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The role of Diffusion Weighted MRI in Evaluation of Neoplastic Hepatic Focal Lesions in Cases of Portal Vein Thrombosis

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Abstract

Background: It is thought that many primary malignant, benign, and metastatic localized lesions share the liver as a location. In order to avoid inoperable tumors being falsely graded and cases with such tumors being scheduled for surgical treatments, accurate diagnosis and characterization of these tumors are essential pre-treatment steps. For individuals at high risk for complications following a biopsy, diffusion-weighted imaging (DWI) may be an ideal non-invasive way to assess particular tissue characteristics.

Objective: To determine how useful diffusion-weighted magnetic resonance imaging (DWI) was for identifying and characterizing hepatic focal lesions (HFL) that were associated with portal vein thrombosis.

Patients and methods: This prospective descriptive study will be done on 50 patients with pathological or radiological proof of focal liver lesion correlated with visible portal vein thrombosis to assess the role of DWI in the detection and characterization of HFL and associated portal vein thrombosis.

Results: Regarding diffusion-weighted MRI in characterization of HFL with PVT, cases with malignant focal lesions had significantly lower mean apparent diffusion coefficient (ADC) when contrasted to cases with benign focal lesions (0.96 ± 0.17 vs 1.88 ± 0.60 ; $P < 0.001$), and among patients with malignant focal lesions, patients with malignant PVT had significantly lower mean ADC PVT (1.08 ± 0.16 vs 2.07 ± 0.13 ; $P < 0.001$), as well as significantly lower ADC ratio (1.07 ± 0.07 vs 2.42 ± 0.50 ; $P < 0.001$) when contrasted with cases with benign PVT.

Conclusion: DW-MRI is a dependable modality for differentiating benign focal liver lesions from malignant ones. The characteristics of the portal vein thrombus can also be ascertained by calculating the ADC ratio between the thrombus and the tumor.

Keywords: Diffusion weighted MRI; ADC; hepatic focal lesions; Portal vein thrombosis

1. Introduction

It is thought that many primary malignant, benign, metastatic localized lesions share the liver as a location. In order to avoid inoperable tumors being falsely graded and cases with such tumors being scheduled for surgical treatments, accurate diagnosis and characterization of these tumors are essential pre-treatment steps.¹

Benign or malignant PVT may manifest in individuals with cirrhosis or neoplastic disorders; also, benign and malignant thrombi can coexist.²

During tumor staging, deciding on the best course of treatment, and gauging prognosis, the

existence of malignant PVT is a critical consideration for individuals with neoplastic conditions.³

Today, computed tomography (CT) and ultrasonography (USG) are used to diagnose focal masses. Furthermore, when additional characterization of these masses is required, magnetic resonance imaging (MRI) is preferable.⁴

Despite ultrasound's great sensitivity for FLLs detection, its specificity for differentiating between entities is limited. To confirm a presumed hepatic neoplasm in the US, CT is advised for patients with confirmed malignancy for staging, chronic liver disease cases, and even healthy individuals. MRI is considered the most sensitive and specific imaging modality for the detection of FLL.⁵

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Historically, triphasic CT has been regarded as the gold standard for FLL diagnosis. It has been noted that triphasic CT studies have a number of limitations involving radiation dosage, renal impairment, and the inability to identify the precise tissue features of localized lesions, which might result in an inconclusive diagnosis in certain circumstances. Thus, an alternative diagnostic method is required to provide accurate spatial resolution and high contrast, which can compensate for invasive procedures utilized to obtain tissue samples and meet the criteria for lesion characterization without the utilization of ionizing radiation or contrast agents.⁴

Patients at risk for problems following a biopsy may find that DWI characterization of particular tissue features is safe and effective.⁶

This study aimed to assess how hepatic focal lesions and related portal vein thrombosis may be detected and characterized utilizing DWI.

2. Patients and methods

This prospective descriptive research was done between October 2022 and October 2023, upon 50 cases with pathological or radiological proof of focal liver lesion accompanied by visible portal vein thrombosis. Patients were referred to the Department of Diagnostic and Interventional Radiology, National Hepatology and Tropical Medicine Research Institute in Cairo. Moreover, A signed permission that was informed was acquired, as well as approval from the ethics committee. All patient information was guarded against unapproved access and kept secret. The monitoring and utilization of any data that was provided was limited to scientific purposes.

Inclusion criteria: Patients aged more than 18 years with radiological proof of focal liver lesion by US or CT, associated with visible portal vein thrombosis.

Exclusion criteria: Young cases < 18 years, individuals with a cardiac pacemaker, those with metallic foreign bodies, and those in a coma.

All patients were subjected to:

Extensive medical history taking that includes noting gender, age, clinical symptoms & laboratory investigations {Alpha fetoprotein}.

MRI of the abdomen (involving pre- and post-contrast (Dynamic) and DWI) was performed on every subject.

Results were contrasted with those of the laboratory, with prior radiological findings, and with the standard dynamic MRI image of lesions.

Ethical approval:

Informed consent was obtained from each patient before inclusion in the study, and approval of the Research Ethics Committee of the faculty of medicine at Al-Azhar University was obtained before the start of the research.

MR Examination:

Research was done utilizing diffusion MR imaging, traditional MRI, and post-Gd-DTPA dynamic MRI. Prior to reviewing the diffusion pictures with ADC values, the focal lesions were characterized and detected. A phased-array torso surface coil was used in conjunction with a high field system (1.5 Tesla) magnet units to acquire MR images of the whole liver (Philips Ingenia, Philips Healthcare).

MR Protocol:

Pre-contrast imaging included:

T1 weighted (T1W) images of echo time TE=4.58msec, repetition time TR=10msec, FOV 355mm, 179x320 matrix, 7-8mm slice thickness, 1-2 mm slice gap.

T2 weighted (T2W) images captured throughout single-shot free breathing of TR ≥445msec, matrix (180-200) x 240, TE 26-28msec, slice gaps 1-2mm, slice thickness 7-8mm & FOV 365.

For adipose suppression utilizing T2 SPAIR (Spectral Attenuated Inversion Recovery), the following parameters are utilized: TE=80msec, TR ≥400msec, matrix dimensions of 204x384, 7-8mm slice thickness, 1-2mm slice gap, and FOV 365.

TE=4.6msec for in-phase and 2.3msec for out-of-phase, 143x240 matrix, TR=75-100msec, 7-8mm slice thickness, 0mm slice gap, and 345mm FOV comprise the in-phase and out-of-phase gradient echo sequence (Dual/FFE).

Dynamic study:

This dynamic research was conducted by administering a bolus injection of 0.1mmol/kg body weight of Gd-DTPA at a rate of 2ml/s, followed by a flush of 20ml of sterile 0.9% saline solution into the antecubital vein. The injections of contrast media and saline solution were performed manually. Following the contrast medium administered, dynamic imaging was carried out in a triphasic way utilizing the T1 THRIVE (High-Resolution Isotropic Volume Examination) approach. This involved an arterial phase lasting 16–20 sec., a porto-venous phase lasting 45–60 sec., and a delayed equilibrium phase lasting 3-5 min.

Diffusion study:

The research employed b values (0, 500, and 1000) sec/mm² to increase sensitivity to cellular packing. Respiratory-triggered fat-suppressed single-shot echoplanar DWI was done in the transverse plane utilizing tri-directional diffusion gradients. The GRAPPA method, short for generalized auto-calibrating partially parallel acquisition, was employed with an acceleration factor of two to improve the image quality. The scan lasted for a length of 3-4 minutes and had a restricted field of vision. The field of view was rectangular and covered 52% of the area. The

remaining parameters were as follows: the echo duration was 70 milliseconds, the number of excitations was 3, the matrix size was 256x256, the slice thickness ranged from 7 to 8 millimetres, and the slice gap ranged from 1 to 2 millimetres.

Imaging Evaluation:

Every lesion's morphological parameters were meticulously documented, involving its shape, size, margin, Characteristics of its signal, and dynamic imaging enhancement pattern, in addition to the number and dimensions of discernible focal lesions. Then, the preliminary diagnosis was revealed. Next, in order to finally discover and characterize localized lesions radiologically, we looked over the diffusion images with the ADC values.

The findings were contrasted with laboratory and additional radiological results (dynamic MRI) for every patient.

ADC Calculation:

In order to calculate the mean ADC of each identified focal lesion, a region of interest (ROI) is traced over the lesion. The ADC was computed by averaging the results of two assessments. In order to guarantee the measurement of identical areas, ROI were transferred from DW images to ADC maps via copy and paste.

Statistical analysis:

The collected, revised, coded & entered data were all performed in version 27 of the Statistical Package for the Social Sciences (IBM SPSS). When

parametric, the quantitative data were shown as means, standard deviations, and ranges. Furthermore, qualitative variables were delineated in percentage form as well.

Qualitative data comparisons among groups were done utilizing the Fisher exact test or the chi-square test in cases where the expected count in any given cell was less than 5.

Utilizing independent t-tests, quantitative data and parametric distributions were contrasted among two distinct groups.

The One-way ANOVA test was employed to contrast quantitative data and parametric distributions of more than two groups.

The optimal cut-off point for the investigated marker was measured utilizing the receiver operating zingcharacteristic curve (ROC), which considered its specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV), and area under the curve (AUC).

The accepted margin of error was 5%, and the confidence interval was established at 95%. The p-value was deemed significant in the subsequent manner:

A P-value greater than 0.05 indicates non-significance (NS).

A P-value less than 0.05 indicates significance (S).

A P-value less than 0.01% indicates high significance (HS).

3. Results

Table 1. Comparison between benign and malignant cases regarding liver status and focal liver lesion by dynamic

		BENIGN FL	MALIGNANT FL	TEST VALUE	P-VALUE	SIG.
		No. = 10	No. = 40			
LIVER	Non-cirrhotic	8 (80.0%)	8 (20.0%)	13.235*	0.000	HS
	Cirrhotic	2 (20.0%)	32 (80.0%)			
FOCAL LIVER LESION BY DYNAMIC	HCC	0 (0.0%)	34 (85%)	26.563*	0.000	HS
	Mets	0 (0.0%)	5 (12.5%)	1.389*	0.239	NS
	Regenerative nodule	2 (20.0%)	0 (0.0%)	8.333*	0.004	HS
	FNH	2 (20.0%)	0 (0.0%)	8.333*	0.004	HS
	Biliary cystadenoma	2 (20.0%)	0 (0.0%)	8.333*	0.004	HS
	Adenoma	2 (20.0%)	0 (0.0%)	8.333*	0.004	HS
	Hemangioma	2 (20.0%)	0 (0.0%)	8.333*	0.004	HS
	Cholangiocarcinoma	0 (0.0%)	1 (2.5%)	0.255*	0.614	NS

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

*: Chi-square test; •: Independent t-test

On dynamic MRI examination, malignant focal lesions were associated with significantly higher prevalence of cirrhotic liver status and the most commonly reported malignant focal lesion was HCC which was reported in 34 (85%) cases, followed by metastasis in 5 (12.5%) cases while cholangiocarcinoma was reported in 1 (2.5%) case. Regarding the benign FLs, regenerative nodule, FNH, biliary cystadenoma, adenoma, and hemangioma each was reported in 2 (20.0%) cases (Table 1).

Table 2. Comparison among malignant and benign cases regarding mean ADC value of focal lesion

		BENIGN FL	MALIGNANT FL	TEST VALUE	P-VALUE	SIG.
		No. = 10	No. = 40			
MEAN ADC	Mean ± SD	1.88 ± 0.60	0.96 ± 0.17	8.591	0.000	HS
	Range	1.13 – 3.12	0.61 – 1.43			

Patients with malignant focal lesions had significantly lesser mean ADC when contrasted with cases with benign focal lesions (0.96 ± 0.17 vs 1.88 ± 0.60; P=0.000) (Table 2).

Table 3. Comparison between malignant FL without PVT and malignant FL with PVT cases regarding liver status and focal liver lesion by dynamic

		MALIGNANT FL WITHOUT PVT	MALIGNANT FL WITH PVT	TEST VALUE	P-VALUE	SIG.
		No. = 10	No. = 30			
LIVER	Non-cirrhotic	4 (40.0%)	4 (13.3%)	3.333*	0.068	NS
	Cirrhotic	6 (60.0%)	26 (86.7%)			
FOCAL LIVER LESION BY DYNAMIC	HCC	6 (60.0%)	28 (93.3%)	6.536*	0.011	S
	Mets	4 (40.0%)	1 (3.3%)	9.219*	0.002	HS
	Cholangiocarcinoma	0 (0.0%)	1 (3.3%)	0.342*	0.559	NS

On dynamic MRI examination, presence of PVT in patients with malignant focal lesions was associated with significantly higher prevalence of HCC (93.3% vs 60% in patients with malignant focal lesions without PVT; $P=0.011$), as well as significantly lower prevalence of Mets (3.3% vs 40% in patients with malignant focal lesions without PVT; $P=0.002$) (Table 3).

Table 4. Comparison between malignant FL without PVT and malignant FL with PVT cases regarding mean ADC value of focal lesion

		MALIGNANT FL WITHOUT PVT	MALIGNANT FL WITH PVT	TEST VALUE	P-VALUE	SIG.
		No. = 10	No. = 30			
MEAN ADC	Mean \pm SD	0.94 \pm 0.21	0.97 \pm 0.16	-0.364*	0.718	NS
	Range	0.74 – 1.43	0.61 – 1.38			

Among cases with malignant focal lesions, no significant variance was reported among cases with and without PVT concerning mean ADC (Table 4).

Table 5. Comparison between cases without PVT, benign and malignant PVT cases with malignant focal lesion regarding mean ADC FL, mean ADC PVT and ADC ratio

		MALIGNANT FL WITHOUT PVT	MALIGNANT FL WITH BENIGN PVT	MALIGNANT FL WITH MALIGNANT PVT	TEST VALUE	P-VALUE	SIG.
		No. = 10	No. = 10	No. = 20			
MEAN ADC FL	Mean \pm SD	0.94 \pm 0.21	0.88 \pm 0.14	1.01 \pm 0.16	1.998*	0.150	NS
	Range	0.74 – 1.43	0.61 – 1.1	0.71 – 1.38			
MEAN ADC PVT	Mean \pm SD		2.07 \pm 0.13	1.08 \pm 0.16	16.825**	0.000	HS
	Range		1.77 – 2.22	0.8 – 1.42			
ADC RATIO	Mean \pm SD	–	2.42 \pm 0.50	1.07 \pm 0.07	12.031**	<0.001	HS
	Range	–	1.88 – 3.51	0.92 – 1.2			

Among cases with malignant focal lesions, cases with malignant PVT had significantly lower mean ADC PVT (1.08 \pm 0.16 vs 2.07 \pm 0.13; $P=0.000$), as well as significantly lower ADC ratio (1.07 \pm 0.07 vs 2.42 \pm 0.50; $P<0.001$) when compared to patients with benign PVT (Table 5).

Table 6. ROC analysis to assess ADC value of FL to detect malignant focal lesion among the studied patients

CUT OFF POINT	AUC	SENSITIVITY	SPECIFICITY	+PV	-PV
≤ 1.12	0.983	87.50	100.00	100.0	66.7

ROC curve revealed that cut off value of ADC 1.12 or less had significant discriminative capability to distinguish among benign & malignant focal lesions with AUC 0.983, 87.5% sensitivity, 100 percent specificity, 100 percent PPV and 66.7% NPV (Table 6).

Table 7. ROC analysis to assess ADC value of PVT to detect malignant PVT among the studied malignant FL cases

CUT OFF POINT	AUC	SENSITIVITY	SPECIFICITY	+PV	-PV
≤ 1.42	1.000	100.00	100.00	100.0	100.0

ROC curve revealed that cut off value of ADC 1.42 or less had significant discriminative capability detect malignant PVT among the studied malignant FL cases with AUC 1.000, 100 percent sensitivity, 100 percent specificity, 100% PPV and 100% NPV (Table 7).

Table 8. ROC analysis to assess ADC ratio of PVT to detect malignant PVT among the studied malignant FL cases

CUT OFF POINT	AUC	SENSITIVITY	SPECIFICITY	+PV	-PV
≤ 1.2	1.000	100.00	100.00	100.0	100.0

ROC curve revealed that cut off value of ADC ratio of PVT 1.2 or less had significant discriminative ability to detect malignant PVT among the studied malignant FL cases with AUC 1.000, 100 percent sensitivity, 100 percent specificity, 100% PPV and NPV (Table 8).

4. Discussion

Our research found that patients with malignant focal lesions in our Study had significantly lesser mean ADC when contrasted with patients with benign focal lesions (0.96 ± 0.17 vs 1.88 ± 0.60 ; $P=0.000$).

In line with our finding, the Study included 31 patients with suspected FLLs observed that benign lesions such as simple hepatic cysts and hemangiomas demonstrated enhanced diffusion, evident by their high signal intensity (SI) on DWI and ADC maps. On the other hand, malignant solid tumors such as hepatocellular carcinoma (HCC) and metastases displayed restricted diffusion, which is evident from the high SI on DWI and low SI on ADC maps. Cancerous metastases or HCC had lower mean ADC than benign localized hepatic lesions such as hemangiomas ($P = 0.001$).⁷

Among patients with malignant focal lesions in the present Study, patients with malignant PVT had significantly lower mean ADC (1.08 ± 0.16 vs 2.07 ± 0.13 ; $P=0.000$), as well as significantly lower ADC ratio (1.07 ± 0.07 vs 2.42 ± 0.50 ; $P<0.001$) when compared to patients with benign PVT.

In agreement with our Study, PVTs were evaluated using DWI in research that involved clinical imaging data from 140 individuals. The PVTs were classified as benign or malignant using improved MRI. The signal intensity ratio (SIR)/ADC values for benign and malignant PVTs were 0.72 ± 0.32 and 0.62 ± 0.17 , correspondingly. This indicates that the (SIR) ADC values for malignant PVTs were significantly lesser ($P=0.034$).⁸

Furthermore, the Study involved 30 individuals diagnosed with liver cirrhosis who had radiographic or pathological evidence of an HCC and who also had evident portal vein thrombosis. They observed that the mean ADC ratios of malignant thrombi were significantly lesser contrasted with non-malignant venous thrombi (1.27 ± 0.4352 vs 2.09 ± 0.6667 correspondingly; $P= 0.000755$). They also reported significantly lower ADC values in neoplastic thrombi compared to non-malignant venous thrombi (1051.25 ± 256.560 vs 1794.29 ± 463.828 mm²/sec, respectively; $P= 0.000035$).⁹

In disagreement with our findings, research was conducted on 39 cases with PVT; they examined DWI and ADC maps. They discovered no statistically significant distinctions in the subjective evaluation of benign and malignant PVT. They attributed that to their method, which differed from previous attempts by utilizing a qualitative review and somewhat different b-values.¹⁰

Among patients with malignant FLs in our research, no significant variance was reported

among cases without PVT, cases with benign PVT and cases with malignant PVT regarding ADC map of HFLs.

ROC curve in our research revealed that the cutoff value of ADC 1.12 or less had significant discriminative capability to differentiate among benign and malignant focal lesions with AUC 0.983, 87.5% sensitivity, 100% PPV, 100% specificity, and 66.7% NPV.

In agreement with our finding, Jahic et al.¹¹ attain the ideal cutoff for the ADC value of 1.341×10^{-3} mm²/s, which was shown to be the defining characteristic distinguishing benign from malignant lesions.¹¹

Moreover, the Study comprised fifty patients who were referred for an MRI in order to confirm or diagnose focal hepatic lesions identified by USG or CT. DWI was observed to be beneficial in conjunction with routine MRI sequences in order to facilitate the diagnosis. Histopathological examination or subsequent analysis validated the final diagnosis. It was determined that 1.25×10^{-3} mm²/s was the appropriate cutoff value of ADC for benign lesions, with a sensitivity of 90.9% and a specificity of 90.6%.¹²

ROC curve in our research revealed that the off value of ADC 1.42 or less had a significant discriminative ability to detect malignant PVT among the studied malignant FLL cases with AUC 1.000, 100% specificity, 100% sensitivity, 100% PPV and 100% NPV.

In line with our finding, a study found that ADC revealed 80% sensitivity and 72.7% specificity with a cutoff value of 1.00×10^{-3} mm²/s.¹³

Also, another ROC curve in the Study revealed the cutoff value of ADC (≤ 1) discriminated malignant from benign PVT with 100% sensitivity and 82.5% specificity.¹⁴

Nevertheless, there is a study that stated an ADC value that discriminates among benign and malignant PVTs with a sensitivity of 22.2% due to the large range and significant overlap of ADC. The ADC value is affected by the thrombus's stage, which might explain why benign PVT and malignant PVT can both have low ADC values.¹⁵

In our Study, the ROC curve revealed that the cutoff value of the ADC ratio of PVT 1.2 or less had a significant discriminative ability to detect malignant PVT among the studied malignant FLL cases with AUC 1.000, 100% sensitivity, and 100% specificity.

In line with our finding, a study reported that a sensitivity of 85% and specificity of 81% were achieved when utilizing a threshold value of 1.25 for the ADC ratio to differentiate between benign and malignant portal vein thrombi.⁹

In addition, another study discovered that a cutoff value of 1.2 for the ADC ratio assisted in thrombus-type discrimination with a sensitivity of 98% and a specificity of 70%.¹⁶

These variances in the cutoff values can be attributed to several factors, such as the use of distinct hardware, the absence of standardized protocols for image collection (employing different b values), diverse approaches for calculating ADC, and variations in the patient population.

4. Conclusion

DW-MRI is a dependable method for differentiating between benign and malignant focal liver lesions. Additionally, it can ascertain the characteristics of portal vein thrombosis by estimating the ADC ratio between the tumor and the thrombus.

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