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The utility of diffusion-weighted magnetic resonance imaging in differentiation of benign and malignant diffuse colon wall thickening**Mustafa Koc, Selami Serhatlioglu***Firat University, Medical Faculty, Department of Radiology, Elazig, Turkey*

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Abstract

To examine the effectiveness of apparent diffusion coefficient (ADC) values in differentiation of benign bowel wall thickening and malignant diffuse scirrhous type's bowel wall thickening. Subject and Methods A total of 81 patients who underwent abdomen diffusion-weighted magnetic resonance imaging (DW MRI) in our clinic between April 2015 and September 2016 was analyzed. Of these patients, 42 had benign bowel wall thickening and 39 had malignant bowel wall thickening. The values of ADC were measured with two different b-values (400, 1000 s/mm²). Benign and malignant ADC values were compared using areas under the receiver-operating characteristic (ROC) curve. Results: According to the ADC values, the mean ADC values (x10⁻³ mm²/s) of benign lesions were 1.42±0.17 for b 400, 1.39±0.12 for b 1000. The mean ADC values (x10⁻³ mm²/s) of malignant lesions were 1.08±0.15 for b 400, 1.02±0.13 for b 1000. There were significantly lower ADC values in malignant lesions in all b values (P=.001 for b 400, P=.001 for b 1000). ROC analysis showed that a cut-off value of 1.24 x 10⁻³ mm²/s between the malignant and benign values with a sensitivity of 91 %, specificity of 85 %, and an accuracy of 84 %. The positive predictive value, negative predictive value, and diagnostic accuracy of ADC values were determined to be 97 %, 86 %, and 88 % respectively. Conclusion: Measurement of ADC values by DWI was effective in differentiation of malignant diffuse scirrhous types of bowel wall thickening from benign bowel wall thickening.

Keywords: Colon cancer, Inflammatory bowel disease, Diffusion-weighted imaging, apparent diffusion coefficient**Introduction**

Colon cancer (CC), which affects 5% of the overall population of the United States of America (USA), Europe, and Western countries, is one of the major causes of cancer-related morbidity and mortality. In the USA, it is the third most common cause of new-onset and fatal cancer disease in men, after prostate and lung cancer and in women after breast and lung cancer. The risk of developing invasive CC increases with age, and 90 % of cases develop the disease after the age of 50 years. It most commonly affects the individuals in the sixth and seventh decades of life [1].

Main risk factors which are considered to play a role in the development of CC include age, diet, medical history, family history, and the presence of inflammatory bowel disease (IBD) [2]. Diagnosis can be easily made radiologically for polypoid or vegetative (cauliflower) types of cancer. However, early diagnosis of CC presenting as diffuse bowel wall thickness (scirrhous types)

is very complicated. Scirrhous cancers can be easily confused with benign pathologies of the colon, such as IBD, ischemic or infectious diseases. Furthermore, it has very rapid dissemination by lymphatic and hematological routes, and delayed clinical obstructive symptoms.

Although multidetector computed tomography (MDCT) has been widely used as the primary imaging modality for the evaluation of colon mural thickening, magnetic resonance imaging (MRI) can yield more detailed information due to its excellent contrast resolution. MRI is also superior to MDCT in the assessment of pericolic invasion, lymph node involvement, evaluation of treatment response [3,4].

Diffusion-weighted MRI (DW MRI) is in which sequence features are adjusted to bring out the differences of the tissues. Strong gradients are added to sensitize the sequential diffusion. It is also a useful method for abdomen. In abdominal imaging, DW MRI has been mainly suggested for the characterization of colorectal cancer, lymph nodes, and metastases [5-8].

In this study, we aimed to evaluate the role of DW MRI on the differentiation of benign and malignant diffuse bowel wall thickening to be use early detection of scirrhous type CC.

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Material and Methods

Patient Enrollment

The study protocol was approved by the Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki. Data of a total of 81 patients who underwent 1.5T MRI and abdominopelvic DW MRI in our clinic between April 2015 and March 2016 were analyzed. The threshold for wall thickening was determined as ≥ 3 mm for the bowel, and ≥ 5 mm for the rectum. The mean diffusion wall thickening apparent diffusion coefficient (ADC) value was calculated by ADC mapping.

MRI examination

The 1.5T MRI device (Philips Ingenia, USA) was used for MRI scanning. All patients were placed in the supine position with the head placed first into the device. The patients were prepared for analysis using a 32-channel body coil, accompanied by pulmonary monitoring. The patients were also informed about the instructions. Communication with the patient during the process was made with the assistance of hearing aid systems compatible with MRI. None of the patients were sedated during the imaging procedure. The ADC mapping of all the patients was drawn via diffusion analysis of b-400 and b-1000 values.

The following parameters were used for the MR images: matrix: 288x251, number of excitations (NEX): 1.0, field of view (FOV): 40x35 cm, cross-sectional thickness: 4 mm, space between cross-sections: 0.5 mm, repetition time (TR): 441 msec, and echo time (TE): 80 msec.

The following parameters were used for the diffusion-weighted imaging (DWI): matrix: 132x114, NEX: 2.0, FOV: 40x35 cm, cross-sectional thickness: 4 mm, space between cross-sections: 0.5 mm, direction of diffusion: all directions, TR and TE: minimum.

Measurements were performed at the General Electric Company (GE) Advantage Workstation Release 4.6 Software station. The ADC mapping was formed by the device via DWI images. Two radiologists carried out all measurements using T2-weighted images as a reference via ADC mapping. The ADC values were measured using the region of interest (ROI). The ROI was standardized at 5 mm², and measurements were made from three zones of the thickened colon wall. The mean ADC values of these three measurements and standard deviation values were calculated. The ADC values and histopathological results of the patients were compared. The DWI images and ADC maps were analyzed in consensus by two radiologists with 10 years of experience.

Statistical analyses

Data were summarized as mean $\pm$ standard deviation for continuous variables and frequencies for categorical variables. The Mann-Whitney U test was used to compare the ADC values between the malignant and benign cases. P value $< .05$ was considered as statistically significant. In order to determine the diagnostic accuracy of ADC measurements, receiver operating characteristic (ROC) analysis was performed. Cut-off ranges were calculated around the optimal cut-off to maximize sensitivity and specificity for discrimination of benign from malignant thickened colon wall.

Results

A total of 81 patients were included in the study. Of these patients, 42 had benign bowel wall thickening and 39 had malignant bowel wall thickening. Diffuse wall thickness was observed on the ascending colon in 15 patients, the cecum in 11 patients, the transverse colon in 8 patients, the descending colon in 13 patients, and the recto sigmoid colon in 34 patients.

The mean age of the patients was 57 years $\pm$ 11.8 (standard deviation; range, 23–77 years). The mean age of the patients with benign group was 32 $\pm$ 12.8 (standard deviation; range, 22–46 years), and that of patients with colon cancer was 45.1 $\pm$ 9.6 (standard deviation; range, 27–68 years). The mean wall thickness was 10.7 mm $\pm$ 5.4 (standard deviation; range, 8.5–16.2 mm) in benign cases and 16 mm $\pm$ 8.7 (standard deviation; range, 11–23 mm) with colon cancer. There was no difference observed in terms of patient age ($P=.218$). The significant difference was seen in the mean wall thickness between the two groups ($p<0.05$). The longest affected segment was 19 cm long, whereas the shortest segment was 5 cm long (mean length: 7.2 cm). No significant difference was found in the segmental length involvement between the benign and malignant cases ($p>0.05$). Histopathological results of the malignant cases were consistent with an adenocarcinoma in 35 patients and neuroendocrine tumor in 4 patients. On the other hand, histopathological results of the benign cases showed IBD in 24 patients, non-specific colitis in 9 patients, infectious colitis in 5 patients, and ischemic colitis in 4 patients.

According to the ADC values obtained from pathological wall thickening, the mean ADC values ($\times 10^{-3}$ mm²/s) of benign lesions were 1.42 $\pm$ 0.17 for b 400, 1.39 $\pm$ 0.12 for b 1000 (Figures 1). The mean ADC values ($\times 10^{-3}$ mm²/s) of malignant lesions were 1.08 $\pm$ 0.15 for b 400, 1.02 $\pm$ 0.13 for b 1000 (Figures 2, 3). There were significantly lower ADC values in malignant lesions in all b values ($P=.001$ for b 400, $P=.001$ for b 1000). The results are summarized in Table 1.

The receiver operating curve (ROC) showed that a cut-off value of 1.24×10^{-3} mm²/s between the malignant and benign values with a sensitivity of 91 %, specificity of 85 %, and an accuracy of 84 %. The positive predictive value, negative predictive value, and diagnostic accuracy of ADC values were determined to be 97 %, 86 %, and 88 % respectively.

Table 1. The details of detected lesions in 81 patients

	Benign group (n=42)	Malignant group	P
Patient age (years)	32 $\pm$ 12.8	45.1 $\pm$ 9.6	.218
Lesion size (cm)	10.7 $\pm$ 5.4	16 $\pm$ 8.7	.005
ADC values for b 400	1.42 $\pm$ 0.17	1.08 $\pm$ 0.15	.001
ADC values for 1000	1.39 $\pm$ 0.12	1.02 $\pm$ 0.13	.001

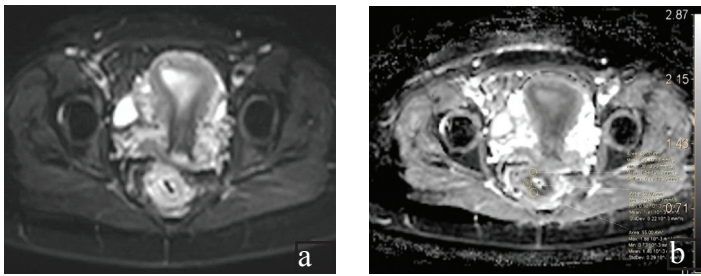


Figure 1 a-b. DW MR image shows narrowed, rigid rectal loop and thickening of the rectum wall (IBD) (a). ADC was measured for the 3 ROIs as 1.41×10^{-3} , as 1.40×10^{-3} , and $1.54 \times 10^{-3} \text{ mm}^2/\text{s}$ with b 400 (b)

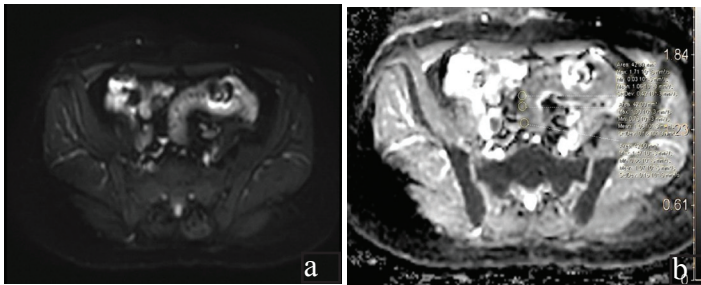


Figure 2 a-b. DW MR image demonstrates diffuse bowel wall thickening in the sigmoid colon (colon cancer) (a). ADC was measured for the 3 ROIs as 1.06×10^{-3} , 1.08×10^{-3} , and $1.07 \times 10^{-3} \text{ mm}^2/\text{s}$ with b 1000 (b). Discussion

CC is slow-growing tumor. A benign adenoma is initially present in most of the cases. These patients usually experience malignant transformation within a long period of seven to 10 years. The most common clinical finding is rectal bleeding. Diagnosis before the appearance of symptoms is advantageous for prognosis. Early diagnosis is life-saving. The carcinoma was seen with diffuse wall thickening have a higher potential for malignant transformation than polypoid carcinoma [9,10].

IBD is a chronic intestinal disease with unknown etiology, characterized by activation and remission episodes. There are two major types, ulcerative colitis (UC) and Crohn's disease (CD). CD may involve all layers of the gastrointestinal system; about 30 to 40% of the small intestine, 15 to 25% of the large intestine, and 40 to 45% both involved. The affected intestinal segments are thickened and mesenteric adipose tissue advances towards the diseased segment.

Ischemic colitis accounts for more than half of all cases of gastrointestinal ischemia. In clinical practice, many cases of colonic ischemia are misdiagnosed as inflammatory bowel disease. The differential diagnosis of ischemic colitis on MDCT depends on the phase and on the appearance of the wall thickening. A stratified thickening suggests infectious colitis, inflammatory colitis, and radiation damage. A homogeneous gray wall thickening (dry form) suggests ulcerative and granulomatous colitis and overall malignancy [11,12].

Radiological procedures which are carried out through appropriate techniques play an important role in the diagnosis, staging, choice of medical or surgical treatment, in the evaluation of postoperative recurrence and residual lesions. Diagnosis can be easily made radiologically for polypoid or vegetative types of cancer. Early diagnosis of cancer presenting as diffuse bowel wall thickness is very difficult due to very rapid dissemination by lymphatic and

hematological routes, and delayed clinical obstructive symptoms. Furthermore, these types of scirrhous cancers can be easily confused with benign pathologies of the colon, such as IBD, ischemic or infectious colon diseases.

Radiologically, the most common findings are mural thickening with infectious colon diseases. Ultrasonography (US) shows circumferential, symmetric, homogeneous, hypoechoic thickening of colon. MDCT images show marked wall thickening of the colon, and rectum with pericolonic stranding [13]. MRI and positron emission tomography-CT (PET-CT) are the other imaging modalities used in the diagnosis of IBD and CC. In addition, tumor diagnosis, characteristic, therapy plan, and treatment response can be also evaluated using advanced functional and molecular imaging procedures [14].

The diagnostic rate of tumors with MDCT is higher with a sensitivity of 69 to 84% and specificity of 59 to 83% [15,16]. On the other hand, although conventional MRI sequences may be helpful to detect a pathological lesion, they cannot adequately differentiate between malignant and benign lesions [16,17].

In DW MRI, sequence features are adjusted to bring out the differences of the tissues. Strong gradients are added to sensitize the sequential diffusion and three least perpendicular planes are applied. There is an inverse relationship between the amount of diffusions and the cellular density of the tissue. Diffusion is inhibited in tissues with excess cell density, and a high signal is obtained, also diffusion increases at low cellular concentrations and low signal is produced at DW MRI. When compared to normal tissue, malignant tumors are labeled with increased cellularity, larger nuclei and more abundant macromolecular proteins, a larger nuclear/cytoplasm ratio with less extracellular space. Due to the reasons, the diffusion of water molecules in malignant tumors is restricted, resulting in decreased ADC [3].

DWI is used for diagnostic purposes in several abdominal organs and for urinary and pelvic cancer [4-6]. Furthermore review of the literature reveals successful results of the examination of the diffuse bowel pathologies with DWI imaging [18-20].

A few studies have demonstrated that ADC values closer to different b-values can be obtained in cases of colorectal cancer. Nasu et al. [21] reported that the mean ADC values of CC were 1.02 ± 0.1 ($\times 10^{-3} \text{ mm}^2/\text{s}$) for b 0, and for b 1000. Solak et al. [22] presented that the mean ADC values of CC were 1.19 ± 0.51 ($\times 10^{-3} \text{ mm}^2/\text{s}$) and of IBD were 1.39 ± 0.53 for b 800. Our study show that the mean ADC values ($\times 10^{-3} \text{ mm}^2/\text{s}$) of malignant lesions were 1.08 ± 0.15 for b 400, 1.02 ± 0.13 for b 1000 and benign lesions were for b 400, 1.39 ± 0.12 for b 1000. Although our study had similar values to the literature, 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 using technique.

There are some limitations to this study. These are retrospective design and evaluation of a small number of patients. Our results should be confirmed with larger clinical studies. The stage and

activity of IBD with some inflammatory processes may cause misdiagnosis.

Conclusions

By the way the signal-to-noise ratio and the geometric resolution are reported to be low with DWI. MRI is also not recommended in patients with contraindications.

In conclusion, our study data suggest that ADC measurements are useful for differentiation of benign bowel wall thickening from malignant diffuse scirrhous types of bowel wall thickening. Thus early detection of scirrhous type CC can be available for patient. ADC parameter can be use particularly in cases where clinic-radiological findings are inconclusive. By the way these findings should be validated with other studies

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