the underlying disease (with or without hepatitis) and the main tumor markers [alpha fetoprotein (AFP), carcinoembryonic antigen (CEA), CA19-9] of the patients. The threshold for AFP, CEA and CA19-9 are respectively 20 ug l^{-1} , 5 ug l^{-1} and 37 U ml^{-1} in Zhongshan Hospital of Fudan University.

Statistical analysis

Statistical analyses were performed using SPSS v. 18.0. Univariate statistical differences among each MRI parameter and baseline clinic characteristics were analyzed using a χ^2 test and Fisher's

exact test for categorical variables. For continuous variables, a Student's *t*-test or the Mann–Whitney *U* test were used. Moreover, for baseline clinic characteristics, we analyzed all patients, small tumor group ($\leq 3 \text{ cm}$) and large tumor group ($> 3 \text{ cm}$) separately. The statistically significant variables obtained from univariate analysis were used to conduct multivariate logistic regression analysis. Factors showing multicollinearity were excluded from the multivariable analyses. For all tests, a *p* value less than 0.05 was considered significant.

RESULTS

Study population

The baseline characteristics of enrolled patients are summarized in Table 2. We observed that in all patients and large tumor group, age, sex, the infection rate of chronic liver disease and the abnormal increase of serum tumor markers (CA199, CEA, AFP) were significantly different between IMCCs and HCCs ($p < 0.001$). And there was no significant difference in the maximum diameter of the largest lesion between two diseases ($p > 0.05$). However, in the small tumor group, age and the maximum diameter of the largest lesion were no statistically significant difference between two diseases ($p > 0.05$). And sex, the infection rate of chronic liver disease and the abnormal increase of serum tumor markers were significantly different ($p : < 0.001$ – 0.018). The average time intervals between the MRI examination and surgery were 5 days (range 3–14 days) for IMCCs and 5 days (range 2–14 days) for HCCs.

Predictive factors of large IMCCs and HCCs ($> 3 \text{ cm}$)

The predictive factors of differentiating IMCCs from HCCs, and the results of the uni- and multivariate analysis are summarized in Table 3. In univariate analysis, except the appearance of nodule-in-nodule architecture, all other characteristics, including rim arterial phase hyperenhancement, peripheral washout appearance, target appearance at DWI, liver surface retraction, biliary dilation, washout appearance, enhancing capsule appearance, non-enhancing capsule appearance, fat in mass, blood products in mass, chronic liver disease, CA19-9, CEA, AFP, sex and age were significantly different

Table 2. Patient baseline characteristics

	ALL		<i>p</i> -value	Size >3 cm		<i>p</i> -value	Size ≤3 cm		<i>p</i> -value
	IMCC (<i>n</i> = 180)	HCC (<i>n</i> = 215)		IMCC (<i>n</i> = 138)	HCC (<i>n</i> = 143)		IMCC (<i>n</i> = 42)	HCC (<i>n</i> = 72)	
Age (yr), median (range)	60 (28–80)	55 (28–80)	<0.001	59 (28–80)	54 (28–77)	<0.001	57 (39–73)	57 (31–80)	0.933
Male/female, <i>n</i>	115/65	183/32	<0.001	89/49	124/19	<0.001	26/16	59/13	0.018
Size (mean ± SD, cm)	5.7 ± 2.9	5.1 ± 3.3	0.059	6.7 ± 2.4	6.6 ± 3.2	0.57	2.2 ± 0.59	2.2 ± 0.56	0.693
Chronic liver disease									
Presence (HBV/HCV)	71 (70/1)	190 (186/4)	<0.001	46 (46/0)	125 (124/1)	<0.001	25 (24/1)	65 (62/3)	0.001
Absence	109	25		92	18		17	7	
CA19-9 (>37 U ml ⁻¹)	95	31	<0.001	79	20	<0.001	16	11	0.006
CEA (>5 ug l ⁻¹)	59	8	<0.001	51	6	<0.001	8	2	0.003
AFP (>20 ug l ⁻¹)	15	130	<0.001	12	97	<0.001	3	33	0.001

AFP, alpha fetoprotein Markk; CA19-9, carbohydrate antigen; CEA, carcino embryonic antigen; ICC, intrahepatic cholangio carcinoma; IMCC, mass-forming type of intrahepatic cholangio carcinoma; SD, standard deviation.

between IMCCs and HCCs (p : < 0.001–0.008). The most prevalent enhancement pattern for IMCCs was rim enhancement with progressive central enhancement in portal venous and delayed phase, whereas hyperenhancement in arterial phase followed by washout in portal venous phase or delayed phase was more common for HCCs (p < 0.001). Enhancing capsule appearance, nonenhancing capsule appearance, fat in mass, blood products in mass were less common in IMCCs than

HCCs, and peripheral washout appearance, target appearance at DWI were more inclined to appear in IMCCs (p : <0.001–0.008). On morphological features, liver surface retraction and biliary dilation were more common in IMCCs than HCCs (p < 0.001).

In multivariable analysis, rim arterial phase hyperenhancement, biliary dilation and abnormal increase of CA19-9 were

Table 3. Results of univariate and multivariate analysis for MRI characteristics in differentiating large IMCC from HCC (>3 cm)

	IMCC (<i>N</i> = 138)	HCC (<i>N</i> = 143)	Univariate analysis			Multivariate analysis		
			OR	95% CI	<i>p</i> -value	OR	95% CI	<i>p</i> -value
Rim hyperenhancement	110 (79.7%)	36 (25.2%)	11.677	6.663, 20.462	<0.001	13.159	1.732, 99.972	0.013
Peripheral washout	16 (11.6%)	4 (2.8%)	4.557	1.484, 14.000	0.008			
Target appearance at DWI	78 (56.5%)	21 (14.7%)	7.552	4.261, 13.387	<0.001			
Liver surface retraction	40 (29.0%)	16 (11.2%)	3.240	1.714, 6.125	<0.001			
Biliary dilation	54 (39.1%)	4 (2.8%)	22.339	7.809, 63.910	<0.001	23.417	1.532, 358.039	0.023
Washout appearance	4 (2.9%)	107 (74.8%)	0.010	0.003, 0.029	<0.001	0.036	0.002, 0.525	0.015
Enhancing capsule	48 (34.8%)	112 (78.3%)	0.148	0.087, 0.251	<0.001	0.039	0.005, 0.326	0.003
Non-enhancing capsule	51 (37.0%)	98 (68.5%)	0.269	0.164, 0.441	<0.001			
Fat in mass	4 (2.9%)	34 (23.8%)	0.096	0.033, 0.278	<0.001	0.057	0.003, 0.958	0.047
Nodule-in-nodule	12 (8.7%)	19 (13.3%)	0.622	0.290, 1.334	0.223			
Blood products in mass	20 (14.5%)	49 (34.3%)	0.325	0.181, 0.584	<0.001			
Chronic liver disease	46 (33.3%)	125 (87.4%)	0.072	0.039, 0.132	<0.001	0.088	0.014, 0.547	0.009
CA19-9 (>37 U ml ⁻¹)	79 (57.2%)	20 (14.0%)	8.235	4.608, 14.716	<0.001	21.446	3.118, 147.504	0.002
CEA (>5 ug l ⁻¹)	51 (37.0%)	6 (4.2%)	13.385	5.510, 32.515	<0.001			
AFP (>20 ug l ⁻¹)	12 (8.7%)	97 (67.8%)	0.045	0.023, 0.090	<0.001	0.019	0.002, 0.149	0.001
Sex (Male)	89 (64.5%)	124 (86.7%)	0.278	0.153, 0.505	<0.001			
Age (>50y)	113 (81.9%)	88 (61.5%)	2.825	1.632, 4.890	<0.001			

AFP, alpha fetoprotein Markk; CA19-9, carbohydrate antigen; CEA, carcino embryonic antigen; CI, confidence interval; DWI, diffusion-weighted imaging; ICC, intrahepatic cholangio carcinoma; IMCC, mass-forming type of intrahepatic cholangio carcinoma; OR, odds ratio.

Figure 2. The surgically confirmed small HCC in a 65-year-old female. (a) Pre-contrast T_1 weighted image shows a 2.7-cm-sized hypointense mass at the hepatic segment V. (b) T_2 weighted image shows a heterogeneous high signal, followed by hyperenhancement in the (c) arterial phase and washout in (d) portal venous and (e) delayed phases (f) with enhancing capsule appearance. On the DWI at $b = 500 \text{ s mm}^{-2}$, the tumor shows a high signal. DWI, diffusion-weighted imaging; HCC, HCC, hepatocellular carcinoma.

independent predictors of IMCCs ($p: 0.002\text{--}0.023$). On the contrary, washout appearance, enhancing capsule appearance, fat in mass, chronic liver disease and abnormal increase of AFP were more frequently found in HCCs ($p: <0.001\text{--}0.047$).

Predictive factors of small IMCCs and HCCs ($\leq 3 \text{ cm}$) The clinical characteristics, including chronic liver disease, CA19-9, CEA, AFP and sex, still maintained their statistical significance for the differentiation between small IMCCs and HCCs ($p: < 0.001\text{--}0.02$). For MRI features, rim arterial phase hyperenhancement, target appearance at DWI and biliary dilation were more common in IMCCs, while washout appearance, enhancing capsule appearance and fat in mass were more common in HCCs in univariate analysis ($p: < 0.001\text{--}0.019$) (Figure 2). Multivariate analysis revealed that rim arterial phase hyperenhancement, target appearance at DWI, AFP and sex were significant independent factors for differentiating IMCCs from HCCs ($p: 0.002\text{--}0.049$) (Figure 3). Detailed description of this subgroup analysis is described in Table 4.

DISCUSSION

The study validated the clinical efficacy of the LI-RADS in differentiating different size of IMCC and HCC. Our results indicated that for tumors larger than 3 cm, MR features that was useful for differential diagnosis of IMCC and HCC, was in concordance with the major features described in LI-RADS and the previous relevant studies.^{16,17} However, only rim arterial phase hyperenhancement and target appearance at DWI were important MRI predictors favoring small IMCCs ($\leq 3 \text{ cm}$).

It follows that different enhancement patterns of IMCCs and HCCs are quite related to tumor size and the imaging performances of small IMCCs and HCCs are more likely to be

confused. Absence of contrast washout was once regarded as an important characteristic MR contrast pattern for IMCCs, independently of its size,¹⁸ which was not completely consistent with our study. We found that absence of washout was valuable MR feature of IMCCs in the large tumor group ($> 3 \text{ cm}$). However, we failed to demonstrate that absence of washout was independent predictors of IMCCs in the small tumor ($\leq 3 \text{ cm}$) by multivariate analysis. This inconformity may be due to the relative small sample size in the study of Rimola et al, in which all the patients with cirrhosis did not evaluate by different tumor size. Comparatively, our study contained all the patients regardless of hepatitis and cirrhosis (only 59.5% of IMCCs and 90.3% of HCCs had a history of chronic liver disease). This may show that the applicability of the results of this study is better.

In the study of Huang et al,¹¹ substantial proportions of small IMCCs and HCCs have similar enhancement patterns in the patients with cirrhosis. Washout may be observed in a noticeable proportion of small IMCCs (5/71, 7.0%). Similarly, eight patients of IMCCs (19.0%) displayed washout appearance in our study. This phenomenon may be attributed to the fact that small IMCCs contain less central fibrotic stroma and necrosis, while they tend to have larger amounts of cellular and cholangiolocellular components.^{18–20} Some studies described that IMCCs with washout pattern were found to be poorly differentiated and early arterial enhancement was a useful factor for longer disease-free survival.^{20–22}

Consistent with previous reports,^{11,12} rim hyperenhancement on arterial phase was a significant feature for diagnosing IMCCs, which was one of the most important independent predictor of differentiating small IMCCs from HCCs in our

Figure 3. The surgically confirmed small IMCC in a 73-year-old female. (a) Pre-contrast T_1 weighted image shows a 2.8-cm-sized hypointense mass at the junction of hepatic segment II and IV. (b) T_2 weighted image shows a homogeneous high signal, followed by peripheral rim enhancement in the (c) arterial phase and progressive central enhancement in (d) portal venous and (e) delayed phases. (f) On the DWI at $b = 500 \text{ s mm}^{-2}$, the tumor shows target appearance that consists of a central hypointense area and a peripheral hyperintense rim. DWI, diffusion-weighted imaging; IMCC, mass-forming type of intrahepatic cholangiocarcinoma.

Table 4. Results of univariate and multivariate analysis for MRI characteristics in differentiating small IMCC from HCC ($\leq 3 \text{ cm}$)

	IMCC (N = 42)	HCC (N = 72)	Univariate analysis			Multivariate analysis		
			OR	95% CI	p-value	OR	95% CI	p value
Rim hyperenhancement	28 (66.7%)	12 (16.7%)	10	4.098,24.401	<0.001	9.684	2.136, 43.898	0.003
Peripheral washout	2 (4.8%)	1 (1.4%)	3.55	0.312,40.386	0.307			
Target sign at DWI	27 (64.3%)	8 (11.1%)	14.4	5.465,37.941	<0.001	12.508	2.500, 62.574	0.002
Liver surface retraction	5 (11.9%)	4 (5.6%)	2.297	0.581,9.081	0.236			
Biliary dilation	13 (31.0%)	5 (6.9%)	6.007	1.961,18.404	0.002			
Washout appearance	8 (19.0%)	52 (72.2%)	0.09	0.036,0.229	<0.001			
Enhancing capsule	19 (45.2%)	50 (69.4%)	0.363	0.165,0.799	0.012			
Non-enhancing capsule	24 (57.1%)	48 (66.7%)	0.667	0.305,1.459	0.310			
Fat in mass	2 (4.8%)	17 (23.6%)	0.162	0.035,0.740	0.019			
Nodule-in-nodule	0	0	NA	NA	NA			
Blood products in mass	2 (4.8%)	8 (11.1%)	0.4	0.081,1.979	0.261			
Chronic liver disease	25 (59.5%)	65 (90.3%)	0.158	0.059,0.428	<0.001			
CA19-9 ($>37 \text{ U ml}^{-1}$)	16 (38.1%)	11 (15.3%)	3.413	1.395,8.347	0.007			
CEA ($>5 \text{ ug l}^{-1}$)	8 (19.0%)	2 (2.8%)	8.235	1.658,40.902	0.010			
AFP ($>20 \text{ ug l}^{-1}$)	3 (7.1%)	33 (45.8%)	0.091	0.026,0.321	<0.001	0.116	0.020, 0.685	0.017
Sex (Male)	26 (61.9%)	59 (81.9%)	0.358	0.151,0.850	0.020	0.200	0.040, 0.996	0.049
Age ($>50\text{y}$)	30 (71.4%)	52 (72.2%)	0.962	0.413,2.239	0.962			

AFP, alpha fetoprotein MarkI; CA19-9, carbohydrate antigen; CEA, carcino embryonic antigen; CI, confidence interval; DWI, diffusion-weighted imaging; ICC, intrahepatic cholangio carcinoma; IMCC, mass-forming type of intrahepatic cholangio carcinoma; OR, odds ratio; NA, not applicable.

study ($p = 0.003$). Although 66.7% of IMCCs showed typical enhancement pattern, there were also 16.7% of small HCCs showed this appearance. This might be due to that the arterial supply of small HCCs were not fully developed, and they were still mostly supplied by the portal blood on arterial phase.^{23–25}

Target appearance at DWI defined as a hypointense area with a peripheral hyperintense rim, was another independent predictor of IMCCs ($p = 0.002$), as in our study, 27 IMCCs (64.3%) showed this feature, while only 8 HCCs (11.1%) showed this feature. It was in accordance with previous studies,^{7,8} especially in the study of Park et al,⁸ which revealed that DWI target appearance was the only significant and independent MR predictor for distinguishing small IMCCs from HCCs. However, we failed to find that target appearance at DWI was an independent predictor of IMCCs in large tumor group by multivariate analysis. This makes us speculate that DWI target appearance may be more meaningful for diagnosing small IMCCs. As shown in previous studies, DWI target appearance was thought to be associated with the pathological characteristics of IMCCs.^{26,27} IMCCs contain peripheral cellular components and central loose fibrosis with accompanying edema which is responsible for central hypointense area at DWI.

There are some limitations in our study. First, this was a retrospective study that selection bias inevitably existed. Second, the MR protocols and machines used in our study were not uniform. However, we used similar parameters to determine image quality to ensure the accuracy of the diagnosis. Third, MRI features of IMCCs and HCCs evaluated in this study only included those recommended on LI-RADS, which was primarily targeted at the diagnosis of HCCs in hepatitis and cirrhosis. Fourth, gadoxetic acid is not routinely used in our department. So target appearance was assessed only on DWI. Study showed that target appearance either on hepatobiliary phase at gadoxetic acid enhanced MRI or on DWI slight higher than only on DWI both for HCCs (87.3% vs 83.5%) and IMCCs (15.7% vs 13.5%).²⁸ Finally, the radiologists may have differences in evaluating MRI features due to their different levels of experience.

In conclusion, the MR features differed for differential diagnosis of IMCC and HCC depending on tumor size. Normally, we can use LI-RADS to diagnose large IMCC and HCC (>3 cm), and for small IMCC and HCC (≤ 3 cm), rim arterial phase hyperenhancement and target appearance at DWI are the most reliable predictors.

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