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FULL PAPER

Differentiating metastatic mucinous colorectal adenocarcinomas from simple cysts of the liver using contrast-enhanced and diffusion-weighted MRI

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Objective: To determine the value of contrast-enhanced and diffusion-weighted (DW) MRI for differentiating metastatic mucinous colorectal adenocarcinomas from simple cysts of the liver.

Methods: 29 patients with 47 metastatic mucinous colorectal adenocarcinomas and/or 19 simple cysts of the liver who underwent contrast-enhanced and DW MRI were included in this retrospective study. Two radiologists assessed the MRI findings by consensus. Qualitative and quantitative analyses were conducted. Significant MRI findings on univariate and multivariate analyses were assessed, and their diagnostic performances for predicting metastatic mucinous colorectal adenocarcinomas were analyzed.

Results: The presence of rim enhancement (odds ratio, 28.43; $p = 0.008$) and intracystic enhancement (odds ratio, 180.15; $p = 0.001$) were independently significant factors for predicting metastatic mucinous colorectal adenocarcinomas. The sensitivity and specificity of rim enhancement, intracystic enhancement, and their combination

for detecting metastatic mucinous colorectal adenocarcinomas were 83% (39/47) and 63.2% (12/19), 87.2% (41/47) and 89.5% (17/19), and 72.3% (34/47) and 94.7% (18/19), respectively. Compared to simple cysts, metastatic mucinous colorectal adenocarcinomas showed significantly lower mean apparent diffusion coefficient (1.92 ± 0.81 vs $2.99 \pm 0.75 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$; $p = 0.001$) and lesion-to-liver apparent diffusion coefficient ratio (1.66 ± 0.75 vs $2.44 \pm 0.56 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$; $p = 0.004$) and higher mean signal intensity (400.3 ± 216.3 vs 222.4 ± 99.3 ; $p = 0.039$) and lesion-to-liver signal intensity ratio on hepatobiliary-phase images (0.58 ± 0.16 vs 0.30 ± 0.14 ; $p < 0.001$).

Conclusion: Contrast-enhanced and DW MRI may be helpful for differentiating metastatic mucinous colorectal adenocarcinomas from simple cysts of the liver.

Advances in knowledge: On contrast-enhanced and DW MRI, rim and intracystic enhancement can be helpful for differentiating metastatic mucinous colorectal adenocarcinomas from simple cysts of the liver.

INTRODUCTION

Metastasis is the most common malignant neoplasm of the liver and may show variable appearances because of different characteristics of the primary malignancy.¹ Cystic metastases from tumors such as neuroendocrine tumor, melanoma, or gastrointestinal stromal tumor, may be due to necrosis of the hypervascular metastases secondary to rapid growth.²⁻⁴ Also, in patients with extrahepatic malignant mucinous neoplasms, such as mucinous adenocarcinomas of the colorectum and mucinous cystadenocarcinomas of the ovary or pancreas, hepatic metastases may show cystic

appearance because of abundant mucin production from the tumor.⁵⁻⁷

Simple hepatic cysts are benign, congenital, and developmental lesion derived from biliary endothelium with no communications with the biliary tree, based on pathology.³ They are commonly found lesions in clinical practice, and have an estimated prevalence of 2.5– to 5% in the general population. In patients with no extrahepatic mucinous adenocarcinoma, diagnosing simple hepatic cysts is usually easy because of their typical findings on various imaging

modalities.^{3,8–10} Studies have reported that metastatic mucinous adenocarcinomas of the liver may appear cystic with thick, irregularly enhanced wall, septa, mural nodule, or intracystic debris.^{5–7,9} However, in clinical practice, we have encountered that metastatic mucinous adenocarcinomas with no solid portion or mural nodule may show nonspecific imaging features, which might be similar to those of common benign cystic lesions of the liver, such as simple hepatic cysts.^{6,7} Therefore, differentiating metastatic mucinous adenocarcinomas with no solid portion or mural nodule from simple cysts of the liver is clinically important to avoid unnecessary management such as invasive biopsy or surgery of simple hepatic cysts, or delayed treatment of metastatic mucinous adenocarcinomas in patients with extrahepatic malignant mucinous adenocarcinomas.

Several studies have compared the imaging findings of primary biliary cystic neoplasms and simple hepatic cysts.^{11–14} However, to the best of our knowledge, no studies have evaluated the imaging findings for differentiating metastatic mucinous adenocarcinomas from simple cysts of the liver. Accordingly, the purpose of this study was to assess the value of contrast-enhanced and diffusion-weighted (DW) MRI for differentiating metastatic mucinous adenocarcinomas from simple cysts of the liver.

METHODS AND MATERIALS

This retrospective study was approved by the institutional review board of Samsung Medical Center, and the need for informed consent was waived.

Patients

We retrospectively searched the database of the Department of Pathology between October 2010 and June 2016, by using the search terms “mucinous adenocarcinoma”, “mucinous cystadenocarcinoma” or “metastatic mucinous (cyst) adenocarcinoma”, and “liver” in patients with extrahepatic mucinous (cyst) adenocarcinomas. 49 patients were identified with histologically proven metastatic mucinous adenocarcinoma of the liver, either by surgical resection or percutaneous biopsy. Of these patients, we excluded 26 patients because of the following reasons: (1) MRI at an outside hospital ($n = 6$); (2) suboptimal MRI with no contrast-enhanced dynamic phases ($n = 3$) or with dynamic phases of inadequate quality due to motion artifact and/or poor image quality ($n = 5$); or (3) enhancing solid portion or mural nodule in metastatic lesions of the liver, which was unmistakable from simple hepatic cysts ($n = 12$) by consensus between two abdominal radiologists (SYC and SL, with 8 and 6 years, respectively, of experience in abdominal MRI interpretation) who did not participate in the image analysis. Finally, 23 patients (13 males and 10 females; mean age, 57.69 years; age range, 30–78 years) with 47 metastatic mucinous adenocarcinomas without an enhancing solid portion or mural nodule in the liver were included. 46 metastatic mucinous adenocarcinomas in 22 patients were proven by surgical resection and only 1 lesion was proven by percutaneous biopsy. All patients had histologically proven primary mucinous adenocarcinomas in the colorectum.

As the control group, patients with histologically proven simple hepatic cysts were included. First, 8 patients among the

above-mentioned 23 patients had 12 simple hepatic cysts in the resected liver with metastatic mucinous colorectal adenocarcinoma. Moreover, among patients with no extrahepatic mucinous neoplasms, six patients with seven surgically confirmed simple hepatic cysts who underwent MRI at our hospital during the same period were identified. Accordingly, 14 patients (9 males and 5 females; mean age, 58.14 years; age range, 30–76 years) with 19 simple hepatic cysts were included.

Among the 47 metastatic mucinous colorectal adenocarcinomas of the liver, 35 were in the right, 11 in the left, and 1 in the caudate lobe. As for the 19 simple cysts of the liver, 5 were in the right, 11 in the left, and 3 in the caudate lobe.

MR image acquisition

In all patients, MR images were acquired using a 3.0 T whole-body MR system (Intera Achieva; Philips Healthcare, Best, Netherlands) with a 16-channel phased-array receiver coil. MRI included a T_1 weighted turbo field echo in-phase and out-of-phase sequence, a breath-hold multishot T_2 weighted sequence, and a respiratory-triggered single-shot T_2 and heavily T_2 weighted sequence. For contrast-enhanced MRI (Primovist; Bayer Healthcare, Berlin, Germany), unenhanced, arterial (20–35 s), portal (60 s), delayed (3 min), and 20 min hepatobiliary phases (HBPs) were obtained using a T_1 weighted three-dimensional turbo field echo sequence (T_1 high-resolution isotropic volume examination, THRIVE; Philips Healthcare, Best, Netherlands). The contrast agent was automatically administered intravenously by using a power injector at 2 ml s^{-1} for a total dose 0.025 mmol/kg body weight, followed by a 20 ml saline flush. For subtraction imaging in the arterial phase, unenhanced images were automatically subtracted from the arterial phase images by the inbuilt software of the MR machine. DW images with b -values of 0, 100, and 800 s mm^{-2} were acquired simultaneously using respiratory-triggered single-shot echoplanar imaging. The apparent diffusion coefficient (ADC) map was generated by using a mono-exponential function with b -values of 0 and 800 s mm^{-2} . The detailed parameters of MRI sequences are shown in Table 1.

Image analysis

All MR images were reviewed by two abdominal radiologists (JEL and SHK, with 6 and 17 years of experience in liver MRI, respectively) with consensus on imaging findings being analyzed. The reviewers were blinded to the clinical or histopathological results of each case. The images were reviewed on a picture archiving and communication system (Centricity; GE Healthcare, Chicago, IL).

Qualitative analysis

For qualitative analysis, the following imaging parameters were evaluated: margin (well-defined or ill-defined), shape (round/oval, lobulated, or irregular), presence of septa, rim enhancement, intracystic debris, intracystic enhancement, content homogeneity (homogenous or heterogeneous), and presence of perilesional bile duct dilatation. Patterns of intracystic enhancement were subcategorized into mesh-like, homogenous, and nodular enhancement. The signal intensity (SI) of the lesion on unenhanced, contrast-enhanced dynamic, HBP, and DW images

Table 1. MRI sequences and parameters

Sequence	TR/TE (ms)	Flip angle (°)	Section thickness (mm)	Matrix size	Bandwidth (Hz/pixel)	Field of view (cm)	Acquisition time (s)	No. of Excitations
T_1 W-2D dual GRE	3.5/1.15–2.3	10	6	256 × 194	434.4	32–38	14	1
BH-MS- T_2 WI	1623/70	90	5	324 × 235	235.2	32–38	55	1
RT-SS- T_2 WI	1342/80	90	5	320 × 256	506.4	32–38	–	2
RT-SS-HT $_2$ WI	1156/160	90	5	320 × 256	317.9	32–38	–	2
T_1 W-3D GRE	3.1/1.5	10	2	256 × 256	995.7	32–38	16.6	1
DWI	1600/70	90	5	112 × 112	79.5	30–38	–	2

BH-MS- T_2 WI, breath-hold multishot T_2 weighted image; DWI, diffusion-weighted imaging; GRE, gradient echo; RT-SS- T_2 WI, respiration-triggered single-shot T_2 weighted image; RT-SS-HT $_2$ WI, respiration-triggered single-shot heavily T_2 weighted image; TE, echo time; TR, repetition time; T_1 WI-2D, T_1 weighted two-dimensional, 3D, three-dimensional.

(b -value, 800 s mm⁻²) and the presence of diffusion restriction were recorded. The SI of the lesion on dynamic, HBP, and DW images was considered high, iso, or low after comparing it to the SI of the surrounding liver parenchyma. Diffusion restriction was defined when a lesion showed high SI on DW images (b -value, 800 s mm⁻²) and iso-to-low SI on the ADC map when compared with the SI of the surrounding liver parenchyma.¹⁵ The detailed definitions of the imaging parameters are summarized in Table 2.

Quantitative analysis

For quantitative analysis, the lesion size, ADC value, lesion-to-liver ADC ratio, SI on the HBP image, and lesion-to-liver SI ratio on the HBP image were measured. The size for all lesions was measured as the longest diameter on axial HBP images. Quantitative analysis was conducted only for lesions equal to or larger than 10 mm in diameter to avoid the partial volume effect, and thus, 19 metastatic mucinous colorectal adenocarcinomas and 11 simple cysts were included. Measurements were conducted three times for each lesion by a third radiologist (JAH, with 7 years of experience in abdominal imaging), and the values were averaged. A largest-possible circular region of interest was drawn on the ADC maps and HBP images for the lesion and the surrounding normal liver parenchyma at the same segment and same level. The mean region of interest size was 109.84 ± 136.48 mm² (range, 12–394 mm²) for metastatic mucinous colorectal adenocarcinomas and 125.1 ± 149.09 mm² (range, 13–502 mm²) for simple hepatic cysts.

Statistical analysis

To compare variables between metastatic mucinous colorectal adenocarcinomas and simple cysts of the liver, categorical variables were analyzed using the χ^2 test or Fisher's exact test. Continuous data were evaluated using a two-sample t -test or Mann–Whitney U test. Data were analyzed using a generalized estimating equation because of the within-subject correlations. In addition, we used receiver operating characteristic curves to determine the appropriate cut-off values for the significant quantitative parameters corresponding to the maximal Youden index. Multivariate logistic regression analyses were conducted with backward selection with significant variables in univariate analysis ($p < 0.2$). The sensitivity, specificity, accuracy,

positive-predictive value (PPV), and negative-predictive value (NPV) of each significant imaging finding and combination of these findings were calculated. The significance level was set at $p < 0.05$. All statistical analysis was executed using SAS v. 9.4 (SAS Institute Inc., Cary, NC) and R 3.3.2 (The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

The results of qualitative analysis are presented in Table 3. Metastatic mucinous colorectal adenocarcinomas more frequently showed septa (74.5%, 35/47 vs 31.6%, 6/19, $p = 0.005$), rim enhancement (83%, 39/47 vs 36.8%, 7/19, $p = 0.001$), and intracystic enhancement (87.2%, 41/47 vs 10.5%, 2/19, $p < 0.001$) than did simple cysts (Figures 1–4). Among 41 metastatic mucinous colorectal adenocarcinomas with intracystic enhancement, 39 lesions (39/41, 95.1%) showed mesh-like enhancement (Figure 1), 1 showed nodular enhancement (1/41, 2.4%) (Figure 3), and 1 showed homogenous enhancement (1/41, 2.4%) (Figure 4). Among simple hepatic cysts, only two lesions showed intracystic mesh-like enhancement.

Quantitative analysis (Table 4) revealed that metastatic mucinous colorectal adenocarcinomas showed significantly lower mean ADC value ($p = 0.001$) and lesion-to-liver ADC ratio ($p = 0.004$), and higher mean SI ($p = 0.039$) and lesion-to-liver SI ratio on HBP images ($p < 0.001$) than did simple hepatic cysts. The optimal cutoff value of significant quantitative variables for differentiating metastatic mucinous adenocarcinomas from simple cysts of the liver were 2.917×10^{-3} mm² s⁻¹ for ADC value, 2.177 for lesion-to-liver ADC ratio, 367.500 for SI on HBP images, and 0.350 for lesion-to-liver SI ratio on HBP images (Figure 5).

On multivariate analysis (Table 5), the presence of rim enhancement ($p = 0.008$) and intracystic enhancement ($p = 0.001$) were significant independent variables for predicting metastatic mucinous colorectal adenocarcinomas.

The sensitivity, specificity, accuracy, PPV, and NPV for identifying metastatic mucinous colorectal adenocarcinomas were 83.0% (39/47), 63.2% (12/19), 77.3% (51/66), 84.8% (39/46), and

Table 2. Definition of MR findings in image analysis

MR finding	Definition
Margin	
Well-defined	Lesions with a discrete boundary all around the lesion on HBP
Ill-defined	Lesions without a well-defined margin
Shape	
Round/oval	Round or ovoid shape with a smooth margin
Lobulated	Round or ovoid shape with a lobulated margin
Irregular	Lesions neither round/oval nor lobulated
Septa	Perceptible septa with enhancement on arterial and/or portal phase
Rim enhancement	Perceptible rim-like enhancement around the lesion on arterial and/or portal phase
Intracystic debris	Focal lesions within the lesion without enhancement
Intracystic enhancement	Any enhancement within the apparent cystic portion of the lesion except for enhancement of the septum
Content	
Homogeneous	Uniform SI within the lesion on T_1 - and T_2 weighted images
Heterogeneous	Non-uniform SI within the lesion
Perilesional bile duct dilatation	Dilatation of intrahepatic bile duct at the peripheral aspect of the lesion
SI on T_2 weighted image	
Very high	Equivalent SI to the CSF
Moderately high	Equivalent SI to or higher SI than the portal vein but lower than the CSF
Slightly high	Lower SI than the portal vein but higher than the surrounding liver parenchyma
SI on T_1 weighted image	
Very low	Lower SI than the portal vein
Low	Equivalent SI to or higher SI than the portal vein but lower than the surrounding liver parenchyma
Iso	Equivalent SI to the surrounding liver parenchyma
High	Higher SI than the surrounding liver parenchyma

CSF, cerebro spinal fluid; HBP, hepato biliary phase; SI, signal intensity.

60.0% (12/20), respectively, for the presence of rim enhancement, and 87.2% (41/47), 89.5% (17/19), 87.9% (58/66), 95.3% (41/43), and 73.9% (17/23), respectively, for the presence of intracystic enhancement. When these two criteria were combined, the sensitivity, specificity, accuracy, PPV, and NPV for identifying metastatic mucinous colorectal adenocarcinomas were 72.3% (34/47), 94.7% (18/19), 78.8% (52/66), 97.1% (34/35), and 58.1% (18/31), respectively.

Table 3. Qualitative analysis

Variable	Metastatic mucinous colorectal adenocarcinoma (n = 47)	Simple cyst (n = 19)	p
Margin			NA
Well-defined	47 (100.0)	19 (100.0)	
Ill-defined	0 (0.0)	0 (0.0)	
Shape			0.351
Round/oval	18 (38.3)	12 (63.2)	
Lobulated	21 (44.7)	5 (26.3)	
Irregular	8 (17.0)	2 (10.5)	
Septa			0.005
Absent	12 (25.5)	13 (68.4)	
Present	35 (74.5)	6 (31.6)	
Rim enhancement			0.001
Absent	8 (17.0)	12 (63.2)	
Present	39 (83.0)	7 (36.8)	
Intracystic debris	0 (0.0)	0 (0.0)	NA
Intracystic enhancement			<0.001
Absent	6 (12.8)	17 (89.5)	
Present	41 (87.2)	2 (10.5)	
Content			0.095
Homogeneous	12 (25.5)	10 (52.6)	
Heterogeneous	35 (74.5)	9 (47.4)	
Perilesional bile duct dilatation	1 (2.1)	0 (0.0)	NA
SI on T_2 weighted image			NA
Very high	16 (34.0)	19 (100.0)	
Moderately high	29 (61.7)	0 (0.0)	
Slightly high	2 (4.3)	0 (0.0)	
SI on T_1 weighted image			NA
Very low	12 (25.5)	17 (89.5)	
Low	35 (74.5)	1 (5.3)	
Iso	0 (0.0)	0 (0.0)	
High	0 (0.0)	1 (5.3)	
SI on arterial phase			
Low	47 (100.0)	19 (100.0)	NA
SI on portal phase			
Low	47 (100.0)	19 (100.0)	NA
SI on 3 min late phase			
Low	47 (100.0)	19 (100.0)	NA

(Continued)

Table 3. (Continued)

Variable	Metastatic mucinous colorectal adenocarcinoma (n = 47)	Simple cyst (n = 19)	p
SI on HBP phase			
Low	47 (100.0)	19 (100.0)	NA
DWI ($b = 800 \text{ s/mm}^2$)			
High	47 (100.0)	9 (47.4)	
Iso	0 (0.0)	5 (26.3)	
Low	0 (0.0)	5 (26.3)	
Diffusion restriction			
Absent	38 (80.9)	19 (100.0)	
Present	9 (19.1)	0 (0.0)	

DWI, diffusion-weighted imaging; HBP, hepato biliary phase; NA, not available; SI, signal intensity.

Data are presented as number (%) of lesions.

DISCUSSION

Several studies have described the imaging features of metastatic mucinous adenocarcinomas of the liver by using various imaging modalities.^{5–7,16,17} Metastatic mucinous adenocarcinomas of

the liver frequently show hypoechoic or anechoic echogenicity on ultrasonography, liquid attenuation on CT, and bright SI on T_2 weighted MR images that is similar to the SI of the cerebrospinal fluid, with rim enhancement, internal septa, or mural nodules after contrast enhancement.^{6,16,17} In contrast, hepatic metastases from colorectal adenocarcinomas other than mucinous adenocarcinomas usually show a moderately high SI on T_2 weighted images.^{5,18} Because metastatic mucinous adenocarcinomas of the liver may show bright SI on T_2 weighted MR images due to abundant mucin production from the tumor,¹⁶ metastatic mucinous adenocarcinomas of the liver may be difficult to differentiate from simple cysts of the liver when the former have no enhancing solid portions or mural nodules. Our study revealed that among the various MRI findings, the presence of rim enhancement (odds ratio, 28.43; $p = 0.008$) and intracystic enhancement (odds ratio, 180.15; $p = 0.001$) were independent significant factors for differentiating metastatic mucinous colorectal adenocarcinomas from simple cysts of the liver. Even though, 59.6% (28/47) of the metastatic mucinous colorectal adenocarcinomas were subcentimeter sized, combining these two criteria resulted in a specificity of 94.7% and PPV of 97.1%.

Sugawara et al⁶ reported that on histopathological examination, metastatic mucinous adenocarcinomas of the liver had internal cystic portions with capsules and internal septa consisting of well-developed fibrous tissue and abundant carcinoma cells. Viable cancerous tissues at the periphery of the tumor were

Figure 1. A 65-year-old male with typical metastatic mucinous colorectal adenocarcinoma of the liver that was confirmed at surgery. He had a history of surgery for mucinous adenocarcinoma of the sigmoid colon. (a) Axial respiratory-triggered single-shot T_2 weighted MRI shows a 5.3 cm lesion (arrow) with a very high SI in the posterior segment of the right liver. It shows a lobulated contour with multiple thin septum-like structures within the lesion. (b, c) On the diffusion-weighted image ($b = 800 \text{ s/mm}^2$) (b) and ADC map (c), the lesion (arrow) shows no diffusion restriction. The ADC value is $2.63 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ for the lesion and $1.24 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ for the surrounding liver parenchyma, and the lesion-to-liver ADC ratio is 2.12. (d) On the unenhanced T_1 weighted MRI, the lesion (arrow) shows a very low SI. (e) On the contrast-enhanced portal-phase MRI, the lesion (arrow) shows rim enhancement and intracystic mesh-like enhancement. (f) On the contrast-enhanced hepatobiliary-phase image, the lesion shows a low SI (arrow), but with progressive and delayed enhancement within the lesion. The SI on the hepatobiliary phase is 409.3 for the lesion and 683.4 for the surrounding liver parenchyma, and the lesion-to-liver SI ratio is 0.60. ADC, apparent diffusion coefficient; SI, signal intensity.

Figure 2. A 58-year-old female with a septated simple cyst of the liver that was confirmed at surgery. (a) Axial respiratory-triggered single-shot T_2 weighted MRI shows a 4.9 cm lesion with a very high SI in the medial segment of the left liver. It shows a lobulated contour with several thin septum-like structures (*arrow*) in the peripheral aspect. (b, c) On the diffusion-weighted image ($b = 800 \text{ s mm}^{-2}$) (b) and ADC map (c) the lesion shows no diffusion restriction. The ADC value is $3.98 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ for the lesion and $1.45 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ for the surrounding liver parenchyma, and the lesion-to-liver ADC ratio is 2.74. (d) On the unenhanced T_1 weighted MRI, the lesion shows a very low SI. (e) On the contrast-enhanced arterial-phase MRI, the lesion shows rim enhancement and no intracystic enhancement. (f) On the contrast-enhanced hepatobiliary-phase image, the lesion shows a low SI, with no intracystic enhancement. The SI on the hepatobiliary phase is 103.4 for the lesion and 476.3 for the surrounding liver parenchyma, and the lesion-to-liver SI on the hepatobiliary phase is 0.22. ADC, apparent diffusion coefficient; SI, signal intensity.

suspected to be the reason for rim enhancement on contrast-enhanced imaging studies.⁶ In contrast, Kanematsu et al⁵ described a case of metastatic mucinous adenocarcinoma of the liver with rim enhancement on contrast-enhanced MR images and suggested that the rim enhancement may be due to perilesional sinusoidal congestion of contrast media. In our study, seven (36.8%) simple hepatic cysts also showed rim enhancement. We speculate that the aforementioned perilesional sinusoidal congestion⁵ enhancement of surrounding compressed liver tissue,¹⁹ or complications such as infection or hemorrhage⁹ may have caused rim enhancement of simple hepatic cysts. Moreover, misrecognition of vascular structures surrounding the simple hepatic cysts as rim enhancement may also occur. Although the mechanism of rim enhancement on metastatic mucinous colorectal adenocarcinomas of the liver remains unclear, our study showed that the presence of rim enhancement was an independently significant MRI feature for differentiating metastatic mucinous colorectal adenocarcinomas from simple cysts of the liver with a sensitivity of 83% and specificity of 63.2%.

The presence of intracystic enhancement was another significant MRI finding for predicting metastatic mucinous colorectal adenocarcinomas of the liver. In our study, metastatic mucinous colorectal adenocarcinomas (87.2%, 41/47) frequently showed intracystic enhancement, particularly a mesh-like enhancement pattern (95.1%, 39/41), on dynamic MR images than did simple hepatic cysts (10.5%, 2/19). Ionilă et al²⁰ reported that on microscopic evaluation of colorectal mucinous adenocarcinomas, clumps of proliferated carcinomatous cells forming glandular lumens of solid or arborizing pattern were found within the mucus lakes. We believe that the high frequency of intracystic

mesh-like enhancement on metastatic mucinous colorectal adenocarcinomas might be explained by the enhancement of intervening stroma and viable cancerous tissue within the mucin lakes of the tumor. In our study, two (10.5%) simple hepatic cysts also showed intracystic enhancement with a mesh-like pattern. We speculate that this might be due to the enhancement of the invisible septum on T_2 weighted MR images or pseudoenhancement caused by motion artifacts, partial volume averaging, or inherent noise in the MR images.

Our study showed that when applying the combination of two significant MRI findings (presence of rim enhancement and intracystic enhancement), the specificity and PPV for predicting metastatic mucinous colorectal adenocarcinomas were 94.7 and 97.1%, respectively. We believe that the interpretation of hepatic cystic lesions based on these two significant imaging findings on contrast-enhanced MRI is important for the accurate discrimination of metastatic mucinous colorectal adenocarcinomas from simple cysts of the liver in patients with mucinous colorectal adenocarcinomas.

In clinical practice, DWI with the ADC map, is widely used to help differentiate benign from malignant hepatic lesions by evaluating tissue cellularity with quantitative information on tissue diffusivity.^{21–23} In our qualitative analysis, 38 (80.9%) of the 47 metastatic mucinous colorectal adenocarcinomas showed no diffusion restriction, which was similar to that of simple hepatic cysts. Therefore, we think that the DWI finding of metastatic mucinous colorectal adenocarcinoma with no enhancing solid portion or mural nodule should be cautiously interpreted because of the similarity of the DWI findings with those of simple

Figure 3. A 52-year-old female with a sub cm-sized metastatic mucinous colorectal adenocarcinoma of the liver that was confirmed at surgery. She had a history of surgery for mucinous adenocarcinoma of the transverse colon. (a) Axial respiratory-triggered single-shot T_2 weighted MRI shows a 0.7 cm round lesion (arrow) with a very high signal intensity in the posterior segment of the right liver. (b, c) On the diffusion-weighted image ($b = 800 \text{ s mm}^{-2}$) (b) and apparent diffusion coefficient map (c), the lesion (arrow) shows no diffusion restriction. (d) On the contrast-enhanced arterial subtraction MRI, the lesion (arrow) shows rim enhancement and nodular intracystic enhancement.

hepatic cysts in patients with extrahepatic mucinous colorectal adenocarcinomas.

Previous studies have reported that the ADC values of hepatic metastases ranged from 0.94 to $2.87 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$,^{5,24} whereas cystic metastases of ovarian carcinoma often have high ADC values equivalent to those of simple hepatic cysts.^{5,15,25} In our quantitative analysis, although some overlap existed between the

ADC values of metastatic mucinous colorectal adenocarcinomas and simple cysts of the liver, metastatic mucinous colorectal adenocarcinomas showed significantly lower ADC values and lesion-to-liver ADC ratios than did simple hepatic cysts.

In our study, all metastatic mucinous colorectal adenocarcinomas (100%, 47/47) and simple hepatic cysts (100%, 19/19) showed low SI on HBP images relative to the surrounding liver parenchyma. However, our quantitative analysis showed that metastatic mucinous colorectal adenocarcinomas had significantly higher mean SI ($p = 0.039$) and lesion-to-liver SI ratio on HBP images ($p < 0.001$) than did simple hepatic cysts. This may be due to the delayed enhancement of the fibrous tissue or retention of contrast material within the extracellular space of metastatic mucinous colorectal adenocarcinomas, as speculated in hepatic metastases from typical colorectal adenocarcinomas²⁶ or breast cancers.²⁷

Although quantitative analysis of our study revealed that the mean ADC value, lesion-to-liver ADC ratio, mean SI and lesion-to-liver SI ratio on HBP images may help differentiate metastatic mucinous colorectal adenocarcinoma from simple hepatic cysts, this may only be of clinical use when the lesion is larger than 10 mm. In subcentimeter-sized lesions, it is hard to rely on the quantitative measurement of the lesion due to limitations such as partial volume artifacts. Thus, it is important to look for previous images or recommend follow up for accurate differentiation between metastatic mucinous adenocarcinoma and simple hepatic cysts, especially if the lesion does not show any rim enhancement or intracystic enhancement.

Our study has some limitations. First, the retrospective nature of this study might have caused a selection bias. Second, the number of simple hepatic cysts ($n = 19$) was lower than that of metastatic mucinous colorectal adenocarcinomas ($n = 47$), which might be attributed to the strict inclusion criteria for simple hepatic cysts in order to minimize the false-negative rates. Third, all of the cases in the metastasis group were from primary mucinous tumors of the colorectum, and none were from the ovary or pancreas. Fourth, the smallest lesions included in our study were of 4 mm, which is smaller than the section

Figure 4. A 53-year-old female with a sub cm-sized metastatic mucinous colorectal adenocarcinoma of the liver that was confirmed at surgery. (a) Axial breath-hold multishot T_2 weighted MRI shows a 0.4 cm round lesion (arrow) with a moderately high signal intensity in the posterior segment of the right liver. (b, c) On unenhanced (b) and contrast-enhanced arterial subtraction MRI (c), the lesion (arrow) shows homogeneous intracystic enhancement.

Table 4. Quantitative analysis

Variable	Metastatic mucinous colorectal adenocarcinoma (n = 47)	Simple cyst (n = 19)	p
Size (cm) ^a	1.35 ± 1.05 (0.4–5.3)	1.81 ± 1.58 (0.4–5.2)	0.570
ADC value (× 10 ⁻³ mm ² s ⁻¹) ^b	1.92 ± 0.81 (0.2–3.1)	2.99 ± 0.75 (1.2–4.06)	0.001
Lesion-to-liver ADC ratio ^b	1.66 ± 0.75 (0.22–2.66)	2.44 ± 0.56 (1.06–3.18)	0.004
SI on HBP image ^b	400.3 ± 216.3 (101–798)	222.4 ± 99.3 (90–354)	0.039
Lesion-to-liver SI ratio on HBP ^b	0.58 ± 0.16 (0.2–0.84)	0.30 ± 0.14 (0.16–0.59)	<0.001

ADC, apparent diffusion coefficient; HBP, hepato biliary phase; SI, signal intensity.

Data are presented as mean ± standard deviation, with ranges in parentheses.

^aAll 47 metastatic mucinous colorectal adenocarcinomas and 19 simple cysts.

^b19 metastatic mucinous colorectal adenocarcinomas and 11 simple cysts equal to or larger than 10 mm.

thickness of the T_2 weighted images of MRI. Thus, there may be some unavoidable limitations in evaluation due to volume averaging, slice selection, or respiratory motion artifacts. Fifth, although hepatic hemangioma also frequently show bright SI on T_2 weighted images, the characteristic enhancement patterns of hepatic hemangioma are quite different from the rim enhancement and intracystic enhancement noted in metastatic mucinous colorectal adenocarcinomas of liver. Thus, hepatic hemangioma was not included in our study. Lastly, our study was performed in a single institute and the number of our cases was relatively small.

Although development of a scoring system using both qualitative and quantitative significant variables would have been clinically useful, our data were limited because only lesions larger than 10 mm were included in the quantitative analysis. Thus, multicenter studies with larger sample sizes and development of a scoring system are warranted for further clinical use.

In conclusion, contrast-enhanced and DW-MRI may be helpful for differentiating metastatic mucinous colorectal adenocarcinomas from simple cysts of the liver. Among various MRI

Figure 5. ROC curve analysis of quantitative variables for differentiating metastatic mucinous adenocarcinomas from simple cysts of the liver. (A) ROC curve of ADC value (cut-off value = $2.917 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$), (B) ROC curve of lesion-to-liver ADC ratio (cut-off value = 2.177), (C) ROC curve of SI on HBP images (cut-off value = 367.500), and (D) ROC curve of lesion-to-liver SI ratio on HBP images (cut-off value = 0.350). Numbers in parentheses are specificity and sensitivity. ADC, apparent diffusion coefficient; HBP, hepatobiliary phase; ROC, receiveroperating characteristic; SI, signal intensity.

Table 5. Univariate and multivariate analyses for predicting metastatic mucinous colorectal adenocarcinomas of the liver

Variable	Univariate		Multivariate	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Shape				
Round/oval				
Lobulated	2.8 (0.51–15.4)	0.351 ^a		
Irregular	2.67 (0.45–15.74)	0.432 ^a		
Septa				
Absent				
Present	6.32 (1.74–22.98)	0.005	2.23 (0.34–14.52)	0.402
Rim enhancement				
Absent				
Present	8.36 (2.32–30.13)	0.001	28.43 (2.37–340.59)	0.008
Intracystic enhancement				
Absent				
Present	58.01 (11.04–305.56)	<0.001	180.15 (7.53–4311.12)	0.001
Content				
Homogeneous				
Heterogeneous	3.24 (0.82–12.88)	0.095	0.05 (0.002–1.09)	0.057

CI, confidence interval; OR, odds ratio.

^a*p* values and 95% CI for OR were corrected using Bonferroni's method because of multiple testing.

findings, rim enhancement and intracystic enhancement were independent MRI findings for predicting metastatic mucinous colorectal adenocarcinomas of the liver.

IRB STATEMENT

This retrospective study was approved by the Institutional Review Board of Samsung Medical Center.

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