

Original Research Article

**Role of Diffusion-Weighted Magnetic Resonance Imaging in Differential
Diagnosis of Splenic Focal Lesions**

Abstract

Background: In computed tomography (CT) and magnetic resonance imaging (MRI), enhancement patterns observed following the injection of a contrast agent are typically used to non-invasively distinguish between malignant and benign localised splenic lesions (MRI). Diffusion-weighted magnetic resonance imaging (DWI) is useful for staging and subsequent imaging of malignant tumours because it gives function information and may be utilised to identify and characterise pathologic processes, including malignant tumours.

Aim of the work: This study's main objective was to assess the extra value of diffusion-weighted MRI in the detection and classification of splenic localised lesions.

Patient and Methods: Thirty patients with splenic focal lesions, of both sexes, participated in this prospective investigation. All patients had complete information about the patient, examination findings, including an abdominal and general examination, an ultrasound, an abdominal MRI, and a DWI investigation.

Results: Considering the mean ADC value of the examined group, we discovered that the benign lesions group's mean ADC value was $(1.46) \times 10^{-3}$ sec/mm², whereas the malignant lesions group's mean ADC value was $(0.73) \times 10^{-3}$ sec/mm². In the individuals under study, we discovered a strong correlation between clinicopathological results and DW-MRI data. ($p < 0.001$). With a sensitivity of 83.33% and specificity of 94.44%, the kind of lesion was a statistically significant predictor of ADC values.

Kindly change the word 'sexes' to 'gender'. :[1]Comment

Conclusions: When used with conventional MRI, diffusion-weighted imaging enhances the ability to distinguish between splenic localised lesions. To verify our findings and resolve any discrepancies with the literature, more research is required.

Keywords: lesion, diffusion-weighted, MRI

Introduction:

The spleen may be affected by a wide variety of benign and malignant lesions, necessitating the creation of a differential diagnosis that encompasses both benign and malignant localised lesions (1).

Solid splenic masses are a common occurrence in clinical practise and can be difficult to diagnose. During imaging scans done for other reasons, lesions might be found by chance. Angiosarcoma, lymphoma, leukemic infiltrates, and metastases are examples of malignant solid splenic lesions (2, 3). Hemangiomas, hamartomas, and granulomas are the most typical benign solid splenic localised lesions (4, 5).

Particularly in patients with extrasplenic malignancies, a splenic biopsy is frequently taken into consideration when localised splenic lesions are seen on imaging examinations. Not all individuals with localised splenic lesions require a biopsy since the majority of incidentally discovered splenic lesions are benign (1).

Due to the spleen's abundant blood supply and the low sonic window, localised splenic lesions may not be accessible for ultrasound-guided biopsy after a splenic biopsy (6).

The traditional alternative to biopsy when pathologic diagnosis is required but difficult to execute is splenectomy or laparoscopy-guided splenic biopsy. Therefore, splenectomy for benign tumours that isn't essential will result in the loss of a crucial immune organ. Consequently, it's crucial to non-invasively distinguish between benign and malignant localised splenic tumours on imaging. In computed tomography (CT) and magnetic resonance

imaging (MRI), enhancement patterns observed following the injection of a contrast agent are typically used to non-invasively differentiate between malignant and benign localised splenic lesions (7, 8).

Diffusion-weighted imaging (DWI) of the abdomen has become more popular due to recent improvements in MR technology. DWI is a desirable method since it is non-invasive, fast, and doesn't involve ionising radiation or exogenous contrast chemicals (9).

For the identification and characterization of pathologic processes, such as malignant tumours, diffusion-weighted magnetic resonance imaging (DWI) gives function information.

It may be useful for staging and subsequent imaging of malignant tumours (10).

This study's objective was to assess the extra value of DWI in the identification and classification of splenic localised lesions.

Patients and Methods:

This prospective study involved 30 patients, 30 of both sexes, with splenic focal lesions who were referred to Tanta University Hospital's Diagnostic Radiology Department from various medical and surgical departments as well as the cancer unit. Each patient provided their informed permission, and the ethics committee authorised the protocol.

Patients with splenic focal lesions meet the inclusion criteria.

All genders are represented.

Exclusion standards: Patients for whom an MRI is not recommended include:

- Patients who declined to take part in the study.
- Patients having metallic foreign bodies inside their eyes.
- Those who have cardiac pacemakers.
- Patients with arterial brain aneurysms that have intracranial clips.
- Patient with claustrophobia.

Kindly change the word 'sexes' to 'gender'. **Comment 2**

- If a situation calls for contrast, individuals with impaired renal function should not get it.

Before contrast administration serum creatinine level was checked for all patients.

Every patient went through the following:

1. A thorough history is taken.
2. Clinical examination: abdominal and general examination.
3. Abdominal U/S examination.
4. Abdominal MRI examination.

MRI sequences:

- T1WI •
- T2WI •
- T1C+(Gd) •
- DWI •
- Dynamic contrast enhanced study (if needed). •

Imaging evaluation:

The difference in signal strength, shape, location, size of the lesions, and their relationships to the surrounding structures at the non-contrast T1-weighted and T2-weighted pulse sequences were taken into consideration while interpreting the images.

To determine the additional diagnostic value in the identification and characterisation of the splenic focal lesions, we then analyzed the DWI study and ADC map.

Lastly, we looked at the dynamic Gd-DTPA MRI images to analyze the different lesion enhancement patterns.

All imaging data were adjusted against a predetermined standard of reference for lesion characterisation. Histopathology or multi-modality and clinical follow up were the standards

of reference. The most suitable and morally acceptable SOR was utilized for each kind of lesion. The acceptable SOR for 9 patients (5 lymphoma cases and 4 secondary cases) was biopsy and histological confirmation within 3 months of the MRI evaluation in 6 cases and splenectomy in 3 lymphoma cases. according to moral concerns.

The established standard of reference for patients who presented with benign lesions was close follow-up with contrast-enhanced MRI or triphasic CT imaging after a few months. For nine instances, histopathological correlation was performed.

Statistical analysis

Microsoft Excel 2016 and the SPSS application (Statistical Package for Social Sciences) version 26.0 were used to tabulate and statistically analyze the gathered data. For numerical parametric data, descriptive statistics were performed using the mean, SD (standard deviation), minimum and maximum of the range; for numerical non-parametric data, they were performed using the median and first and third interquartile ranges; and for categorical data, they were performed using the number and percentage. For quantitative variables, inferential analyses were performed using the independent t-test when there were two independent groups and parametric data, and the Mann Whitney U when there were two independent groups and non-parametric data. Chi square test for independent groups was used for inferential analysis of qualitative data. If the P value is less than 0.001, then the level of significance is significant; otherwise, it is not.

Results:

The thirty patients in this prospective research all had splenic localised lesions. These individuals were sent for an MRI test to Tanta University Hospital's Diagnostic Radiology Department from its various medical and surgical departments as well as its cancer section. Males represent 63.3% and females represent 36.7% of the study group. Patients' age in this study ranges from 35 to 67 years old with mean 49.0 ± 11.29 years old (table1).

Can rephrase the following sentence marked in following manner: 'was close follow up' to 'was followed up closely.'

According to lesion margin, (73.7%) of the benign group had lesions with well-defined margin and (26.3%) ill-defined, while (45.5%) of the malignant group had lesions with well-defined margin and (54.5%) ill-defined.(table 2)

According to the splenic focal lesions in this study's MR signal intensity. On T1 weighted image, 60% of the benign group were hypointense and 35% were isotense, and for malignant group there were 55% of them were isointense and 41.8% were low. On T2-weighted images 68.5% of the benign group were high and 30.4% were low, and for malignant group there were 48% of them were high and 41% were low. There was a statistically significant difference between the two groups in terms of DWI for SI on DW images, with low signal intensity being more common in the benign group (free diffusion) and high signal intensity being more common in the malignant group (limited diffusion).(table 3) The dynamic MRI study shows that on arterial phase half of splenic lesions (50%) had low signal,(40%) had high signal and (10%) had intermediate signal. On portal venous phase (50%) lesions had low signal, (30%) had high signal, (20%) had intermediate signal. On late phase (40%) lesions had high signal,(30) displayed low signal , (30%) displayed intermediate signal.(table 4)

Change into following, ' on' to :[4]Comment 'with.

The haemangioma had the greatest values, followed by cysts and infarction, while lymphomas and metastases had the lowest values. The mean ADC values of benign and malignant lesions differed significantly from one another. There were no discernible changes in ADC values between the various benign lesions or the various malignant lesions at any sequence. (table 5)

In terms of the mean ADC value of the group under study, we discovered that the benign lesions group's mean ADC value was 1.46×10^{-3} sec/mm², but the malignant lesions group's mean ADC value was 0.73×10^{-3} sec/mm².

In the individuals under study, we discovered a strong correlation between clinicopathological results and DW-MRI data (p= 0.001).(table 6)

Table (1): Distribution of the research group's age and gender (n=30)

Age(yrs)	Sex	Total No.	%
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	Male	Female		
30 - < 40	2	1	3	10
40 - < 50	7	4	11	36.67
50 - < 60	5	4	9	30
60 - < 70	5	2	7	23.33
Total	19	11	30	100

Table (2): Distribution of the studied patients regarding lesion margin.

Lesion margin	Lesion			
	Benign		Malignant	
	N	%	N	%
Well defined	14	73.7	5	45.5
Ill defined	5	26.3	6	54.5

Table (3): Each focal lesions in our research had a specific MR signal intensity.

Lesion	T1WI	T2WI	DWI	ADC map
Cysts	Low/Iso	High	Low	High
Lymphoma	Low /Iso	Variable intensity	High/ mixed	Low
Metastasis	Low/Iso	Low / Iso	High/Mixed	Low
Haemangioma	Low/Iso	High	high	High
Infarction	Low	High/intermediate	Low	High
Calcification	Low	Low	Low	High
Siderotic nodules	Low	Low	Low	Low

Iso= isointense, please note. Varying means varying intensity (hyperintense, hypointense, isointense). Signal Intensity, or SI.

Table (4): Distribution of patients with splenic focal lesions who underwent triphasic MRI according to signal intensity

	Lesion intensity					
	Hyperintense		Hypointense		Isointense	
	N	%	N	%	N	%
Arterial phase	4	40	5	50.0	1	10
Portal venous phase	3	30	5	50	2	20
Late phase	4	40	3	30	3	30

Table (5): ADC values (mean and range) in different splenic focal lesions in this study.

Lesion	ADC values	
	Range	Mean
Cyst	$(1.2-1.6) \times 10^{-3} \text{ sec/mm}^2$	$1.29 \times 10^{-3} \text{ sec/mm}^2$
Lymphoma	$(0.56-0.82) \times 10^{-3} \text{ sec/mm}^2$	$0.68 \times 10^{-3} \text{ sec/mm}^2$
Metastasis	$(0.61-1.1) \times 10^{-3} \text{ sec/mm}^2$	$0.78 \times 10^{-3} \text{ sec/mm}^2$
Haemangioma	$(1.4-1.9) \times 10^{-3} \text{ sec/mm}^2$	$1.62 \times 10^{-3} \text{ sec/mm}^2$
Infarction	$(1.4-1.6) \times 10^{-3} \text{ sec/mm}^2$	$1.5 \times 10^{-3} \text{ sec/mm}^2$

Table (6): The findings of the ROC curve between benign and malignant regard ADC values and the mean ADC values of benign and malignant splenic focused lesions in this study

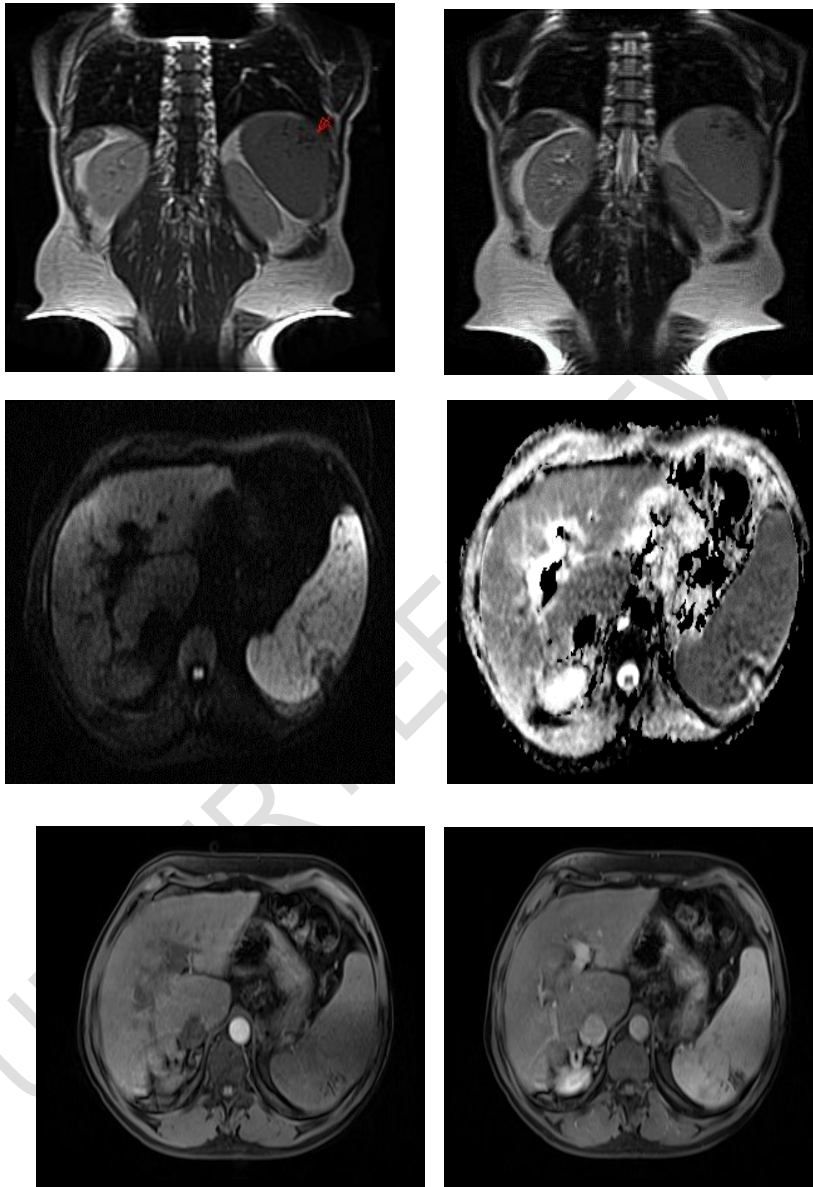
Lesion	ADC values			ROC curve between benign and malignant as regard ADC values						
	Mean	SD	P-value	Cut off	Sensitivity	Specificity	PPV	NPV	Accuracy	P-value
Benign	1.46	0.24	<0.001							
Malignant	0.73	0.15		≤0.98	83.33	94.44	90.9	89.5	94.9	<0.001*

Positive predictive value is PPV, whereas negative predictive value is NPV.

Case NO. (1)

Clinical history:

Sixty one years old male patient was presented clinically by generalized weakness, weight loss and jaundice. Patient was diabetic. He was proven to have hepatic cell carcinoma by histopathological analysis.



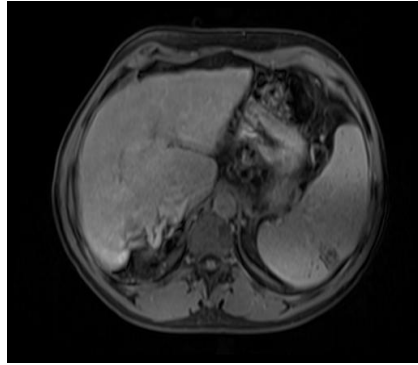


Fig 1. (A) Coronal T1WI, (B) Coronal T2WI, (C) DWI, and (D) ADC Map were found by MRI. Phases (E) Arterial (F) Portal and (G) An enlarged spleen was discovered by delayed phase, measuring 15.3 cm at its widest point, with an upper polar focal lesion that had poor signal in both T1WI and T2WI. Free diffusion was seen in the lesion, with a mean ADC value of 1.5×10^{-3} sec/mm². Throughout the whole research, the lesion didn't exhibit any post-contrast enhancement. Based on the MRI results, the diagnosis of splenic infarction was made.

Case NO.(2)

Cinical history:

Fifty –three years old male patient was presented clinically by upper abdominal pain,jaundice and generalized weakness. Patient was smoker and hypertensive.

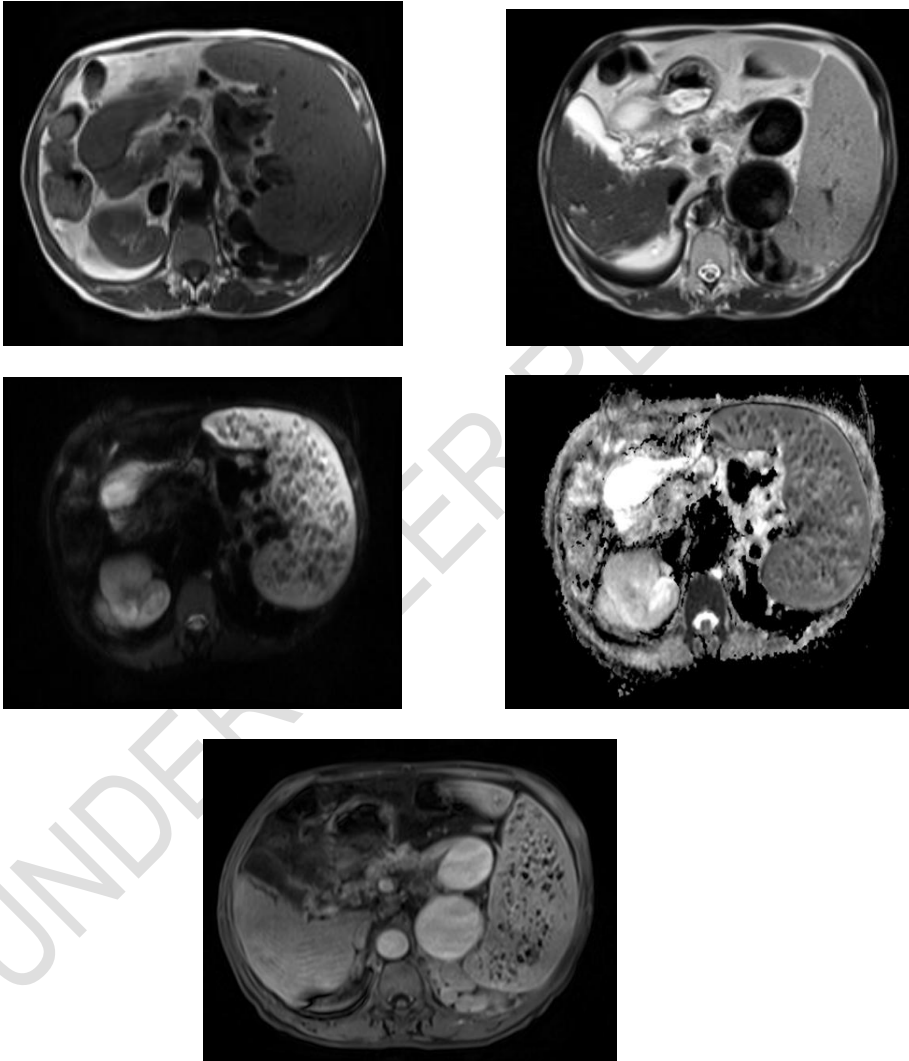


Fig 2. Axial T1WI, Axial T2WI, DWI, ADC Map, Post contrast T1WI, and Axial T1WI(A) revealed enlarged spleen measuring around 20 cm in its maximal bipolar span with numerous small foci of low signal on both T1WI(A) and T2WI. Free diffusion was visible in the lesion. Absence of post-contrast enhancement evidence. Based on the MRI results, the diagnosis of gandy gamma bodies was made.

Case NO. (3)

Cinical history:

Forty –eight years old female patient was presented clinically by loss of weight, nausea and left upper hypochondrium pain. Patient was diabetic and hypertensive.

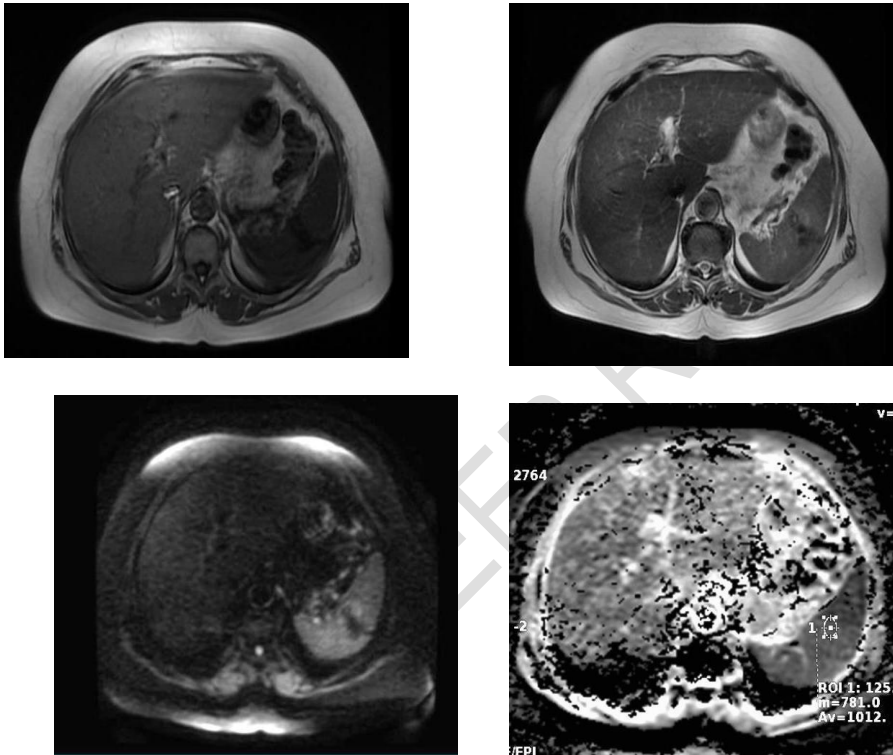


Fig 3, Axial T1WI, Axial T2WI, DWI, and ADC were discovered using MRI. The splenic focal lesion was seen on the map to have low signal on T1WI and mixed low and high signal on T2WI. Restricted diffusion was seen at the mass's periphery, with a mean ADC value of 0.66×10^{-3} sec/mm². A biopsy and histological examination led to the non-Hodgkin lymphoma (NHL) diagnosis.

Discussion:

Distribution of the studied patients regarding lesion margin & enhancement pattern revealed that the benign group (72.2%) had lesions with well-defined margin and (27.8%) had ill-defined, while in the malignant group (41.7%) of patients had lesions with well-defined margin and (58.3%) ill-defined.

In contrast, the study by Choi et al. (11) found that in the malignant group, 25% of patients had lesions with well-defined margins and 75% had ill-defined lesions, with no statistically significant difference between the two groups. In the benign group, 51.4% of patients had lesions with well-defined margins and 48.6% had ill-defined lesions.

In contrast, the research by Jang et al. (12) found that there was no statistically significant difference between the benign and malignant groups and that the majority of the benign and malignant groups had well-defined margins at 66.7% and 63.6%, respectively.

Our findings also showed that, in terms of patient signal intensity on a T1 weighted picture, 60% of the group with cancer was hypointense and 35% was intense, and for Malignancy group there were 55% of lesions were isointense and 41.8% were low. On T2-weighted images 68.5% of the benignancy group were high and 30.4% were low, and for malignancy group there were 48% of lesions were high and 41% were low. Regarding SI on DW image,

Kindly remove 'there were.': [5] Comment

There was a statistically significant difference between the two groups in terms of DWI, with low signal intensity being more common in the benign tumour group (free diffusion) and high signal intensity being more common in the malignant tumour group (limited diffusion).

In contrast, the research by Jang et al. (12) found that the majority of the benign and malignant groups exhibited isointense T1-weighted images (73.8% and 72.7%, respectively) in terms of signal intensity. and in the Benign group's T2-weighted pictures, 47.6% of the images were hyperintense, 31% were hypointense and 21.4% were isointense, while in malignant group 45.4% were hyperintense, 36.4% were hypointense and 18.2% were

isointense. And regarding Signal intensity of hepatobiliary phase: hypointense, isointense and hyperintense were (4.8, 42.8 and 52.4 respectively) for benign group and for malignant group were (18.2%, 36.4% and 45.4% respectively). Regarding T1-weighted imaging and the hepatobiliary phase, there was no statistically significant difference between the two groups. Diffusion-weighted images SI for the Benign group there were, 61.9 % were hypointense, 23.8 % were isointense and 14.3% were hyperintense, while for the malignant group there were, 9.1 % were hypointense, 36.4 % were isointense and 54.5% were hyperintense. Regarding Gadoteric acid-enhanced images of the studied group who undergo triphasic MRI, we found that on arterial phase half of splenic lesions (50%) had low signal,(40%) had high signal and (10%) had intermediate signal .On portal venous phase (50%) lesions had low signal, (30%) had high signal, (20%) had intermediate signal .On late phase (40%) lesions had high signal,(30) displayed low signal , (30%) displayed intermediate signal . According to the study by Choi et al. (11), 100% of the Malignancy group had low SI on arterial phase, compared to 60% of the Benignancy group's low SI on arterial phase and 34.3% of the group's high SI. Moreover, 60% of SI at the portal phase of the Benignancy group have low SI portal phase and 40% have Iso SI, whereas there were 100% of the Malignancy group have low SI, and for the SI on 3-min delayed phase there were 62.9% of the Benignancy group have high SI and 22.9% had Iso SI, whereas there were 80% of the Malignancy group have low SI. In the two groups, there was a statistically significant difference in the SI of the arterial phase, portal phase, and 3-min delayed phase. In terms of the mean ADC value of the group under study, we discovered that the benign lesions group's mean ADC value was 1.46×10^{-3} sec/mm², but the malignant lesions group's mean ADC value was 0.73×10^{-3} sec/mm². We found that there was significant relationship between clinicopathological findings and DW-MRI findings in the studied patients ($p = 0.001$).

Although Choi et al. study (11), which found a statistically significant difference between benign and malignant groups in terms of the signal intensity of diffusion-weighted images (p value = 0.014), did not

Kindly rephrase this sentences. :[6]Comment
The sentence seems incomprehensible.

Also, the study by Jang et al. (12) found that the signal intensity of the diffusion-weighted images differed statistically significantly between the benign and malignant groups (p value = 0.003).

Many papers, including those by Palas et al. (13), Vancauwenbergheet al. (14), Choi et al. (2016, 86), Luna et al. (15), and Elsayes et al. (16), describe the imaging characteristics of focal splenic lesions using CT and MR. The descriptions of the imaging characteristics of each disease—Lewis et al. (17), Lu et al. (18), Nunes et al. (19), Yazici et al. (20), and Ramani et al. (5)—concentrate mostly on this rather than on the distinction between benign and malignant splenic lesions.

As far as we are aware, contrast enhanced ultrasound (CEUS), von Herbay et al (23), contrast enhanced ultrasound (CEUS), and DW MR imaging have all been used to distinguish between benign and malignant splenic tumours. Jang et al. (12), Choi et al (12). Nevertheless, it is unknown which dynamic MRI phase can aid in differentiating between benign and malignant splenic lesions, as well as if the results of dynamic MRI and CEUS are equivalent. Further research with a greater geographic scope and sample size will be conducted to underline our findings. To precisely determine the function of DWI in the identification of splenic focal lesions, more patients, a longer period of follow-up, and multicenter experience are all required. The DWI approach will be improved with more widespread use, which will lead to better patient care.

Conclusions:

When used with conventional MRI, diffusion-weighted imaging enhances the ability to distinguish between splenic localised lesions. Further research is required to verify our findings and resolve any discrepancies with the literature.

Recommendations:

- Further research with a bigger sample size and a wider geographic scope would underscore our findings. ▪
- To precisely determine the function of diffusion-weighted magnetic resonance imaging in the identification of splenic focal lesions, more patients, a longer period of follow-up, and multicenter experience are all required. ▪
- More people using the DWI approach will help it get better, which will lead to improved patient care. ▪

References:

- Abbott RM, Levy AD, Aguilera NS, Gorospe L, Thompson WM, et al** :(2004) 1.
primary vascular neoplasms of the spleen: radiologic-pathologic correlation.
Radiographics.;24(4):1137-63.
- Kutok JL and Fletcher CD.**:(2003) Splenic vascular tumors. Semin Diagn 2.
Pathol.;20(2):128-39.
- Bragg DG, Colby TV and Ward JH**:(1986). New concepts in the non-Hodgkin 3.
lymphomas: radiologic implications. Radiology. 1986;159(2):291-304.
- Danon O, Duval-Arnould M, Osman Z, et al**:(2000) Hepatic and splenic 4.
involvement in cat-scratch disease: imaging features. Abdom Imaging.;25(2):182-3.

- Ramani M, Reinhold C, Semelka RC, et al** :(1997) Splenic hemangiomas and hamartomas: MR imaging characteristics of 28 lesions. *Radiology*;202(1):166-72. 5.
- Gómez-Rubio M, López-Cano A, Rendón P, et al** (2009) Safety and diagnostic accuracy of percutaneous ultrasound-guided biopsy of the spleen: a multicenter study. *J Clin Ultrasound*;37(8):445-50. 6.
- Ito K, Murata T and Nakanishi T.**:(1995) Cystic lymphangioma of the spleen: MR findings with pathologic correlation. *Abdom Imaging*.;20(1):82-4. 7.
- Robertson F, Leander P and Ekberg O.**:(2001) Radiology of the spleen. *Eur Radiol*;11(1):80-95. 8.
- Padhani AR, Liu G, Koh DM, et al.**:(2009) Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations. *Neoplasia*. 2009;11(2):102-25. 9.
- Ichikawa T, Haradome H, Hachiya J, Nitatori T, Araki T.**:(1999) Diffusion-weighted MR imaging with single-shot echo-planar imaging in the upper abdomen: preliminary clinical experience in 61 patients. *Abdom Imaging*.;24(5):456-61. 10.
- Choi SY, Kim SH, Jang KM, Kang TW, et al.**:(2016) The value of contrast-enhanced dynamic and diffusion-weighted MR imaging for distinguishing benign and malignant splenic masses. *Br J Radiol*.;89(1063):20160054. 11.
- Jang KM, Kim SH, Hwang J, Lee SJ, Kang TW, Lee MW, et al.**:(2014) Differentiation of malignant from benign focal splenic lesions: added value of diffusion-weighted MRI. *AJR Am J Roentgenol*. 2014;203(4):803-12. 12.
- Taha Ali TF and El Hariri MA.**:(2017) Diffusion-weighted MRI in liver fibrosis staging: Added value of normalized ADC using spleen and renal cortex as reference organs. *The Egyptian Journal of Radiology and Nuclear Medicine*.;48(1):23-30. 13.

- Vancauwenberghe T, Snoeckx A, Vanbeckevoort D, et al.:(2015)** Imaging of the spleen: what the clinician needs to know. *Singapore Med J*.;56(3):133-44. 14.
- Luna A, Ribes R, Caro P, Luna L, Aumente E, Ros PR. :(2006)**MRI of focal splenic lesions without and with dynamic gadolinium enhancement. *AJR Am J Roentgenol.*;186(6):1533-47. 15.
- Elsayes KM, Narra VR, Mukundan G, Lewis JS, Jr., et al. :(2005)**MR imaging of the spleen: spectrum of abnormalities. *Radiographics.*;25(4):967-82. 16.
- Lewis RB, Lattin GE, Jr., Nandedkar M, Aguilera NS.(2013)** Sclerosing angiomatoid nodular transformation of the spleen: CT and MRI features with pathologic correlation. *AJR Am J Roentgenol.* 2013;200(4):W353-60. 17.
- Lu T, Yang C.:(2015):** Computed tomographic and clinicopathological features of inflammatory pseudotumor of the spleen. *J Comput Assist Tomogr.*;39(3):409-13. 18.
- Nunes TF, Szejnfeld D, Miiji LN, Goldman SM.:(2012)** Isolated metachronous splenic metastasis from renal cell carcinoma after 5 years. *BMJ Case Rep.* 2012;2012. 19.
- Yazici P, Aydin U, Ersin S, Kaplan H. :(2008)**Hamartoma - a rare benign tumor of the spleen: a report of four cases. *Eurasian J Med.*;40(1):48-51. 20.
- Stang A, Keles H, Hentschke S, von Seydewitz CU,, et al.:(2011)** Incidentally detected splenic lesions in ultrasound: does contrast-enhanced ultrasonography improve the differentiation of benign hemangioma/hamartoma from malignant lesions? *Ultraschall Med.* 2011;32(6):582-92. 21.
- Stang A, Keles H, Hentschke S, von Seydewitz CU, et al.:(2009)** Differentiation of benign from malignant focal splenic lesions using sulfur hexafluoride-filled microbubble contrast-enhanced pulse-inversion sonography. *AJR Am J Roentgenol.*;193(3):709-21. 22.

von Herbay A, Barreiros AP, Ignee A, et al.:(2009) Contrast-enhanced 23.
ultrasonography with SonoVue: differentiation between benign and malignant lesions of the
spleen. J Ultrasound Med.;28(4):421-34.

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