Original Article

The Efficacy of Diffusion MRI in Differentiating Bland and Malignant Portal Vein Thrombosis in Hepatic Patients Using ADC Values

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ABSTRACT

Background: Portal vein thrombosis may occur because of various hepatic or systemic conditions such as liver cirrhosis, neoplasms, inflammatory disorders and coagulopathy. Patients having cirrhosis or hepatic focal lesions may develop PVT, which could be either bland or malignant. Detecting malignant PVT plays a vital role in tumour staging, deciding treatment options, and predicting patient outcomes.

Aim: This work goals to evaluate the efficacy of diffusion MRI in distinguishing between bland and malignant PVT in hepatic patients by measuring the ADC value.

Material & method: The present retrospective study was performed on 35 patients confirmed, either pathologically or radiologically, to have hepatic focal lesions accompanied by visualized PVT based on the accepted radiological criteria. Patients were divided to benign and malignant PVT groups and the ADC values and ratios were calculated in the focal lesion and the thrombus.

Results: The ADC value of the portal vein thrombus showed a significant difference between the malignant and benign groups, scoring a cut off value at 1.3 which is convenient in differentiating between bland and malignant thrombi. The ADC ratio between the hepatic lesion and the thrombus also was found to have a significant difference at a cut off value at 1.2.

Conclusion: Diffusion MRI is a reliable method that can help in differentiating malignant and bland PVT by measuring the ADC value and ratio between the ADC of the PV thrombus and the hepatic focal lesion, yet dynamic contrast enhanced MRI or CT is still the standard used in practice with the aid of LI-RADS.

Key Words: ADC, cirrhosis, Diffusion weighted imaging, HCC, PVT.

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INTRODUCTION

Portal vein thrombosis has an incidence between 0.05% and 1%, which increases in patients with primary or secondary neoplasms. Cirrhosis is the most frequent of bland PVT, presenting 24% to 32% of cases. HCC is the most frequent cause of malignant PVT[1]. Both bland and malignant PVT can occur in patients having cirrhosis or neoplastic diseases. Detecting malignant PVT plays a vital role that impacts in tumor staging and treatment approaches[2].

Although contrast CT and MRI are used to distinguish bland from malignant PVT in, the differentiation is not always straightforward. Therefore, this study assesses the efficacy of diffusion MRI in identifying the nature of PVT[3].

Portal vein biopsy has several limitations as it relies on the skills of the physician. There is also a risk of errors in sampling, as cells could be taken from the adjacent tumor instead of the thrombus, which leads to inaccurate diagnoses. The procedure also carries other drawbacks such as bleeding. Other contraindications, such as renal function impairment and allergic reactions to contrast media, can also curb the use of contrast-based techniques[4].

In practice, the diagnosis relies on of laboratory tests and imaging findings together. The MRI can help differentiate malignant from bland PVT depending on the characterizations of the malignant thrombi that include dilatation of the calibre of the portal vein, having intermediate or high T2 signal, and showing arterial-phase enhancement similar to the associated tumor[5].

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Diffusion-weighted imaging (DWI) provides tissue characterization by evaluating water molecule diffusion. Malignant tissues show restricted diffusion due to increased cellularity, which results in lower apparent diffusion coefficient (ADC value) compared to bland ones. Adding, DWI does not require contrast agents, making it a safer alternative for patients contraindicated to receive contrast[6].

PATIENTS & METHODS

This retrospective study included 35 patients with a mean age of 60.4 years. All participants were diagnosed with liver cirrhosis or had focal lesions confirmed through pathological or radiological evidence, accompanied by visualized PVT on imaging based on the acknowledged radiological criteria as a standard of reference.

ETHICAL APPROVAL

An approval on the study protocol has been provided by Ain Shams University Faculty of Medicine's local research ethics committee (REC). No. FWA 000017585 (FMASU MS 524/2023).

Patient data was handled with strict confidentiality, ensuring it was protected against unauthorized access. The collected information was exclusively utilized for scientific purposes, and no personal details were disclosed.

Patient selection:

- **The Inclusion Criteria:** Patients aged above 18 years and pathologically or radiologically proven to have hepatic focal lesions along with the presence of PVT.
- **The exclusion criteria:** Clinically unstable patients. Patients younger than 18 years. Contraindicated patients for MRI, including those with: Pacemakers or other implanted cardiac devices, metallic foreign bodies, and claustrophobia.

Standard of Reference:

Based on the criteria used by Sandrasegaran[7] and Sakata[8], a portal vein thrombus is considered malignant when at least two out of three criteria are present which are: the enhancement within the thrombus, the size of the focal lesion is larger than 5 cm and the distance between the thrombus of the portal vein and the hepatic lesion is less than 2 cm. Otherwise the thrombus is however considered a benign PV thrombus. A rapid increase of the size of thrombus (within 3 months) during follow-up treatment indicates a malignant thrombus; therefore the stability of the thrombus for 12 months. By following these criteria, we reach the diagnosis of the malignant PVT by 94-100% sensitivity and specificity at 85-90%. In our study, we ensured the availability of all these criteria in our selected patients.

MR Examination:

This research utilized traditional MRI sequences, including: Axial T1TFE, Axial T2 TSE, Axial T2 SPAIR. In addition, post-Gd-DTPA and diffusion-weighted imaging (DWI) were taken by 1.5 Tesla Philips Ingenia, Philips Healthcare.

MR Protocol:

Pre-Contrast Parameters:

- The acquisition parameters of T1 (T1W) images were: TE=4.58msec, TR=10msec, FOV 355mm, 179x320 matrix, 7- 8mm slice thickness, 1- 2 mm slice gap.
- TR ≥445msec, matrix (180-200) x 240, TE 26-28msec, slice gaps= 1-2mm, in addition, the slice thickness of 7-8mm and the FOV 365 are characteristics of T2 weighted images captured throughout single-shot free breathing.
- Regarding Fat suppression T2 SPAIR, these parameters were used: TE of 80msec, TR ≥400msec, matrix dimensions of 204x384, 7-8mm slice thickness, slice gap of, 1-2mm, and the FOV was 365.

Dynamic Study:

This study employed the injection of a bolus of Gd-DTPA (0.1 mmol/kg body weight), after which 20 ml of 0.9% saline was flushed. Dynamic imaging was conducted in a triphasic manner after contrast administration The imaging phases included:an arterial phase lasting 16–20 seconds, a porto-venous phase lasting 45–60 seconds & a delayed equilibrium phase lasting 3-5 minutes.

Diffusion Study:

DWI was conducted at b values of 0, 500, and 1000 sec/mm² and the respiratory-triggered fat-suppressed single-shot echoplanar diffusion weighted imaging was performed in the transverse plane utilizing tri-directional diffusion gradients. The acquisition parameters were as follows: the TE was 70 milliseconds, with matrix size measuring 256x256, the number of excitations was3, the slice thickness ranged from 7 to 8 millimetres, the slice gap ranged from 1 to 2 millimeters and the FOV was rectangular and covered 52% of the area.

Imaging Evaluation:

The features of hepatic lesions were analysed, including the pattern of enhancement, the size of the lesion, and the distance between PVT and the tumor.

ADC values (mean and standard deviation) of the focal lesion and the thrombus (PVT) were carefully measured. We calculated the ADC ratio by diving the ADC value of the thrombus by the ADC value of the lesion

ADC Calculation:

To determine the ADC of the thrombus and the ADC ratio (which means the ratio between the ADC value of the thrombus and the ADC value of the tumour) ADC values were measured by manually placing ROIs (oval regions of interest) over the lesion and the thrombus. Care was taken to exclude areas outside the lesion or thrombus from the ROI to ensure accurate measurement.

Statistical Analysis:

All analyses were achieved using IBM SPSS. Qualitative variables were presented as percentages. Quantitative data with parametric distributions were expressed as means, standard deviations, and ranges.

Utilizing independent t- test, 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.

To determine the exact cut-off point, the ROC curve was utilized which considered its specificity, sensitivity, positive predictive value (PPV), negative predictive value(NPV), and area under the curve (AUC). The p-value at less than 0.05 is considered significant and at 0.01 is highly significant, yet, non-significant when it scores less than 0

RESULTS

Out of the 35 studied patients, there were 25 malignant PVT and 10 bland PVT patients based on the standard reference criteria.

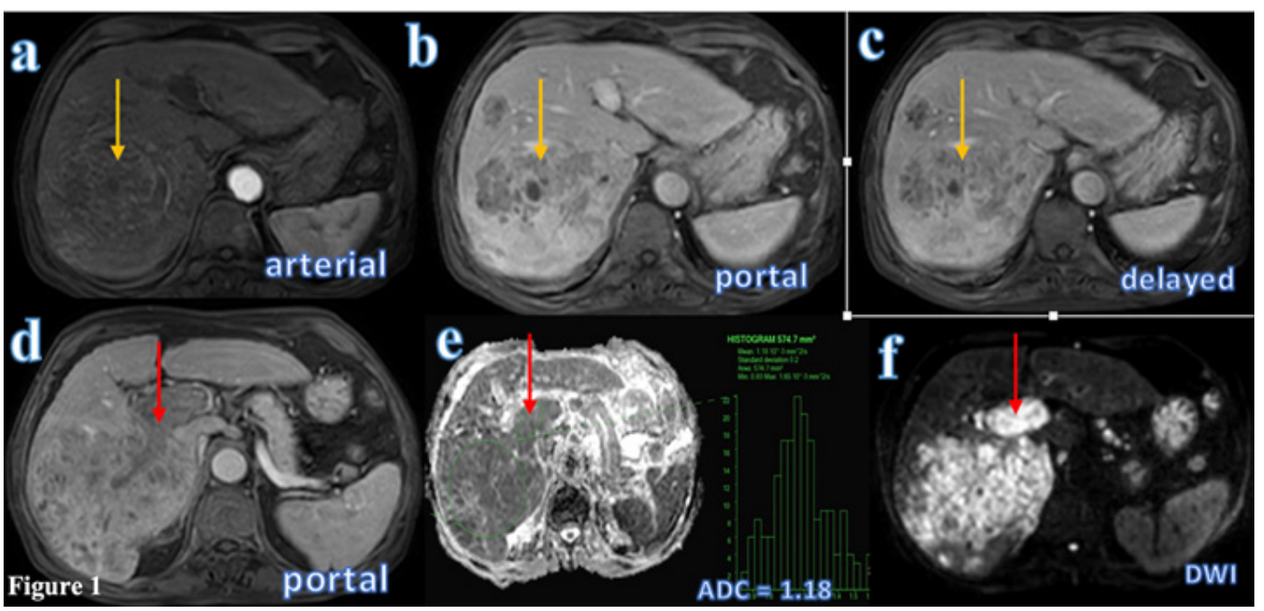

Fig. 1 : A 71 year-old cirrhotic patient. (a) Arterial, (b) porto-venous and (C) Delayed images show ill-defined heterogeneously enhancing lesion occupying most the right hepatic lobe segments and smaller segment VIII focal lesions with enhancement pattern keeping with HCC(yellow arrows). (d) Portal phase showing a mass is seen infiltrating the right main portal vein (red arrows). (e) ADC map showing PVT; ADC value = 1.18 x 10^{-3} mm^2/s keeping with malignant PVT. (f) DWI showing restricted diffusion.

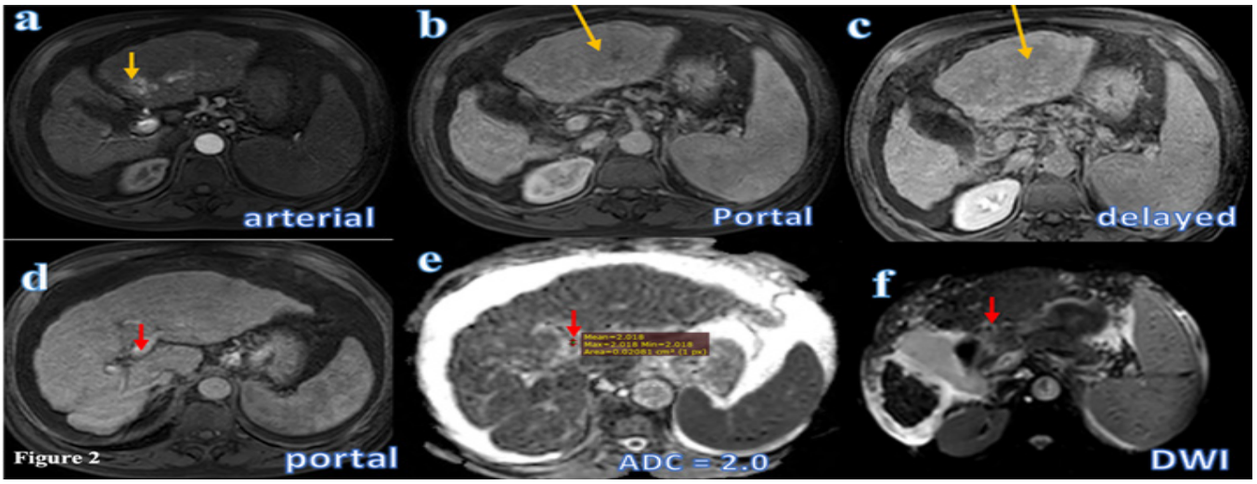

Fig. 2: A 72 year-old cirrhotic male patient. (a) Arterial, (b) porto-venous and (C) Delayed images show ill-defined heterogeneously enhancing lesion, keeping with HCC (yellow arrows). (d) Portal phase showing partial left PVT (red arrows). (e) ADC map showing PVT; the ADC value = 2.0 x 10^{-3} mm^2/s keeping with bland PVT. (f) DWI showing restricted diffusion.

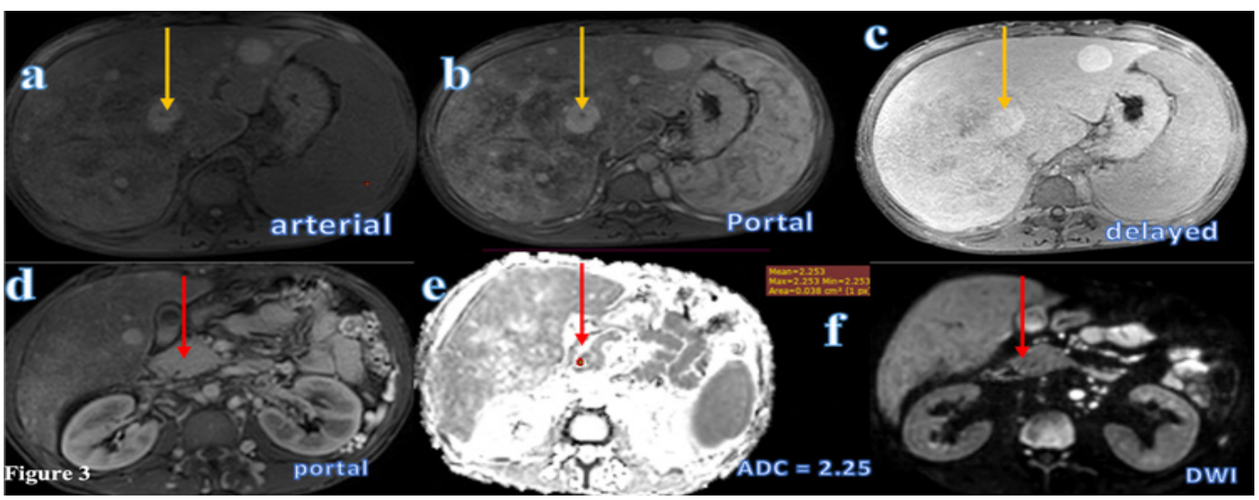

Fig. 3: A 31 year-old known case of Budd-Chiari Syndrome. (a) Arterial, (b) porto-venous and (C) delayed images showing hepatomegaly, with multiple bi-lobar focal dysplastic nodules (yellow arrows). (d) Portal phase showing chronic portal vein thrombosis and portal vein cavernoma(red arrows).(e) ADC map showing PVT ; ADC value = 2.25 x 10^{-3} mm^2/s keeping with bland PVT. (f) DWI showing restricted diffusion

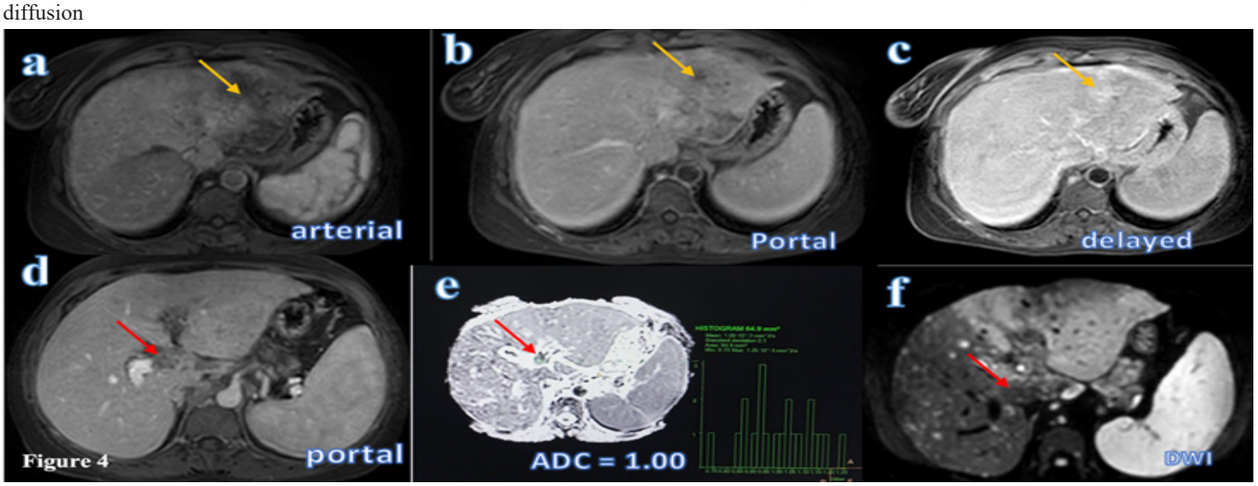

Fig. 4 : A 41 year-old female, a reported case of HBV and previously treated for HCV. (a) Arterial, (b) porto-venous and (C) Delayed phases images show ill-defined infiltrative lesion centered to the left hepatic lobe, showing enhancement pattern keeping with HCC (yellow arrows). (d) Portal phase shows that the left PV and its segmental branches are distended and occluded by a thrombus showing enhancement (red arrows). (e) ADC map showing PVT; ADC value = 1 x 10^{-3} mm^2/s keeping with malignant PVT. (f) DWI showing restricted diffusion.

Table 1: Comparing benign and malignant portal vein thrombosis cases regarding the liver focal lesion, PV distribution and tumor size.

		Malignant PVT	Benign PVT	Test value	*P-value*	Sig.
		No.= 25	No.= 10			
Lesion	HCC	20 (80%)	7 (70%)	0.405	0.524	NS
	FNH	0 (0%)	1 (10%)	2.574	0.109	NS
	Mets	1 (4%)	0 (0%)	0.412	0.521	NS
	HCC + Mets	1 (4%)	0 (0%)	0.412	0.521	NS
	Cirrhotic	0 (0%)	1 (10%)	2.574	0.109	NS
	Cholangio	3 (12%)	0 (0%)	0.412	0.521	NS
	Buddchiari	0 (0%)	1 (10%)	2.574	0.109	NS
PV distribution	Right	12 (48%)	0 (0%)	8.960*	0.030	S
	Left	4 (16%)	3 (30%)			
	Main	9 (36%)	6 (60%)			
	Right + Left	0 (0%)	1 (10%)			
Tumor size (cm)	Mean ± SD	8.25 ± 3.72	3.38 ± 0.68	4.077•	0.000	HS
	Range	3.5 – 18	2.2 – 4.4			

The hepatic focal lesion size in patients with malignant PVT ranges from 3.8 cm to 18 cm (8.25 cm) and the size in patients with benign PVT ranges from2.2 cm to 4.4 cm (3.38 cm).

Table 2: Comparing benign and malignant PVT cases regarding mean ADC value of the portal vein thrombus and the ratio between the PV thrombus and the hepatic focal lesion.

		Malignant	Benign	Test value	*P-value*	Sig.
		No.= 25	No.= 10			
Mean ADC PVT	Mean ± SD	1.07 ± 0.14 x10^{-3} mm^2/s	2.03 ± 0.14 x 10^{-3} mm^2/s	-17.999•	0.000	HS
	Range	0.82 – 1.3 x10^{-3} mm^2/s	1.77 – 2.25 x 10^{-3} mm^2/s			
Ratio	Mean ± SD	1.06 ± 0.1	2.24 ± 0.46	-12.372•	0.000	HS
	Range	0.7 – 1.2	1.7 – 3.4			

Patients with malignant PVT cases regarding mean ADC value of the portal vein thrombus and the ratio between twhen compared to patients with benign PVT (1.07 x 10^{-3} mm^2/s ± 0.14vs 2.03 x 10^{-3} mm^2/s ± 0.14; *P*=0.000).

Patients with malignant PVT show a significantly lower ADC ratio (1.06 ± 0.1vs 2.24 ± 0.46; *P*=0.000) when compared to patients with benign PVT.

The ROC curve revealed that a cut off value of ADC at 1.3 x 10^{-3} mm^2/s or less had significant discriminative ability to detect malignant PVT among the studied cases with sensitivity at 100% and specificity 100%.Also, a cut off value of ADC ratio of PVT 1.2 or less can detect malignant PVT among the studied cases.

DISCUSSION

The presence of malignant (PVT) is considered crucial in tumor staging and treatment options because it is considered an absolute contraindication for liver transplantation, therefore, it is necessary to accurately distinguish between bland and malignant PV thrombosis[9]. Although biopsy stays the gold standard test to distinguish bland from malignant PVT, it unfortunately is an invasive procedure with potential complications. To counter these limitations, non-invasive imaging procedures, such as ultrasonography[10], CT scan[11], and MRI[12] are used. However, accurately distinguishing bland from malignant PVT remains challenging.

Dynamic contrast-enhanced imaging can help in differentiation, as malignant PVTs often exhibit thrombus enhancement and lumen expansion[13]. However, some patients are contraindicated for contrast because of renal function impairment or prior contrast media reactions. Therefore, deploying a reliable and a non-invasive diagnostic technique with high accuracy is essential for distinguishing benign from malignant PVT[14].

The current study goals to validate the usage of DWI in detecting and characterizing portal vein thrombosis (PVT) associated with hepatic focal lesions by measuring ADC

values of 35 patients with confirmed hepatic lesions and visible PVT who were categorized into two groups:

- Benign PVT group: 10 patients
- Malignant PVT group: 25 patients

In the present study, malignant PVT cases had significantly lower mean ADC values (1.07 ± 0.14 vs. 2.03 ± 0.14; $P = 0.000$) and ADC ratios (1.06 ± 0.1 vs. 2.24 ± 0.46; $P = 0.000$) compared to patients with benign PVT.

Similarly, ***Ali et al.***[15] found that neoplastic thrombi had significantly lower ADC values than non-malignant venous thrombi (1051.25 ± 256.56 vs. 1794.29 ± 463.83 mm²/s, $P = 0.000035$).In addition, the ADC ratios of neoplastic thrombi were markedly low compared to non-malignant venous thrombi (1.27 ± 0.4352 vs. 2.09 ± 0.6667, $P = 0.000755$).

Also, ***Huang et al.***[16] results obtained from 140 patients with portal vein thrombosis (PVT) showed that the ADC values in malignant thrombi were lower than the bland ones (0.62 ± 0.17 vs. 0.72 ± 0.32, $P = 0.034$).

In addition, ***Aumann et al.***[9] studied 35 patients with PVT and reported that the ADC values of malignant thrombi were considerably lower than the benign PVTs ($P = 0.005$). They attributed this difference to the restricted diffusion in malignant tissues caused by their greater cell density. Malignant PVTs exhibit greater cellular content compared to benign PVTs, resulting in lower ADC values.

Moreover, a similar study that included 50 patients (33 patients with malignant PVT & 17 benign PVT cases) reported that mean ADC values for malignant PVT was obviously less than the ADC the benign PVT (0.7 ± 0.1 vs 1.1 ± 0.1 respectively; P=0.001)[17].

In disagreement with our findings, in ***Gawande et al.***[13] study which was conducted on 39 patients with PVT, they found no significant differences evaluating DWI and ADC maps. ***Gawande et al.*** attributed that to that the method was different than other approaches, depending on a qualitative assessment and using different b-values.

The variation in these cut-off values is due to several factors such as the use of different MRI hardware, variations in image acquisition protocols (e.g., differences in b-values), diverse methods for calculating ADC, and variations in patient populations across studies.

In the present study, the ROC curve analysis demonstrated that an ADC cut-off value at ≤1.3 × 10^{-3} mm²/s had a significant discriminative ability for detecting malignant PVT among the studied cases. This threshold achieved a 100% sensitivity and 100% specificity. Also, acut off value of ADC ratio of PVT of 1.2 or less has the ability to detect malignant PVT.

Similarly, Osman and Samy[17] reported that the ROC curve analysis revealed a cut-off value of ADC ≤1.0 for distinguishing malignant from benign PVT, with 100% sensitivity & 82.5% specificity ($P = 0.001$).

Also, according to ***Abd El et al.***[18] observed that an ADC ratio cut-off value at 1.2 distinguished malignant from non-malignant thrombi with 98% sensitivity & 70% specificity.

Additionally, ***Aumann et al.***[9] reported that ADC values revealed a sensitivity at 80.0% and specificity at 72.7% for distinguishing malignant from benign PVT, using a cut-off value of ≤1.00 × 10^{-3} mm²/s ($P = 0.005$).

Similar to our study, ***Ali et al.***[15] reported that the ADC ratio cut-off value of 1.25 effectively differentiated malignant from non-malignant PVT, with 85% sensitivity & 81% specificity.

Huang et al.[16] however revealed area under the ROC curve for SIRADC 0.619 with a 45.9% sensitivity and 83.3% specificity with a cutoff value of 0.791.

Instead, ***Ahn et al.***[19] observed that ADC value had a sensitivity of only 22.2% for differentiating benign from malignant PVT. This low sensitivity was due to a wide range of ADC values and significant overlap between the two groups. They referred the variability to some factors such as the stage of the thrombus, as benign PVT could sometimes exhibit low ADC values similar to malignant PVT.

CONCLUSION

Diffusion MRI is a reliable method that can help in differentiating malignant and bland PVT by measuring the ADC value and ratio between the ADC of the PV thrombus and the hepatic focal lesion, yet dynamic contrast enhanced MRI or CT is still the standard used in practice with the aid of LI-RADS.

AUTHOR CONTRIBUTIONS

All the authors have added to the work in the design of the study, analysis and reviewing the article.

CONFLICT OF INTERESTS

There is no conflicts of interest.

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فعالية التصوير بالرنين المغناطيسي الموزن بمعامل الانتشار في التفريق بين تجلط الوريد البابي الحميد والخبيث في مرضى الكبد

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المقدمة: يحدث تجلط الوريد البابي نتيجة لعدة حالات منها تليف الكبد، الأورام، الأمراض الالتهابية، وحالات فرط التخثر و يُعد تليّف الكبد هو السبب الأكثر شيوعًا لتجلط الوريد البابي الحميد عند البالغين، كما يزداد حدوث تجلط الوريد البابي في المرضى الذين يعانون من الأورام الخبيثة الأولية أو الثانوية. المرضى الذين يعانون من تليّف الكبد أو الأورام قد يصابون إما بتجلط الوريد البابي الحميد أو الخبيث. يُعد وجود تجلط الوريد البابي الخبيث عاملاً مهمًا في تحديد النهج العلاجي المناسب والتشخيص.

هدف هذه الدراسة: تهدف هذه الدراسة إلى تحديد فعالية التصوير بالرنين المغناطيسي المنتشر في التمييز بين تجلط الوريد البابي الحميد والخبيث في مرضى الكبد.

المرضى و طرق البحث: هذه الدراسة هي دراسة بأثر رجعي. تم إجراء فحص التصوير بالرنين المغناطيسي الديناميكي والتصوير الموزون بالانتشار على ٣٥ مريضًا.

يتم حساب قيم و نسب ADC معامل الانتشار الظاهر من الآفة البؤرية و الجلطة.

تُستخدم المعايير الإشعاعية المقبولة المحددة كمعيار مرجعي للكشف عن طبيعة الآفة البؤرية و الجلطة والتمييز بين الجلطة الحميدة والجلطة الخبيثة.

النتائج: قمنا بتضمين مجموعة ٣٥ حالة مصابة بتجلط الوريد البابي. أظهرت قيم معامل الانتشار الظاهر والنسبة بين الخثرة والآفة البؤرية فرقًا كبيرًا بين المجموعتين الخبيثة والحميدة، حيث سجلت قيمة قطع للخثرة عند ١,٣ وهو أمر مفيد في التمييز بين الخثرات الحميدة والخبيثة و قيمة قطع ١.٢ للنسبة بين الخثرة والآفة البؤرية.

الاستنتاج: التصوير بالرنين المغناطيسي المنتشر هو وسيلة موثوقة في التمييز بين تجلط الوريد البابي الخبيث و الحميد عن طريق قياس نسبة معامل الانتشار الظاهر بين الخثرة والآفة البؤرية الكبدية. يظل التصوير بالرنين المغناطيسي أو التصوير المقطعي المحوسب المعزز بالتباين الديناميكي هو المعيار المستخدم في الممارسة العملية بمساعدة LIRADS.