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Orginal Article

The role of dynamic and diffusion weighted magnetic resonance imaging in differentiating malignant and benign portal vein thrombosis

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Abstract

Aim: The aim of this study was to evaluate the role of dynamic and diffusion-weighted (DW) magnetic resonance imaging (MRI) in the differentiation of benign from malignant thrombus in patients diagnosed with portal vein thrombosis.

Material and Methods: A total of 56 patients were analyzed, 27 with benign and 29 with malignant thrombus on abdomen dynamic and DW MRI. The b-value of DW MRI was 400 and 1,000 mm2/sec. ADC of portal vein thrombosis was measured. Characteristics of the DW MRI signal were recorded. Contrast imaging of the thrombus was performed. The diameter of the portal vein was measured. A comparison of the ADC values between the malignant and benign groups was made using the Mann-Whitney U test.

Results: The mean ADC values of benign thrombus were calculated as 1.03±0.27 x 10-3 mm2/sec for b400, and 1.01±0.23 x 10-3 mm2/sec for b1000. The mean ADC values were calculated as 0.93±0.13 x 10-3 mm2/sec for b400 and 0.88±0.26 x 10-3 mm2/sec for b1000 for malignant thrombus. No statistically significant difference was found between the groups (p=0.778). Malignant thrombus was reported to have higher signal intensity compared to the benign cases in DW MRI. Arterial mild contrasting was found with malignant thrombus with dynamic MRI on subtraction images. Statistically, a significant difference was found between the groups for portal vein diameter (p<0.05).

Conclusion: Our results show that the DW MRI signal characteristics and dynamic MRI contrast media enhancement, with measurements of thrombosed portal vein diameters, are helpful in the differential diagnosis.

Keywords: Dynamic MRI; Diffusion-Weighted Imaging; Apparent Diffusion Coefficient; Portal Vein; Thrombus.

INTRODUCTION

Portal vein thrombosis (PVT) is a common pathological condition. It is one of the important causes of non-cirrhotic portal hypertension. Many pro-thrombotic factors and local abdominal conditions (myeloproliferative diseases, cirrhosis, pancreatitis, pregnancy, trauma, etc.) may cause PVT (1,2).

The most common cause of PVT is chronic liver disease, followed by malignancies such as a hepatocellular carcinoma (HCC), pancreatic cancer, and carcinoma of the bile ducts. Of the patients diagnosed with a HCC, 10 to 44% had a malignant thrombus in the portal vein, also 42% had a benign thrombus (3,4).

Establishing the definite diagnosis of PVT is very important for treatment and prognosis. Particularly in cirrhotic patients, malignant PVT can be a problem during advanced treatment interventions (resection, or liver transplantation) (5). In addition, the presence of malignant PVT for malignant patients plays an important role in determining tumor staging, appropriate therapeutic approach and their prognosis (6,7).

Radiologically, ultrasonography (US), Doppler US, multidetector computed tomography (MDCT) and endoscopic US (EUS) were used for diagnosis of PVT. They may serve as supportive measures, not definitive diagnosis. Laboratory analysis also may not provide definitive results.

In Doppler US, if the current signal is taken in the thrombus mass with form of an arterial wave during spectral examination, it may be considered for malignant thrombosis (8). Intravenous contrast media (IVCM) uptake with MDCT is valuable in the diagnosis of malignant thrombosis (9).

However, it may not be possible always to make the definite diagnosis in cases where optimal Doppler US cannot be evaluated and in those an IVCM uptake cannot

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be clearly detected to conditions such as iodine allergy and renal impairment with MDCT.

In the present study, we aimed to evaluate the role of dynamic MRI and DW-MRI in the differentiation of benign from malignant thrombus.

MATERIAL and METHODS

After obtaining an approval for the study from the Institutional Ethics Committee of Firat University, between March 2014 and May 2017, the files of 56 patients who were diagnosed with PVT were analyzed. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The mean apparent diffusion coefficient (ADC) of the thrombosis was measured using ADC mapping. Characteristics of the DW-MRI signal were recorded. Contrast imaging of the thrombus was performed during arterial phase imaging using dynamic abdominal MRI. Contrast agent was used (0.1 mL/kg) (Primovist; Bayer Healthcare, Berlin, Germany) at a rate of 1 mL/s followed by a saline flush using a power injector. The diameter of the main portal vein with thrombosis was measured. Thrombosis leading to expansion and portal vein direct invasion with contrast enhancement was evaluated as a malignant.

MRI examination

The 1.5T (Ingenia, Philips) MRI device was used for MRI analysis. All patients were analyzed using the 32-channeled body coil and under respiratory monitoring. Diffusion analyses were performed on all patients with the b 400 and b 1000 values, and ADC mappings were obtained from these analyses. The ADC mappings and other measurements were performed by a radiologist with experience in abdominal radiology.

The following parameters were used in the T2A fast spin-echo images obtained from the patients: Matrix: 288x251, Number of Excitations (NEX): 1.0, Field of view (FOV): 40x35 cm, cross-sectional thickness: 5 mm, space between cross-sections: 0.5 mm, Repetition Time (TR): 441 msn, TE: 80 msn.

The following parameters were obtained from the DW images: Matrix: 132x114, Number of Excitations (NEX): 2.0, Field of view (FOV): 40x35 cm, cross-sectional thickness: 5 mm, space between cross-sections: 0.5 mm, Diffusion direction: All directions, Repetition Time (TR) and Echo Time (TE): minimum.

A dynamic series consisted of one pre-contrast series followed by early arterial, late arterial and portal phase imaging with 32-second intervals for the start of each phase imaging.

The ADC measurements were performed at the General Electric Company (GE) Advantage Workstation Release 4.6 software working station. The ADC mappings were generated by the device using DW images. The ADC values were measured through circular examination of the region of interest (ROI). The circular examination area was standardized to be 5 mm², and the measurements were performed in each patient from three sites of thrombosis.

Statistical Analysis

The mean ADC values and standard deviation values of these three measurements were calculated. The ADC values of the patients were compared with the clinical and histopathological results of the patients. A comparison of the ADC values between the malignant and benign groups was made using the Mann-Whitney U test. A p value of <0.05 was considered statistically significant.

RESULTS

Of the patients, 36 were men (64%), remaining 20 were women (36%) with a median age of 62 years (range: 43 to 79 years). Of the PVT, 27 were benign and 29 were malignant. The patients diagnosed with malignant PVT, 20 had HCC (69%), six had cholangiocellular carcinoma (21%), two had gastric cancer (7%), and one had hepatoblastoma (3%). On the other hand, of the patients diagnosed with benign PVT, 13 had pancreatitis (48%), five had collagenous vascular disease (19%), four had a history of surgical operation (14%), and five had a history of trauma (19%). 5 patients had concomitant mesenteric and splenic thrombosis (17%)with malignant PVT.

The mean ADC values of benign thrombus were calculated as 1.03±0.27 x 10-3 mm2/sec and for b 400, and 1.01±0.23 x 10-3 mm2/sec for b 1000, median (1.1). Values of malignant thrombus were calculated as 0.93±0.13 x 10-3 mm2/sec for b 400 and 0.88±0.26 x 10-3 mm2/sec for b 1000, median (0.9). No statistically significant difference was found between the benign and malignant groups for both b values of mean ADC values (p=0.778).

All patients diagnosed with a malignant thrombus had high signal intensity with DW-MRI examination, whereas there was no diffusion limitation in the benign group. Mild arterial contrasting was observed in malignant thrombus cases on arterial phase images with dynamic MRI on subtraction images (Figure 1A-D, 2A-D).

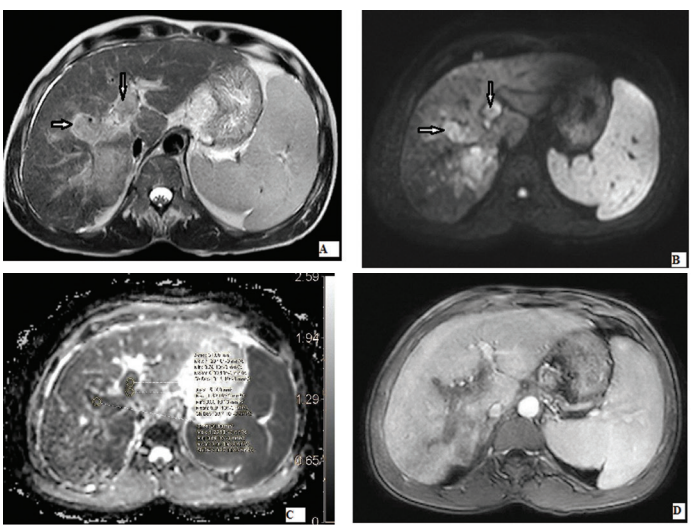

Figure 1. Axial T2 MR Image shows thrombus in the right and left portal vein with HCC **(a).** DW MR Image shows high signal intensity in the thrombus **(b).** Mean ADC was measured for the 3 ROIs as 0.91×10−3, 0.99×10−3 and 0.93×10−3, mm2/s with b 400 **(c).** Dynamic MR Image demonstrates mild arterial contrasting in malignant thrombus **(d).**

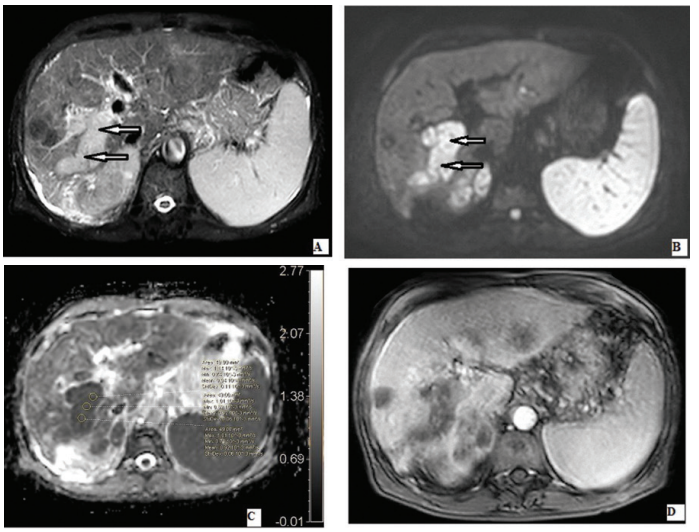

Figure 2. Axial T2 MR Image revealed a large thrombus in the right portal vein **(a).** DW MR Image shows high signal intensity in the thrombus **(b).** Mean ADC was measured for the 3 ROIs as 0.92×10−3, 0.94×10−3 and 0.92×10−3, mm2/s with b 400 **(c)**. Dynamic MR Image shows mild arterial contrasting in malignant thrombus with liver metastasis **(d).**

However, contrast uptake in the benign group was very poor and could not be clearly assessed (Figure 3a-c).

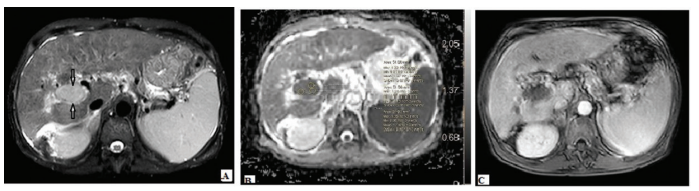

Figure 3. Axial T2 MR Image revealed a large thrombus in the main portal vein **(a).** Mean ADC was measured for the 3 ROIs as 1.07×10−3, 1.13×10−3 and 1.14×10−3, mm2/s with b 400 **(b).** Dynamic MR Image shows no arterial contrasting in benign thrombus **(c).**

The median main portal vein diameter of the benign group was 15.8 mm (12-18 mm), and 18.2 mm (13-22 mm) in the benign and malignant group respectively. Statistically significant difference was found between the benign and malignant groups in vein diameters with thrombosis ($p<0.05$). The results are summarized in Table 1.

Table 1. The details of detected lesions in 56 patients

	Benign group (n=27)	Malignan group (n=29)	P
Patient age (years)	48±12.6	54.1±9.8	.201
Diameter (cm)	15.8±5.6	18.2±5.7	.171
ADC values of b400	1.03±0.27	0.93±0.13	.775
ADC values of b1000	1.01±0.23	0.88±0.26	.778

Data are mean ± S.D. ($\times 10^{-3}$ mm^2/s)

DISCUSSION

Portal vein thrombosis is an important cause of pre-sinusoidal portal hypertension. Two forms of the disease have been described, the acute and chronic forms. Sudden onset clinical findings have been reported in patients with acute portal vein thrombosis. However, in chronic cases, portal hypertension and cavernous transformation are known to develop. Although the etiology is generally multifactorial, cirrhosis of the liver is the most common cause. In non-cirrhotic and non-malignant patients, other diseases leading to a thrombophilic process are the leading cause (10). The clinical course of acute PVT is associated with the dissemination of thrombosis and rate of formation. Patients may sometimes be asymptomatic, but also present with abdominal pain, fever or dyspeptic symptoms. Bleeding esophageal varices may be the first finding, particularly in patients with cirrhosis. Although patients with chronic PVT may be asymptomatic, findings associated with portal hypertension (esophageal varices, gastric varices, splenomegaly, hypersplenism) are generally remarkable (11,12).

The main predisposing factors for PVT in cirrhosis include, slow portal blood flow, decreased liver synthesis function (protein C, S, and anti-thrombin 3), and increased incidence of HCC (10). The main factor in malignant cases is intravascular invasion of the tumor. This may also be caused by thrombogenic factors released by the tumor and a decrease in flow associated with mass compression (13).

Tumor thrombus in the portal vein is an important complication and a prognostic factor in the patients with malignancy. Particularly in patients examined due to HCC, definition of malignant and benign differentiation is very important (5-7). Rapid initiation with appropriate treatment and improvement of prognosis with PVT is achieved through making of the definite diagnosis as early as possible. By the way, in clinical practice, the definite diagnosis of malignant and benign PVT cannot always be possible. Laboratory analysis may not provide definitive results during the diagnostic stage. They may serve as supportive measures. Laboratory abnormalities may include, elevation of liver enzymes, elevation of inflammatory markers such as CRP, white blood cells, and erythrocyte sedimentation rate, elevated hematocrit levels secondary to hemoconcentration, hyperbilirubinemia, elevated INR, leukopenia-thrombocytopenia-anemia associated with hypersplenism, elevated urea-creatinine levels, and hypoalbuminemia (13).

Radiological analysis should be made in suspected patients to detect the presence of thrombus. Although the superiority of imaging analyses is similar, Doppler US is primarily used for diagnostic procedures. Doppler US is a useful modality due to its low cost, repeatable, noninvasive nature, and its ability to easily reveal biliary pathologies. In Doppler US, thrombus is observed as a hypo-hyperechoic solid material in the portal vein. In addition, increase in the diameter of the portal vein may be occurring. The thrombus may sometime extend to the superior mesenteric vein and/or the splenic vein depending on the severity of the disease (9).

The contrast enhanced by US (CEUS), has been reported to show lack of luminal flow. CEUS has been shown to

have a high sensitivity (88-97.7%), and 100% specificity, and also an approximately 92.5 to 95 % accuracy rate. The sensitivity of CEUS is higher than MDCT (67%). The sensitivity of CEUS is reported particularly increased in non-occlusive PVT cases (14,15). However, it is quite expensive to use in routine diagnosis.

The superiority of MDCT from other modalities permits the easy visualization of predisposing factors such as HCC. It can also be more informative about the presence of other intraabdominal pathologies. On the other hand, MRI can be preferable in cases where exposure to radiation is to be avoided. It has a similar diagnostic specificity and sensitivity ratio to MDCT. In dynamic MRI, a thrombus is observed as a soft tissue value that fills the portal vein. In MR angiography it is observed as a partial or complete filling defect. In patients with chronic PVT, collaterals in the porta hepatica can be visualized well (16,17).

DW-MRI is known as MRI with sequential features adjusted to diffusion differences between tissues. In DW-MRI, strong gradients are added to make the sequence susceptible to diffusion (18). An inverse relationship has been demonstrated between the amount of diffusion and cellular density of the tissue. Diffusion is inhibited in tissues with excess cellular density, and under conditions where a high signal is obtained in DW-MRI, diffusion increases and a low signal is observed when the cellular density is low (19).

DW-MRI was first used in cranial imaging in the diagnosis and follow-up of stroke, and its use has been accelerated by the in other parts of the body using of rapid MRI sequences such as echo-planar imaging (18,19). DW-MRI can be used in all MRI devices, with 1.5 Tesla and above. It does not involve any extra cost, and can be said to be cheaper when compared to routine abdominal MRI due to lack of the need for contrast medium. Moreover, since DW-MRI sequence is a rapid sequence, it is also advantageous for patient comfort in terms of duration involved.

ADC measurement with DW-MRI is effective in the differential diagnosis of benign and malignant tumors of different regions of the body. It is used for the diagnosis of many abdominal organs, and in urinary and pelvic cancers (20-21).

The ADC value is an indication of the numerical amount of diffusion. The main determinant of the ADC signal is the amount of diffusion in the tissues. However, perfusion and blood flow also affect signal, although in small quantities. The unit of ADC is mm2/sec. The ADC value has been demonstrated to have a negative correlation with cellular density of the tumor. Cellular density of malignant tumors is generally higher than that of benign tumors and normal surrounding tissue. As a result, when compared to benign tumors, in malignant tumors DW-MRI also provides a bright signal reflecting the restricted diffusion, and low ADC values in ADC mapping. However, signal intensities of the blood clot cause various signal intensities on the DW-MRI, with T2 brightness or T2 dimming effects, depending on the age of bleeding (22). Most studies on hematoma ADC measurements have shown results with a predisposition for low values (23,24). In cases with hyper acute hematoma, ADC values may decrease due to the high viscosity secondary to extracellular space shrinkage. Moreover, in acute and early subacute stages, low values may be observed in ADC due to magnetic susceptibility effects caused by paramagnetic intracellular deoxyhemoglobin and methemoglobin (24).

In this study and in a few of literature studies, no statistically significant differences were demonstrated between different b values with malignant and benign PVT ADC values due to reasons mentioned above (25). Beside this, particularly in malignant thrombotic tissues, high signal intensities are observed in DW-MRI, due to high cell density and secondary to prevented diffusion. In addition to these findings, the thrombotic diameter measurement and evaluation of contrast media uptake would have contributed to the literature about the differential diagnosis.

There are some limitations to this study. Benign and malignant mean ADC values that have been reported, and consequently recommended ADC threshold values can vary widely in the literature. The reason for this is the fact that the ADC value is affected by the specifications of the device; the shooting parameters and the b value are used. Every center may have to determine its own ADC threshold according to the technique used by the center. Although it can be seen as an alternative, attempts to decide depending only of DW-MRI signals can be misleading. The signal-to-noise ratio and the geometric resolution are reported to be low with DW-MRI. MRI is also not recommended in patients with contraindications (18,19).

CONCLUSION

Particularly in patients with PVT who are examined due to malignancy, definite malignant and benign differentiation is very important to treatment and following the prognosis. When the laboratory and routine radiological examinations may not give definitive results, dynamic and DW-MRI findings may contribute to the differential diagnosis of malignant PVT.

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