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FULL PAPER

The value of contrast-enhanced dynamic and diffusion-weighted MR imaging for distinguishing benign and malignant splenic masses

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Objective: To assess the value of contrast-enhanced dynamic and diffusion-weighted (DW) MR imaging for differentiating malignant from benign splenic lesions.

Methods: This retrospective study included 51 patients with 35 benign and 16 malignant focal splenic lesions. All patients underwent contrast-enhanced dynamic and DW MR imaging. Two radiologists evaluated the MR images in consensus. Significant imaging findings on univariate and multivariate analyses were identified and their diagnostic performance for predicting the malignant splenic lesion was analyzed. Using receiver-operating characteristic analysis, the optimal cut-off of the apparent diffusion coefficient (ADC) value corresponding to the maximal Youden's index (*J*) for differentiating the two groups was determined.

Results: In univariate analysis, low signal intensity (SI) on the arterial, portal and 3-min delayed-phase images, high or iso SI on the DW image, iso or low SI on the ADC map, the presence of diffusion restriction and arterial hypovascularity with a progressive enhancement pattern were more frequently observed ($p < 0.05$) in malignant splenic lesions. The ADC value was significantly lower

for malignancy than for benignancy (0.78 ± 0.24 vs $1.16 \pm 0.53 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$; $p < 0.001$). The optimal cut-off ADC value for differentiating the two groups was $0.995 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$. In multivariate analysis, findings that differentiated malignant from benign splenic lesions were low SI on the 3-min delayed-phase image [odds ratio (OR), 27.68; $p = 0.006$] and the presence of diffusion restriction (OR, 48.01; $p = 0.002$). When two of these criteria were combined, 12 (75.0%) of 16 malignant splenic masses were identified with a specificity of 100%.

Conclusion: Contrast-enhanced dynamic and DW MR imaging may be helpful for differentiating malignant from benign splenic lesions. A low SI on the 3-min delayed phase and diffusion restriction are the most reliable findings for the differentiation of malignant from benign splenic lesions.

Advances in knowledge: Dynamic and DW MR imaging help in distinguishing malignant from benign splenic lesions. A low SI on the 3-min delayed phase and diffusion restriction are the most reliable findings for the differentiation of malignant from benign splenic lesions.

INTRODUCTION

Various solid splenic masses are often discovered incidentally in routine clinical practice on imaging studies performed for other causes. However, the differential diagnosis of a solid splenic mass still remains a diagnostic challenging to the radiologist. Although most of the focal splenic lesions detected incidentally are benign, a variety of primary and secondary malignant diseases can affect the spleen.^{1,2} As the differential diagnosis of the focal splenic lesion is not clear with imaging features, splenic biopsy is usually considered

for the next step, especially in patients with extrasplenic malignancies. However, it has a high risk of bleeding or pneumothorax and has a technical difficulty in cases of poor sonic window.³ When splenic biopsy is not feasible, the only alternative method left for tissue confirmation is splenectomy or laparoscopic splenic biopsy. However, as the spleen plays a crucial role in the body's immune system, these surgical procedures must be performed carefully. For these reasons, an accurate discrimination of benign and malignant splenic lesions

is important to avoid unnecessary splenectomy for the benign splenic lesion.

There have been few attempts to differentiate benign and malignant splenic lesions using several imaging modalities^{4–9} and most of these studies were conducted using an ultrasonography or positron emission tomography–CT scan.^{5–7,9} Since MRI has the best ability to demonstrate tissue characteristics among the various imaging tools, it is usually performed after ultrasonography or CT as a problem-solving tool.^{10,11} In addition, with advances in MR technology, diffusion-weighted (DW) imaging is widely used to evaluate tissue cellularity and the apparent diffusion coefficient (ADC) map generated in post-processing by calculating ADC values can provide quantitative information on tissue diffusivity. Decreased movement of water molecules in a highly cellular tissue correlates with a low ADC value. Many studies for the differentiation of malignant and benign lesions in organs other than the spleen using MRI have been published. However, to the best of our knowledge, no study has been established for what are the significant MRI features and what is the optimal cut-off ADC value for differentiating malignant from benign splenic lesions.

The purpose of this study was to assess the value of contrast-enhanced dynamic and DW MR imaging for differentiating malignant from benign splenic lesions.

METHODS AND MATERIALS

Patient population

The institutional review board approved the study and waived the requirement for informed consent because of the retrospective nature of clinical and imaging data collection. We reviewed radiologic reports for the MR examination acquired between June 2010 and June 2015 using the search terms “spleen” or “splenic”, and we found 975 patients. Of these 975 patients, 851 patients had no focal splenic lesion and an

additional 73 patients were excluded for the following reasons: typical MRI findings of the cystic lesion ($n = 61$), disseminated malignancy such as metastases in the extrasplenic upper abdominal organs and/or peritoneal seeding ($n = 8$) for minimizing bias while making a decision in the blinded review and a poor image quality for interpretation ($n = 4$). A typical cystic lesion was defined as bright signal intensity (SI) equal to cerebrospinal fluid on a T_2 weighted image without an enhancing solid component. Finally, 51 patients with focal splenic lesions were enrolled in the study, in which 35 patients (19 males and 16 females, mean age 51.8 years; age range, 41–77 years) were the benign group and 16 patients (4 males and 12 females, mean age 48.7 years; age range, 22–73 years) were the malignant group. Among the 35 benign lesions, 15 lesions were pathologically proven by surgery [$n = 12$; 5 sclerosing angiomatoid nodular transformations (SANTs), 3 inflammatory pseudotumours, 3 haemangiomas, 1 hamartoma, 1 haematoma, 1 sarcoidosis and 1 vascular malformation] or biopsy ($n = 3$; 2 inflammatory pseudotumours and 1 hamartoma) and the remaining 20 lesions were clinically diagnosed as benign when the lesions disappeared, decreased or remained constant in size and morphology without treatment during the follow-up of over 2 years in patients with no extrasplenic malignancy. Among 16 malignant lesions, 14 lesions were pathologically proven by surgery [$n = 13$; 9 metastases (6 from colorectal cancer, 2 from ovarian cancer and 1 from hepatocellular carcinoma), 2 lymphomas, 1 angiosarcoma and 1 histiocytic sarcoma] or biopsy ($n = 1$; metastasis from pancreatic cancer) and the remaining 2 malignant lesions were clinically diagnosed in patients with advanced colon cancer and thymic lymphoma based on the development of the new focal splenic lesion that increased in size at follow-up CT and MRI and decreased in size after chemotherapy. Of the 51 patients with focal splenic lesions, 39 patients had a single lesion and 12 patients had multiple lesions (>2 lesions). We included some cases that were enrolled in a previous study⁴ because this study was retrospectively designed.

Table 1. MRI sequences and parameters

Sequence	TR/TE (ms ⁻¹)	Flip angle (degree)	Section thickness (mm)	Matrix size	Bandwidth (Hz/pixel)	Field of view (cm)	Acquisition time (s)	Number of excitations
T1W-2D dual GRE	3.5/ 1.15–2.3	10	6	256 × 194	434.4	32–38	14	1
BH-MS-T2WI	1623/70	90	5–7	324 × 235	235.2	32–38	55	1
RT-SS-T2WI	1342/80	90	5–7	320 × 256	506.4	32–38	–	2
RT-SS-HT2WI	1156/160	90	5–7	320 × 256	317.9	32–38	–	2
T1-3D GRE	3.1/1.5	10	2	256 × 256	995.7	32–38	16.6	1
DWI (b -value = 0, 800 s m ⁻²)	1600/70	90	5	112 × 112	79.5	30–38	–	2

BH-MS-T2WI, breath-hold multishot T_2 weighted image; DWI, diffusion-weighted image; RT-SS-HT2WI, respiration-triggered single-shot heavily T_2 weighted image; RT-SS-T2WI, respiration-triggered single-shot T_2 weighted image; T1W-2D dual GRE, T_1 weighted two-dimensional dual gradient echo; T1-3D GRE, T_1 weighted three-dimensional gradient echo; TE, repetition time; TR, echo time.

“–” indicates variable value depending on patient breathing and number of respiratory interval in respiratory-triggered techniques.

Table 2. Qualitative analysis

Variables		Benignancy	Malignancy	<i>p</i> -value
		<i>n</i> = 35	<i>n</i> = 16	
Sex	Male	19 (54.3)	4 (25.0)	0.071
	Female	16 (45.7)	12 (75.0)	
Multiplicity	Single	27 (77.1)	12 (75.0)	0.867
	Multiple	8 (22.9)	4 (25.0)	
Shape	Round to oval	21 (60)	6 (37.5)	0.221
	Lobulated	10 (28.6)	6 (37.5)	
	Irregular	4 (11.4)	4 (25.0)	
Margin	Well defined	18 (51.4)	4 (25.0)	0.127
	Ill defined	17 (48.6)	12 (75.0)	
SI on T_2 weighted image	High	17 (48.6)	8 (50.0)	0.544
	Iso	6 (17.1)	1 (6.3)	
	Low	12 (34.3)	7 (43.8)	
SI on T_1 weighted image	High	1 (2.9)	1 (6.3)	0.675
	Iso	21 (60.0)	8 (50.0)	
	Low	13 (37.1)	7 (43.8)	
SI on arterial phase	High	12 (34.3)		0.006
	Iso	2 (5.7)		
	Low	21 (60.0)	16 (100)	
SI on portal phase	High			0.002
	Iso	14 (40.0)		
	Low	21 (60.0)	16 (100)	
SI on 3-min delayed phase	High	22 (62.9)		<0.001
	Iso	8 (22.9)	2 (20.0)	
	Low	5 (14.3)	14 (80.0)	
SI on DW image ($b = 800 \text{ s mm}^{-2}$)	High	6 (17.1)	9 (56.3)	0.014
	Iso	10 (28.6)	4 (25.0)	
	Low	19 (54.3)	3 (18.8)	
SI on ADC map	High	24 (68.6)	1 (6.3)	<0.001
	Iso	7 (20.0)	5 (31.3)	
	Low	4 (11.4)	10 (62.5)	
Diffusion restriction	Presence	2 (5.7)	13 (81.3)	<0.001
	Absence	33 (94.3)	3 (18.8)	
Homogeneity	Heterogeneous	16 (45.7)	4 (25.0)	0.221
	Homogeneous	19 (54.3)	12 (75.0)	
Enhancement pattern	No enhancement			0.002
	Hypervascularity with persistent enhancement	14 (40.0)		
	Hypervascularity with washout			
	Hypovascularity with progressive enhancement	21 (60.0)	16 (100)	

(Continued)

Table 2. (Continued)

Variables		Benignancy	Malignancy	<i>p</i> -value
		<i>n</i> = 35	<i>n</i> = 16	
Perisplenic fluid collection	Presence			NA
	Absence	35 (100)	16 (100)	
Cystic/necrotic portion	Presence	4 (11.4)	4 (25.0)	0.24
	Absence	31 (88.6)	12 (75.0)	
Haemorrhage	Presence	5 (14.3)	1 (6.3)	0.651
	Absence	30 (85.7)	15 (93.8)	
Splenomegaly	Presence			NA
	Absence	35 (100)	16 (100)	
Lymphadenopathy	Presence		1 (6.3)	0.314
	Absence	35 (100)	15 (93.8)	

ADC, apparent diffusion coefficient; DW, diffusion-weighted; NA, not available; SI, signal intensity. Data in parentheses are percentage values.

MRI examination

In all patients, MR images were acquired using a 3.0-T whole-body MR system (Intera Achieva 3.0T; Philips Healthcare, Best, Netherlands) with a 16-channel phased-array coil as the receiver coil. Baseline MRI included a T_1 weighted turbo field-echo in-phase and opposed-phase sequence, a breath-hold multishot T_2 weighted sequence and a respiratory-triggered single-shot T_2 weighted and heavily T_2 weighted sequence. All T_2 weighted imaging were performed with fat saturation (Table 1). Dynamic images were obtained using a T_1 weighted three-dimensional turbo field-echo sequence [T_1 weighted high-spatial-resolution isotropic volume examination]. Unenhanced and contrast-enhanced arterial phase images (20–35 s), portal phase images (60 s), delayed-phase (3 min) and hepatobiliary phase images (20 min) were acquired before and after the i.v. bolus administration of gadoxetic acid (Primovist®; Bayer Schering Pharma AG, Berlin, Germany). The timing for arterial phase imaging was determined using the MR fluoroscopic bolus detection technique. The contrast agent was administered intravenously using a power injector (Mark V; Medrad, Indianola, PA) at a dose of $0.025 \text{ mmol kg}^{-1}$ (0.1 ml kg^{-1} body weight) at the rate of 2 ml s^{-1} and was immediately followed by a 20-ml saline flush. DW imaging was performed using single-shot echoplanar imaging with respiratory triggering before the contrast media injection. b -values of 0, 100 and 800 s mm^{-2} were used. The acquisition time ranged from 3 to 4 min depending on the respiratory rhythm of each patient. The ADC was calculated using a monoexponential function with b -values of 0 and 800 s mm^{-2} .

Imaging analysis

2 abdominal radiologists with 7 and 16 years' experience in abdominal MRI interpretation reviewed all MR images in consensus on a picture archiving and communication system (Centricity Radiology RA 1000; GE Healthcare, Chicago, IL). When both observers were divided into different opinions, another observer with 14 years' experience in abdominal MRI interpretation additionally reviewed the relevant case and the

final decision was made by the majority rule. All observers were blinded to the clinical or histopathologic results of each case. When multiple lesions were observed in a single patient, image review focused on the largest dominant lesion.

For qualitative analysis, the following imaging parameters were evaluated: (a) multiplicity (single or multiple; two or more lesions), (b) shape (round to oval, lobulated or irregular), (c) margin (well defined or ill defined), (d) homogeneous (diffuse uniform enhancement with no definite hypointense area) or heterogeneous enhancement, (e) enhancement pattern (no enhancement, arterial hypervascularity with persistent enhancement, arterial hypervascularity with washout or arterial hypovascularity with progressive enhancement), (f) the presence of internal cystic or necrotic portion, (g) the presence of haemorrhage, (h) the presence of perisplenic fluid collection, (i) the presence of splenomegaly (longest diameter $>12 \text{ cm}$) and (j) lymph node enlargement (shortest diameter $>1 \text{ cm}$). Arterial hypervascularity was defined as iso or higher SI compared with normal splenic parenchyma because the spleen is known to be a highly vascular organ owing to its abundant vascular structures of red pulp¹² and shows heterogeneously well enhancement during arterial phase imaging.^{1,13} Washout was defined as low SI on portal or 3-min delayed-phase imaging among hypervascular lesions. The SI of the lesion on unenhanced, contrast-enhanced and DW MR images (b -value of 800 s mm^{-2}) with ADC map were recorded with categorization into three groups of high, iso or low SI compared with unaffected splenic parenchyma. Normal splenic parenchyma has been reported to have the greatest degree of restricted diffusion^{4,14,15} and shows the lowest ADC value ($1.26 \pm 0.23 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) among all solid abdominal organs. Based on above findings, we defined the presence of diffusion restriction as iso or high SI on the DW image ($b = 800 \text{ s mm}^{-2}$) with iso or low SI on the ADC map compared with unaffected splenic parenchyma.

For quantitative analysis, the age, size and ADC value of the lesions were compared between the two groups. For ADC

measurement, the reviewers manually drew a region of interest (ROI) on the ADC maps at the corresponding area of the enhancing solid portion of the focal splenic lesion at its largest diameter. Contrast dynamic enhanced images and ADC maps were set side by side and were evaluated using a spatial cursor key on our picture archiving and communication system that assisted in matching the matching corresponding sites on different images using multiplanar localization. The drawn ROI avoided necrotic or cystic areas and the edge of the focal splenic lesions for minimizing the partial volume-averaging effect. The

ADC value was measured three times, and the average value was calculated. The mean ROI size was 80.1 mm^2 (range, $40\text{--}121 \text{ mm}^2$).

Statistical analysis

χ^2 test or Fisher's exact test was used to compare the frequencies of categorical variables for differentiating benign and malignant splenic lesions. The Student's *t*-test or Mann–Whitney test was performed for continuous variables. To determine the predictors of the malignant splenic lesion, multivariable logistic regression

Figure 1. A malignant splenic mass in a 65-year-old female: (a) on the fat-saturated T_2 weighted image, a 6.4-cm mass (arrows) shows a slightly high signal intensity (SI) relative to the splenic parenchyma (arrowheads) and heterogeneity owing to tumour necrosis. On unenhanced (b) and contrast-enhanced dynamic arterial (c), portal (d) and 3-min delayed (e) phase images, the peripheral solid portion of the mass (arrows) with progressive enhancement shows arterial hypovascularity relative to the splenic parenchyma (arrowheads) and the central portion (asterisks) of the tumour shows necrosis. The peripheral solid portion of the mass (arrows) shows a low SI on the 3-min delayed phase (e) compared with the splenic parenchyma (arrowheads). (f, g) The peripheral solid portion of the mass (arrows) shows diffusion restriction with high SI on the diffusion-weighted MR image ($b = 800 \text{ s mm}^{-2}$) (f) and low SI on the apparent diffusion coefficient (ADC) map (g) compared with the splenic parenchyma (arrowheads). The ADC value of the peripheral solid portion of the mass (arrows) is $0.790 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$. The mass was confirmed to be a diffuse large B-cell lymphoma on biopsy.

analyses were conducted with backward selection using significant variables on univariate analysis. Using receiver-operating characteristic (ROC) analysis, the appropriate cut-off value of ADC was determined according to the Youden's index (J), which is a commonly used function of sensitivity and specificity to measure overall diagnostic effectiveness. The sensitivity, specificity, accuracy, positive-predictive value (PPV) and negative-predictive value of each significant imaging finding and combination of findings were calculated. All statistical analyses were performed using SPSS® v. 17 for Windows (SPSS Inc., Chicago, IL). The significance level was set at $p < 0.05$.

RESULTS

The results of qualitative analysis are shown in Table 2. On dynamic images, malignant splenic lesions more frequently displayed a low SI on the arterial ($p = 0.006$), portal ($p = 0.002$) and 3-min delayed ($p < 0.001$) phases compared with benign lesions. Furthermore, malignant splenic lesions more commonly showed high or iso SI on the DW image ($p = 0.014$), iso or low SI on the ADC map ($p < 0.001$) and the presence of diffusion restriction ($p < 0.001$). In terms of enhancement pattern, all malignant splenic lesions showed arterial hypovascularity with progressive enhancement ($p = 0.004$) (Figures 1–3).

Figure 2. A benign splenic mass in a 46-year-old male with renal cell carcinoma: (a) on the fat-saturated T_2 weighted image, a 4.4-cm mass (arrows) shows homogeneously high signal intensity (SI) relative to the splenic parenchyma (arrowheads). On the unenhanced (b) and contrast-enhanced dynamic arterial (c), portal (d) and 3-min delayed (e) phase images, the mass (arrows) shows arterial hypovascularity with progressive enhancement. On the 3-min delayed phase (e), the mass (arrows) shows a slightly high SI compared with the splenic parenchyma (arrowheads). (f, g) The mass (arrows) shows no diffusion restriction, with iso SI on the diffusion-weighted MR image ($b = 800 \text{ s mm}^{-2}$) (f) and a slightly high SI on the apparent diffusion coefficient (ADC) map (g) compared with the splenic parenchyma (arrowheads). The ADC value of the mass (arrows) is $0.810 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$. The mass was confirmed to be a cavernous haemangioma after splenectomy.

Figure 3. A malignant splenic mass with false-negative finding in a 53-year-old male: (a, b) a 11.5-cm mass (arrows) shows arterial hypovascularity with progressive enhancement on arterial (a) and 3-min delayed (b) phases. On the 3-min delayed phase (b), the mass (arrows) shows iso signal intensity (SI) compared with splenic parenchyma (arrowheads). (c, d) The mass (arrows) shows no diffusion restriction, with low SI on both the diffusion-weighted MR image ($b = 800 \text{ s mm}^{-2}$) (c) and the apparent diffusion coefficient (ADC) map (d) compared with the splenic parenchyma (arrowheads). The ADC value of the mass (arrows) is $0.708 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$. The mass was confirmed to be a histiocytic sarcoma on biopsy.

On quantitative analysis (Table 3), the mean lesion size was not significantly different between benign and malignant splenic lesions [$3.69 \pm 2.05 \text{ cm}$ (range, 1.10–7.90 cm) vs $3.91 \pm 2.46 \text{ cm}$ (range, 1.30–11.50 cm), respectively; $p = 0.761$]. Patients in the benign group were significantly younger than those in the malignant group [48.74 ± 12.16 years (range, 22–73 years) vs 58.81 ± 12.3 years (range, 41–77 years); $p = 0.009$]. The mean ADC value of the malignant group [$0.78 \pm 0.24 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ (range, 0.35 – $1.12 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)] was significantly lower than that of the benign group [$1.16 \pm 0.53 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ (range, 0.52 – $2.61 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$); $p < 0.001$]. Based on ROC curve data, the optimal cut-off ADC value for differentiating malignancy from benignancy was $0.995 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, and the area under the ROC curve was 0.758 [95% confidence interval (CI), 0.626–0.890] (Figures 4 and 5). Applying this cut-off value gave the best sensitivity and specificity for diagnosing malignant splenic masses (81.3% and 65.7%, respectively).

In multivariate analysis (Table 4), low SI on 3-min delayed phase ($p = 0.006$) and the presence of diffusion restriction ($p = 0.002$) were significant independent variables for differentiating benign and malignant splenic lesions (Figures 1 and 2). All five benign lesions that showed a low SI on the 3-min delayed phase (one haemangioma, one inflammatory pseudotumour, two SANTs and one clinically benign lesion) demonstrated no diffusion restriction. Of the two malignant lesions with iso SI on the 3-min delayed phase (one lymphoma and one histiocytic sarcoma), one lymphoma showed diffusion restriction and one histiocytic sarcoma showed no diffusion restriction (Figure 3). Both benign splenic lesions with diffusion restriction (one hamartoma and one vascular malformation) showed an iso SI on the 3-min delayed phase. The other two malignant lesions with no diffusion restriction (one angiosarcoma and one metastasis from hepatocellular carcinoma) showed a low SI on the 3-min delayed phase. The sensitivity, specificity, accuracy, PPV

Table 3. Quantitative analysis

Variables	Benignancy	Malignancy	<i>p</i> -value
	<i>n</i> = 35	<i>n</i> = 16	
Age (years), mean (SD)	48.74 (12.16)	58.81 (12.3)	0.009
Size (cm), mean (SD)	3.69 (2.05)	3.91 (2.46)	0.761
Tumour ADC ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$), mean (SD)	1.16 (0.53)	0.78 (0.24)	<0.001

ADC, apparent diffusion coefficient; SD, standard deviation.

Figure 4. A box plot showing the apparent diffusion coefficient (ADC) value of benign and malignant splenic masses. The optimal cut-off value was $0.995 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ for differentiating the two groups.

and negative-predictive value for these two significant imaging features and their combination are demonstrated in Table 5. When these 2 criteria were combined, 75.0% (12/16) of malignant splenic lesions were identified with a specificity of 100% (35/35).

DISCUSSION

Our study demonstrated that among the various MRI findings, low SI on the 3-min delayed phase (odds ratio, 27.68; $p = 0.006$)

Figure 5. The receiver-operating characteristic curve evaluating the optimal apparent diffusion coefficient cut-off value for distinguishing malignant from benign splenic lesions. When the cut-off value was $0.995 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, the sensitivity and specificity were the best, 66.7% and 81.0%, respectively. The area under the curve (AUC) was 0.758. CI, confidence interval.

and the presence of diffusion restriction (odds ratio, 48.01; $p = 0.002$) were significant independent variables for differentiating malignant from benign splenic masses, and combining these two criteria resulted in a specificity of 100%, which could be considered reliable for decreasing unnecessary invasive procedures or surgery for the treatment of splenic lesions.

There are several articles that summarize the imaging features of focal splenic lesions with CT and MR,^{1,2,4,10,11} and many sporadic reports of variable focal splenic lesions^{16–20} mainly focus on the description of imaging features of each disease and not on the differentiation of benign and malignant splenic lesions. To the best of our knowledge, there have been attempts to discriminate benign and malignant splenic masses using contrast-enhanced ultrasound (CEUS)^{6,7,9} and DW MR imaging.⁴ However, it has not been established that which phase on dynamic MRI can help in the differentiation of benign and malignant splenic lesions and whether dynamic MRI findings are comparable with CEUS.

Stang et al⁷ reported that an isoenhancing lesion compared with normal splenic parenchyma at the parenchymal phase obtained at 150–300 s after contrast injection on CEUS was suggestive of splenic benignancy with a PPV of 100% and that a progressively hypoenhancing lesion (increasing lesion-to-parenchyma contrast while moving to the parenchymal phase, but lower echogenicity than splenic parenchyma) was suggestive of splenic malignancy with a PPV of 87%. Similar to this study, other CEUS studies reported that hypoenhancement in the parenchymal phase (60–300 s after contrast injection) is a characteristic finding of malignant splenic lesions irrespective of arterial enhancement.^{6,9} In addition, Jang et al⁴ reported that SI on the 3-min delayed phase on dynamic MRI was significantly different between benign and malignant splenic masses on univariate analysis. However, in this report, only the value of the DW image was evaluated for differentiating malignant from benign splenic lesions, and the role of the 3-min delayed phase on contrast-enhanced dynamic MRI was not assessed. Our study showed that a low SI on the 3-min delayed phase was an independently significant dynamic feature suggesting malignancy than benignancy, with a sensitivity of 87.5% and a specificity of 85.7%, which are comparable with the results of previous reports using CEUS and contrast-enhanced dynamic MRI.^{4,6,7,9} The reasons for different SIs on the 3-min delayed phase between the two groups are not clear, but a previous report that dealt with dynamic contrast enhancement of haemangiomas or hamartomas, the most common benign solid splenic vascular tumours with typically uniform delayed enhancement,²⁰ could support our results. However, in our study, some benign (5/35, 14.3%) lesions and malignant (2/16, 12.5%) lesions showed overlapping findings on the 3-min delayed phase, and thus the clinical application of dynamic characteristic on the 3-min delayed phase for determining benign or malignant splenic lesions should be taken carefully.

Stang et al⁶ reported that arterial hyperenhancement or iso-enhancement was an independent CEUS predictor of benign splenic neoplasms compared with malignant splenic lesions. Corresponding to this previous study, our results showed that

Table 4. Multivariate analysis for predicting malignant splenic lesion

Variables		Univariate			Multivariate		
		OR	95% CI	p-value	OR	95% CI	p-value
SI on 3-min delayed phase (ref: non-low)	Low	42.00	(7.24, 243.7)	<0.001	27.684	(2.560, 299.313)	0.006
SI on DW image (ref: low)	Iso	2.53	(0.47, 15.11)	0.279			
	High	9.50	(2.11, 54.91)	0.006			
	Non-low	11.33	(1.88, 68.44)	0.008			
SI on ADC map (ref: high)	Iso	17.14	(2.29, 359.02)	0.016			
	Low	60.00	(8.4, 1274.8)	0.001			
	Non-high	57.78	(5.56, 599.98)	0.001			
Diffusion restriction (ref: absence)	Presence	71.50	(13.02, 647.49)	<0.001	48.013	(4.250, 542.372)	0.002
Tumour ADC ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) (ref: >0.995)	≤ 0.995	8.306	(1.975, 34.928)	0.004			

ADC, apparent diffusion coefficient; CI, confidence interval; DW, diffusion-weighted; OR, odds ratio; ref, reference; SI, signal intensity.

arterial hypervascularity was observed only in benign splenic (14/35, 40%) lesions. However, there have been reported cases of malignant lesions with arterial hyperenhancement or iso-enhancement on CEUS^{6,9} and MRI.¹⁸

In our study, 21 (60%) of 35 benign splenic lesions showed arterial hypovascularity, which was a major overlapping finding with malignant splenic lesions because they all showed arterial hypovascularity. Several reasons for the arterial hypovascularity of benign lesions can be considered; most of the enrolled inflammatory pseudotumours or SANTS showed arterial hypovascularity corresponding to previous reports^{16,17,21,22} and a substantial number of cases of splenic haemangiomas showed atypical radiologic features with poor contrast enhancement on the arterial phase as in our case (Figure 2), whereas typical hepatic haemangiomas showed peripheral globular enhancement.^{23–25} Taibbi et al²⁴ reported that 8 (29.6%) of 27 haemangiomas showed some degree of contrast enhancement but remained substantially hypoechoic throughout CEUS. In addition, transient patterns of heterogeneous well enhancement during the arterial phase in the spleen could also lead us to interpret the focal splenic lesion as a lower SI than the actual SI.^{1,13} Although some hypervascular malignant splenic lesions have been reported,¹⁸ we think that arterial hypervascularity could play a supportive role in the differentiation of malignant from benign splenic lesions if arterial hypervascularity is

interpreted in combination with findings on the 3-min delayed phase because no hypervascular benign lesions showed a washout pattern.

Jang et al⁴ reported that malignant splenic masses had a lower ADC value ($0.73 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) compared with benign splenic masses ($1.21 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ and 1.43 , respectively). Similar to this previous study, our results showed that SI on the DW image and ADC map, diffusion restriction and the mean ADC value were significantly different between the two groups in univariate analysis. However, among them, the presence or absence of diffusion restriction was the only independently significant imaging feature on multivariate analysis. Furthermore, our results showed that the optimal cut-off of the ADC value for distinguishing the two groups was set at $0.995 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ maximizing the sensitivity and specificity to 81.3% and 65.7%, respectively. To the best of our knowledge, this study is the first attempt to set an optimal cut point of ADC value for distinguishing benign and malignant splenic masses. We are not sure why the ADC value is different between the two groups, but we presume that compared with benign splenic lesions, increased tissue cellularity owing to tumour cell infiltration in malignant splenic lesions would play an important role in diffusion restriction with a low ADC value. However, in our study, there were two benign splenic lesions with diffusion restriction and three malignant splenic lesions without diffusion restriction.

Table 5. Diagnostic performance of magnetic resonance imaging findings for predicting malignant splenic lesion

Magnetic resonance finding	SEN	SPE	ACC	PPV	NPV
Low SI on 3-min delayed phase	14/16 (87.5)	30/35 (85.7)	44/51 (86.3)	14/19 (73.7)	30/32 (93.8)
Presence of diffusion restriction	13/16 (81.3)	33/35 (94.3)	46/51 (90.2)	13/15 (86.7)	33/36 (91.7)
Combination of two findings	12/16 (75.0)	35/35 (100)	47/51 (92.2)	12/12 (100)	35/39 (89.7)

ACC, accuracy; NPV, negative-predictive value; PPV, positive-predictive value; SEN, sensitivity; SI, signal intensity; SPE, specificity. Data are presented as the number over the total with the percentage in parentheses.

In this regard, although diffusion restriction is an important imaging finding for predicting malignant splenic lesions, we should keep in mind that the use of diffusion restriction may lead to a false-positive or false-negative finding in the differentiation of benign and malignant focal splenic lesions.

Applying the combination of two significant imaging features (low SI on the 3-min delayed phase and the presence of diffusion restriction), there was 100% specificity and 100% PPV for predicting malignant splenic lesions with no false-positive lesion. There was only one malignant splenic lesion with a false-negative finding, which showed neither a low SI on the 3-min delayed phase nor diffusion restriction. We believe that comprehensive MRI interpretation with both SI on the 3-min delayed phase and diffusion restriction may be helpful for making a correct differentiation between benign and malignant splenic lesions.

Our study had several limitations. First, as the study was retrospectively designed, there was an inevitable selection bias. Second, the number of patients with malignant splenic masses was small compared with that of benign splenic masses. Third, not all splenic lesions were confirmed histopathologically. However, we tried to include clinically benign and malignant lesions based on the aforementioned criteria to minimize false-negative or false-positive cases. Fourth, we used gadoxetic acid, known for being a liver-specific agent, as the contrast agent, which might have resulted in the suboptimal contrast enhancement on dynamic phases. However, in previous studies,^{26–28} there was no significant difference in the dynamic enhancement pattern of the spleen between gadoxetic acid and gadobutrol. Also, with the greater enhancement effect of gadoxetic acid on 3.0-T MRI compared with 1.5-T MRI, the higher protein-binding property of gadoxetic

acid resulted in increased relaxivity, which compensated for the low gadolinium concentration.^{29,30} Therefore, the lower gadolinium dosage may not have lessened the characteristic dynamic enhancement pattern on the spleen and focal splenic lesions in our study. Fifth, the CI range of the variables is wide in Table 4. We think that it would be derived from the small sample size. However, to the best of our knowledge, this study has a relatively larger sample size than previous other studies dealing with the imaging findings of the solid splenic mass, because of its scarcity. Furthermore, we think that the multivariable analysis on our study is meaningful because the tendency and the significance of the variables were evident, in spite of the wide CI range of the variables. Last, our study enrolled 15 overlapping splenic lesions (8 benign and 7 malignant lesions) which were included in a previous study by Jang et al⁴ for comparing the imaging findings of benign and malignant splenic lesions. However, we believe that the similarity between the 2 studies is limited because the overlapped subjects were only 15 of the total 51 lesions in our study. In addition, the importance of 3-min delayed phase on dynamic MRI was newly emphasized in this study, in this respect, we think that the purpose of our study was quite different from the previous study by Jang et al.

In conclusion, dynamic contrast-enhanced and DW MR imaging may be helpful for differentiating malignant and benign splenic lesions. A low SI on the 3-min delayed phase, the presence of diffusion restriction and the combination of these two factors could raise the diagnostic performance for the discrimination of splenic masses.

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REFERENCES

1. Palas J, Matos AP, Ramalho M. The spleen revisited: an overview on magnetic resonance imaging. *Radiol Res Pract* 2013; **2013**: 219–97. doi: <http://dx.doi.org/10.1155/2013/219297>
2. Vancauwenberghe T, Snoeckx A, Vanbeckevoort D, Dymarkowski S, Vanhoenacker FM. Imaging of the spleen: what the clinician needs to know. *Singapore Med J* 2015; **56**: 133–44. doi: <http://dx.doi.org/10.11622/smedj.2015040>
3. Tam A, Krishnamurthy S, Pillsbury EP, Ensor JE, Gupta S, Murthy R, et al. Percutaneous image-guided splenic biopsy in the oncology patient: an audit of 156 consecutive cases. *J Vasc Interv Radiol* 2008; **19**: 80–7. doi: <http://dx.doi.org/10.1016/j.jvir.2007.08.025>
4. Jang KM, Kim SH, Hwang J, Lee SJ, Kang TW, Lee MW, et al. Differentiation of malignant from benign focal splenic lesions: added value of diffusion-weighted MRI. *AJR Am J Roentgenol* 2014; **203**: 803–12. doi: <http://dx.doi.org/10.2214/AJR.13.11914>
5. Wan YL, Cheung YC, Lui KW, Tseng JH, Lee TY. Ultrasonographic findings and differentiation of benign and malignant focal splenic lesions. *Postgrad Med J* 2000; **76**: 488–93. doi: <http://dx.doi.org/10.1136/pmj.76.898.488>
6. Stang A, Keles H, Hentschke S, von Seydewitz CU, Dahlke J, Habermann C, et al. Incidentally detected splenic lesions in ultrasound: does contrast-enhanced ultrasonography improve the differentiation of benign hemangioma/hamartoma from malignant lesions? *Ultraschall Med* 2011; **32**: 582–92. doi: <http://dx.doi.org/10.1055/s-0031-1282034>
7. Stang A, Keles H, Hentschke S, von Seydewitz CU, Dahlke J, Malzfeldt E, et al. Differentiation of benign from malignant focal splenic lesions using sulfur hexafluoride-filled microbubble contrast-enhanced pulse-inversion sonography. *AJR Am J Roentgenol* 2009; **193**: 709–21. doi: <http://dx.doi.org/10.2214/AJR.07.3988>
8. Metser U, Even-Sapir E. The role of 18F-FDG PET/CT in the evaluation of solid splenic masses. *Semin Ultrasound CT* 2006; **27**: 420–5. doi: <http://dx.doi.org/10.1053/j.sult.2006.06.005>
9. von Herbay A, Barreiros AP, Ignee A, Westendorff J, Gregor M, Galle PR, et al. Contrast-enhanced ultrasonography with SonoVue: differentiation between benign and malignant lesions of the spleen. *J Ultrasound Med* 2009; **28**: 421–34.
10. Luna A, Ribes R, Caro P, Luna L, Aumente E, Ros PR. MRI of focal splenic lesions without and with dynamic gadolinium enhancement. *AJR Am J Roentgenol* 2006; **186**: 1533–47. doi: <http://dx.doi.org/10.2214/AJR.04.1249>
11. Elsayes KM, Narra VR, Mukundan G, Lewis JS Jr, Menias CO, Heiken JP. MR imaging of

- the spleen: spectrum of abnormalities. *Radiographics* 2005; **25**: 967–82. doi: <http://dx.doi.org/10.1148/rg.254045154>
12. Cesta MF. Normal structure, function, and histology of the spleen. *Toxicol Pathol* 2006; **34**: 455–65. doi: <http://dx.doi.org/10.1080/01926230600867743>
 13. Donnelly LF, Foss JN, Frush DP, Bisset GS 3rd. Heterogeneous splenic enhancement patterns on spiral CT images in children: minimizing misinterpretation. *Radiology* 1999; **210**: 493–7. doi: <http://dx.doi.org/10.1148/radiology.210.2.r99fe16493>
 14. Morani AC, Elsayes KM, Liu PS, Weadock WJ, Szklaruk J, Dillman JR, et al. Abdominal applications of diffusion-weighted magnetic resonance imaging: where do we stand. *World J Radiol* 2013; **5**: 68–80. doi: <http://dx.doi.org/10.4329/wjr.v5.i3.68>
 15. Yoshikawa T, Kawamitsu H, Mitchell DG, Ohno Y, Ku Y, Seo Y, et al. ADC measurement of abdominal organs and lesions using parallel imaging technique. *AJR Am J Roentgenol* 2006; **187**: 1521–30. doi: <http://dx.doi.org/10.2214/AJR.05.0778>
 16. Lewis RB, Lattin GE Jr, Nandedkar M, Aguilera NS. Sclerosing angiomatoid nodular transformation of the spleen: CT and MRI features with pathologic correlation. *AJR Am J Roentgenol* 2013; **200**: W353–60. doi: <http://dx.doi.org/10.2214/AJR.12.9522>
 17. Lu T, Yang C. Computed tomographic and clinicopathological features of inflammatory pseudotumor of the spleen. *J Comput Assist Tomogr* 2015; **39**: 409–13. doi: <http://dx.doi.org/10.1097/RCT.0000000000000215>
 18. Nunes TF, Szejnfeld D, Mijji LN, Goldman SM. Isolated metachronous splenic metastasis from renal cell carcinoma after 5 years. *BMJ Case Rep* 2012; **2012**. doi: <http://dx.doi.org/10.1136/bcr-2012-006992>
 19. Yazici P, Aydin U, Ersin S, Kaplan H. Hamartoma—a rare benign tumor of the spleen: a report of four cases. *Eurasian J Med* 2008; **40**: 48–51.
 20. Ramani M, Reinhold C, Semelka RC, Siegelman ES, Liang L, Ascher SM, et al. Splenic hemangiomas and hamartomas: MR imaging characteristics of 28 lesions. *Radiology* 1997; **202**: 166–72. doi: <http://dx.doi.org/10.1148/radiology.202.1.8988207>
 21. Karaosmanoglu DA, Karcaaltincaba M, Akata D. CT and MRI findings of sclerosing angiomatoid nodular transformation of the spleen: spoke wheel pattern. *Korean J Radiol* 2008; **9**: S52–5. doi: <http://dx.doi.org/10.3348/kjr.2008.9.s.s52>
 22. Bhatt S, Simon R, Dogra VS. Radiologic-pathologic conferences of the university of Rochester School of Medicine: inflammatory pseudotumor of the spleen. *AJR Am J Roentgenol* 2008; **191**: 1477–9. doi: <http://dx.doi.org/10.2214/AJR.08.1011>
 23. Vilgrain V, Boulos L, Vullierme MP, Denys A, Terris B, Menu Y. Imaging of atypical hemangiomas of the liver with pathologic correlation. *Radiographics* 2000; **20**: 379–97. doi: <http://dx.doi.org/10.1148/radiographics.20.2.g00mc01379>
 24. Taibbi A, Bartolotta TV, Matranga D, Midiri M, Lagalla R. Splenic hemangiomas: contrast-enhanced sonographic findings. *J Ultrasound Med* 2012; **31**: 543–53.
 25. Abbott RM, Levy AD, Aguilera NS, Gorospe L, Thompson WM. From the archives of the AFIP: primary vascular neoplasms of the spleen: radiologic-pathologic correlation. *Radiographics* 2004; **24**: 1137–63. doi: <http://dx.doi.org/10.1148/rg.244045006>
 26. Kuhn JP, Hegenscheid K, Siegmund W, Froehlich CP, Hosten N, Puls R. Normal dynamic MRI enhancement patterns of the upper abdominal organs: gadoxetic acid compared with gadobutrol. *AJR Am J Roentgenol* 2009; **193**: 1318–23. doi: <http://dx.doi.org/10.2214/AJR.09.2412>
 27. Tamada T, Ito K, Sone T, Yamamoto A, Yoshida K, Kakuba K, et al. Dynamic contrast-enhanced magnetic resonance imaging of abdominal solid organ and major vessel: comparison of enhancement effect between Gd-EOB-DTPA and Gd-DTPA. *J Magn Reson Imaging* 2009; **29**: 636–40. doi: <http://dx.doi.org/10.1002/jmri.21689>
 28. Zizka J, Klzo L, Ferda J, Mrklovský M, Bukac J. Dynamic and delayed contrast enhancement in upper abdominal MRI studies: comparison of gadoxetic acid and gadobutrol. *Eur J Radiol* 2007; **62**: 186–91. doi: <http://dx.doi.org/10.1016/j.ejrad.2007.02.035>
 29. Goncalves Neto JA, Altun E, Elazzazi M, Vaidean GD, Chaney M, Semelka RC. Enhancement of abdominal organs on hepatic arterial phase: quantitative comparison between 1.5- and 3.0-T magnetic resonance imaging. *Magn Reson Imaging* 2010; **28**: 47–55. doi: <http://dx.doi.org/10.1016/j.mri.2009.05.041>
 30. Soher BJ, Dale BM, Merkle EM. A review of MR physics: 3T versus 1.5T. *Magn Reson Imaging Clin N Am* 2007; **15**: 277–90. doi: <http://dx.doi.org/10.1016/j.mric.2007.06.002>