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The value of diffusion-weighted magnetic resonance imaging in the differential diagnosis in diffuse bowel wall thickening

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Background/aims: *We aimed to investigate the value of diffusion-weighted magnetic resonance imaging in the differentiation of benign-malignant diffuse bowel wall thickening (scirrhous colon carcinoma) and to discuss the diagnostic importance and potential use of apparent diffusion coefficient measurements.* ***Materials and Methods:*** *A total of 41 patients (32 males, 9 females; mean age, 57 years) with diffuse bowel wall thickening diagnosed on computed tomography were included in this study. The magnetic resonance imaging was performed on a 1.5 T scanner (Siemens-Espree). Changes in the signal intensity of the lesions were determined by their appearance in images at b800 s/mm², and apparent diffusion coefficient values were also calculated. Lesions were classified in two groups according to the presence of hyperintensity on b800 images and results of endoscopic biopsies. The differences in mean apparent diffusion coefficient values between the two groups were compared with the Mann-Whitney U test, and threshold values were determined with receiver operating characteristic curve analysis.* ***Results:*** *The difference between the mean apparent diffusion coefficient values of benign and malignant groups was statistically significant, and the apparent diffusion coefficient values of benign lesions were significantly higher than of malignant lesions ($p<0.05$). By using a cut-off value of 1.21 x 10-3mm²/s, apparent diffusion coefficient had a sensitivity of 100%, specificity of 87.3%, and accuracy of 89.3% in the discrimination of malignant colorectal pathologies. With the visual assessment of the diffusion weighted images and the measurement of apparent diffusion coefficient values, malignant and benign lesions could be differentiated, with 100% sensitivity, 89.2% specificity, and 90.4% accuracy. Although some benign lesions were interpreted as malignant, no malignant lesion was determined as benign in the visual assessment.* ***Conclusions:*** *Diffusion-weighted magnetic resonance imaging and apparent diffusion coefficient values together can successfully differentiate malignant from benign diffuse bowel wall thickening.*

Key words: Bowel wall thickening, diffuse colorectal cancer, diferential diagnosis, diffusion weighted magnetic resonance imaging, inflammatory bowel disease

Diffüz kolon duvarı kalınlaşmasının ayırıcı tanısında diffüzyon ağırlıklı manyetik rezonans görüntülemenin değeri

Amaç: *Bu çalışmada amacımız diffüzyon ağırlıklı manyetik rezonans görüntüleme'nin malign (skirökarsinom) ve benign diffüz kolon duvarı kalınlaşmasının ayırdedilmesindeki değerini araştırmak ve apparent diffusion coefficient ölçümlerinin kullanılabilirliğini ve tanısal değerini tartışmaktır.* ***Gereç ve Yöntem:*** *Tomografik incelemede 32'si erkek toplam 41 diffüz kolon duvarı kalınlaşması olan hasta çalışmaya alınmıştır. Manyetik rezonans görüntüleme incelemeleri 1.5T cihazla yapılmıştır (Siemens-Espree). Lezyonların b800 difüzyon ağırlıklı manyetik rezonans görüntülemedeki sinyal değişiklikleri gözlenmiş ve apparent diffusion coefficient ölçümleri yapılmıştır. Lezyonlar biyopsi sonuçlarına ve b800 incelemedeki görünümlerine göre malign-benign olarak iki gruba ayrılmıştır. İki grup arasındaki ortalama apparent diffusion coefficient değerleri Mann-Whitney U testi kullanılarak karşılaştırılmıştır, karakteristik ROC analiziyle eşik değeri belirlenmiştir.* ***Bulgular:*** *Benign ve malign gruptaki apparent diffusion coefficient değerleri arasında istatistiksel olarak anlamlı farklılık mevcuttur ve benign gruptaki apparent diffusion coefficient değerleri malign gruptan belirgin yüksektir ($P < 0.05$).1.21 x 10-3mm²/s cut-off değeri kullanarak apparent diffusion coefficient ölçümleriyle malign-benign ayırımı %100 sensitivite, %87.3 spesivite ve %83.3 doğrulukla yapılabilir. Apparent diffusion coefficient ölçümlerine diffüzyon ağırlıklı görüntülemenin görsel olarak değerlendirilmesi eklenirse sensitivite %100, spesivite %89.2, doğruluk %90.4'e ulaşmaktadır. Bazı benign lezyonlar maligne yakın ölçüm gösterse de hiçbir malign lezyon görsel olarak ve apparent diffusion coefficient ölçümlerinde benign lezyon görünümüne sahip değildir.* ***Sonuç:*** *Diffüzyon ağırlıklı manyetik rezonans görüntüleme ve apparent diffusion coefficient ölçümleri malign-benign diffüz kolon duvarı kalınlaşmasını başarıyla ayırdedebilir.*

Anahtar kelimeler: Kolon duvarı kalınlaşması, diffüz, kolorektal kanser,ayırıcı tanı, diffüzyon ağırlıklı manyetik rezonans görüntüleme, inflamatuar barsak hastalığı

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INTRODUCTION

Colorectal cancer (CRC) affects about 5% of the population, with up to 150,000 new cases per year in the United States alone. Cancer of the large intestine accounts for 21% of all cancers in the United States, ranking second in mortality only to lung cancer among both males and females. It is, however, one of the most potentially curable of the gastrointestinal cancers, if early diagnosis is made. Age is a known risk factor for CRC for those aged over 40 years. A study published online in the *Journal of Cancer* has reported an increase in rectal cancer cases in adults under the age of 40 over the past several decades. In cauliflower type malignancies and polypoid masses invading adjacent structures, the diagnosis is straightforward. However, the diagnosis is difficult to reach in scirrhous type malignancies, which result in late obstructive symptoms and tend to spread early via the lymphatic and hematogenic route. Furthermore, this pathology may be confused clinically and radiologically with various benign conditions, including inflammatory, ischemic, or infectious bowel disease. Our aim in this preliminary study was to evaluate the usefulness of diffuse bowel wall thickening in diffusion weighted-magnetic resonance imaging (DW-MRI) in the diagnosis of CRC and its differentiation from benign conditions.

MATERIALS AND METHODS

During a period of 11 months between June 2011 and May 2012, 41 consecutive patients (32 males, 9 females; mean age, 57 years; age range, 31-77 years) with diffuse bowel wall thickening were included in this study. Contrast enhanced computed tomography (CT) was performed in all patients before MR examinations. Exclusion criteria were as follows: a history of CRC or inflammatory bowel disease (IBD), polypoid mass filling the colonic lumen, peritoneal effusion, liver metastasis, presence of a pacemaker, metallic implants in the central nervous system, and claustrophobia. The research protocol was approved by the local ethics committee, and written consent was obtained from all the patients prior to the study.

The patients did not undergo any preparation such as bowel cleansing before the examinations, and intravenous contrast medium was not administered. The MRI was performed on a 1.5 T scanner (Espree VB13; Siemens, Erlangen, Germany) with a 33 mT/m maximum gradient capability using an eight-channel phased-array body coil. Pathologic segment on CT examination was noted, and routine conventional and DW-MRI sequences were taken according to the location of these segments. The sequences used for abdominopelvic MRI were as follows: axial, turbo spin-echo T2-weighted sequence repetition time (TR), 4320 ms, echo time (TE), 87 ms; axial fat-saturated 3D gradient-echo T1-weighted MRI sequence (VIBE) TR, 5.32 ms, TE, 2.53 ms; axial, turbo spin-echo T1-weighted sequence TR, 536 ms, TE, 11 ms; sagittal, turbo spin-echo T2-weighted sequence TR, 5030 ms, TE, 101 ms; and coronal, turbo spin-echo TIRM sequence TR, 4980 ms, TE, 84 ms. This sequence was followed by a diffusion weighted single-shot spin-echo echoplanar sequence using chemical shift selective fat-suppression technique: TR/TE, 4900/93; matrix, 192?192; slice numbers, 30-50; slice thickness, 6 mm; interslice gap, 35%; FOV, 45 cm; averages, 5; acquisition time, approximately 3 minutes; PAT factor, 2; and PAT mode, GRAPPA with b factors of 50, 400 and 800 s/mm^2. The DW-MRI images were of diagnostic quality in all cases, and no cases were excluded from the study.

All images were reviewed on an image archiving and communication system workstation monitor (PACS with Leonardo console software 19A version, Siemens, Erlangen, Germany) by two gastrointestinal radiologists (A.S., B.G.), each having at least 7 years of clinical experience in interpretation of abdominal MR images. The reviewers were aware that the study was performed to detect colonic cancers. However, they were blinded to all other information, such as patient identity, clinical history and the results of other imaging examinations. The location and length of the lesions were evaluated on routine conventional MRI scans. Therefore, high b value (b=800) diffusion MR images were detected visually according to the signal intensities on b800 and apparent diffusion coefficient (ADC) map images, and ADC values were also calculated. Lesions were grouped according to the histopathological results of endoscopic biopsy. For quantitative analysis in DW-MRI, the radiologist measured the thickened colonic wall ADC values in the three regions of interest by using a dedicated software at the workstation. The measurements from the three regions of interest were averaged. A circular region of interest with a diameter of at least 4 mm^2 (larger than 2 mm in minimum diameter) was placed on three different portions of the thickened wall to obtain average ADC values of the lesion. Within a period of 2-11 days

(mean, 6.6 days) following MRI, a colonoscopy was performed by an experienced gastroenterologist. After visual assessment, a biopsy of the colonic wall was obtained. The reports of the endoscopic examination and the results of the pathology report were reviewed. The quantitative DW-MRI findings were compared to the results of the traditional colonoscopy and biopsy.

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) 21.0 software. The ADC values are reported as the mean ± standard deviation. The normality of distribution of the parameters was assessed using the Kolmogorov-Smirnov test. The difference between the mean size of hyperintense and hypointense lesions and ADC values between the two groups were compared with the Mann-Whitney U test. P values of less than 0.05 were considered to be statistically significant. The receiver operating characteristics (ROC) analyses were performed in order to determine cut-off ADC values for differentiation of the benign and malignant lesion groups.

RESULTS

The location of the lesions in our series was anorectal region in 11 cases, descending colon and/or splenic flexura in 9 cases, ascending colon in 8 cases, rectosigmoid region in 7 cases, and cecum in 6 cases (Figure 1A-E). Maximum and minimum lengths of the affected segment were 17 cm and 3.5 cm, respectively (mean, 6.3 cm; SD, 4.7). According to histopathologic results of the endoscopic biopsy, the patients were divided into malignant (n=26) and benign (n=15) groups. Microscopically, all of the tumors were adenocarcinomas. Three pedunculated polyps were extirpated (1-2 cm in size) and five flat polyps were seen during endoscopic examination in patients with malignancy. All 26 lesions were hyperintense (group A-malignant group) on DWI at high b value (b=800) images (Figures 1, 2); 7 of the remaining lesions were mildly hyperintense, and 8 lesions were hypointense in group B (benign group). The size difference between these two groups was not significant ($p>0.05$). In group A, tumor locations were as follows: anorectal region (n=7) (Figure 2A-F), left colon (n=5), rectosigmoid region (n=5), right colon (n=5), and cecum (n=2). Group B consisted entirely of benign lesions according to endoscopic biopsy results: 6 patients were diagnosed with IBD (Figure 3A-C), 4 with non-specific colitis, 3 with infectious colitis, and 2 with normal findings.

In quantitative analysis, ADC values of all pathologic regions were measured. The mean ADC values were 1.19±0.51 mm^2/s (min: 0.57, max: 1.64) in group A and 1.93±0.87 mm^2/s (min: 1.20, max: 2.59) in group B. In group B, the mean ADC value of 6 cases with IBD was lower than that of other benign pathologies (1.39±0.53 vs 2.69±0.81) (Figure 3). A comparison between IBD and other benign pathologies was not possible due to the small number of patients included in this group. The difference between the mean ADC values of the benign and malignant groups was statistically significant, and the ADC values of benign lesions were significantly higher than of malignant lesions ($p<0.05$). In the ROC curve analysis, the cut-off value of ADC to differentiate benign from malignant wall thickening was found as 1.21 mm^2/s, which had a sensitivity of 100%, specificity of 87.3%, and accuracy of 89.3% in the discrimination of malignant colorectal pathologies. With visual assessment of the DWIs and measurement of ADC values, malignant and benign lesions could be differentiated with a sensitivity of 100%, specificity of 89.2%, and an accuracy of 90.4%.

DISCUSSION

Most CRCs are polypoid type, which may cause early obstructive symptoms. However, it must be emphasized that non-polypoid lesions also occur. These are classified as protruded, slightly elevated (small flat adenoma), lateral spreading tumor, and depressed type. The existence of flat or depressed type colorectal carcinomas has been reported in recent studies, and it has been suggested that they may have a higher malignant potential than polypoid type carcinomas (6-8). Therefore, early diagnosis is very important. There are several diagnostic methods that can be used for early detection of the lesion. Ultrasound (US) and CT have been used for many years, but the success of these methods is controversial. The sensitivity of US in the diagnosis of diffuse CRC has been reported as 67%-86% and the specificity as 79%-87%. The main problem with US is that the rectum is a relatively inaccessible area; rectal wall thickening is correctly detected by suprapubic ultrasound in only 15% of cases. The reported sensitivity for diffuse rectal carcinoma detection by transrectal US is 67%-81%. The sensitivity of CT for detecting diffuse CRC has been reported as 69%-84% and specificity as 59%-83%. Moreover, CT leads to ionizing radiation exposure and requires intravenous contrast agent administration (6,9-11).

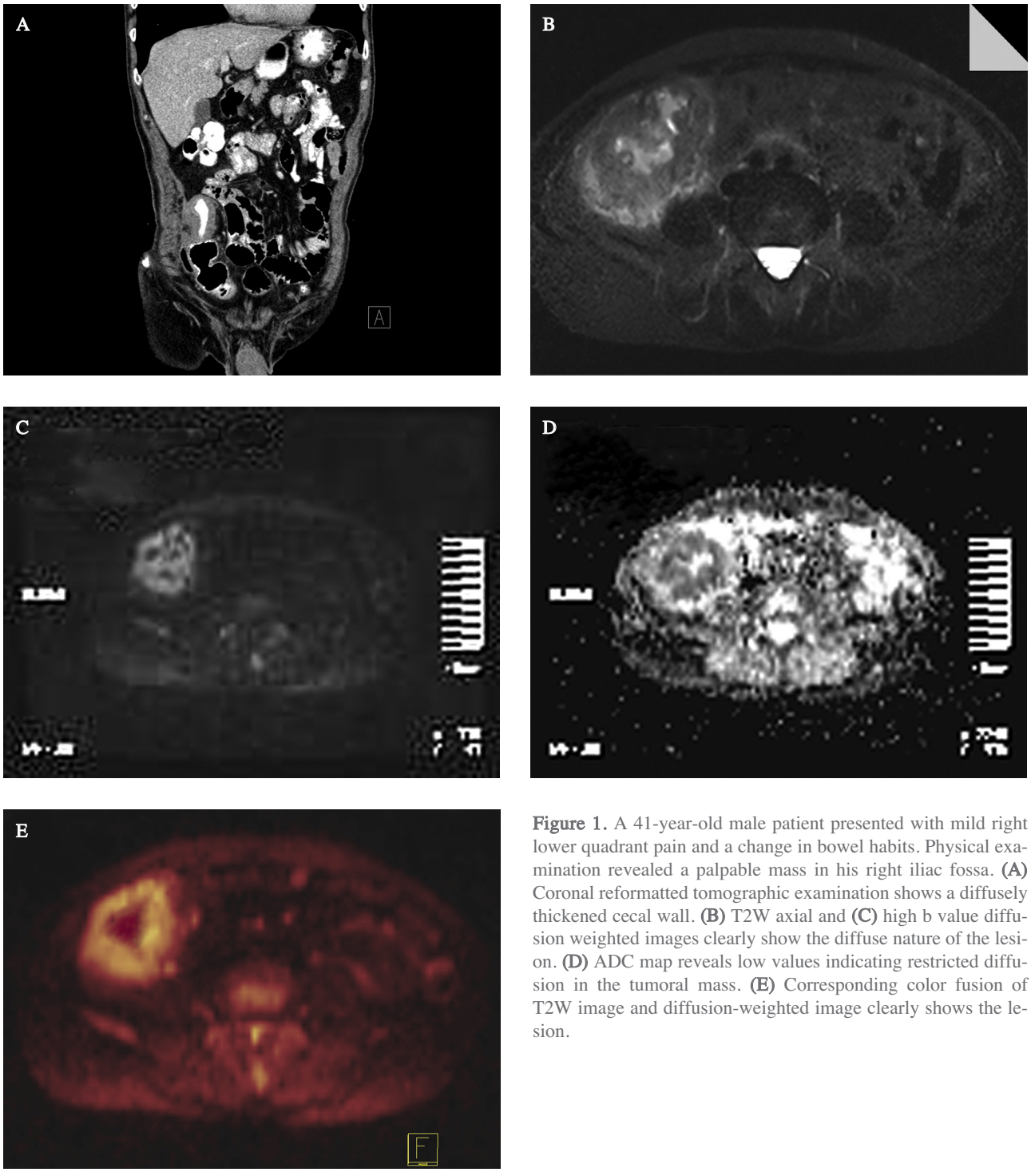

Figure 1. A 41-year-old male patient presented with mild right lower quadrant pain and a change in bowel habits. Physical examination revealed a palpable mass in his right iliac fossa. **(A)** Coronal reformatted tomographic examination shows a diffusely thickened cecal wall. **(B)** T2W axial and **(C)** high b value diffusion weighted images clearly show the diffuse nature of the lesion. **(D)** ADC map reveals low values indicating restricted diffusion in the tumoral mass. **(E)** Corresponding color fusion of T2W image and diffusion-weighted image clearly shows the lesion.

Several authors have described the MR features of normal and abnormal bowel wall in both patients and healthy volunteers in the early and mid 1990s. A thickness ≥4 mm has to be considered pathologic, whereas a thickness of 3-4 mm should raise suspicion. However, conventional MRI scans cannot differentiate between benign and malignant bowel wall thickening (11,12).

DW-MRI, which is frequently used in neuroradiology, is a relatively new technique that can be used for the evaluation of abdominal diseases, especially in oncology. The diagnostic value of DW-MRI for hepatic, urinary, and pelvic malignancies has been shown in multiple studies. In addition, the ADC values determined using this method have been lower in kidney and liver failure, concor-

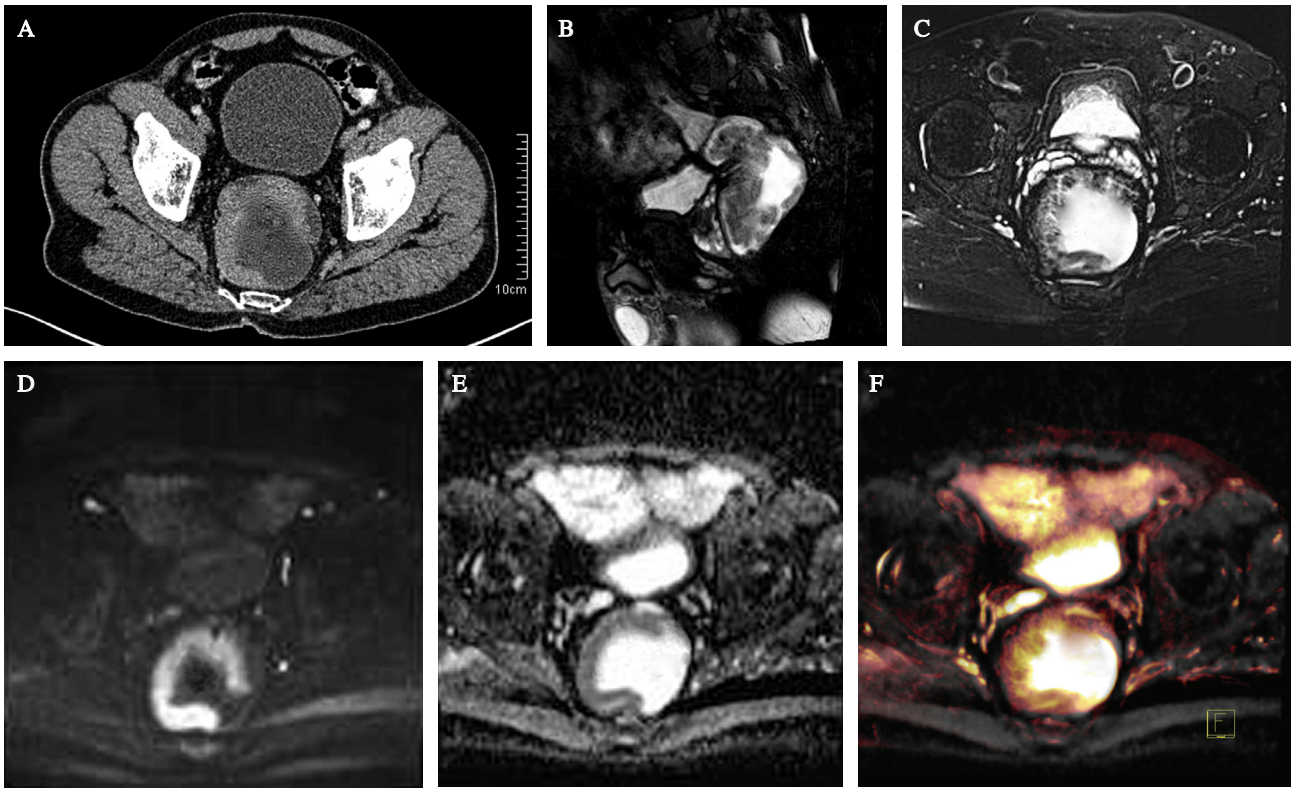

Figure 2. A previously healthy 61-year-old male presented with a 3-month history of rectal tenesmus and progressive constipation. Rectal examination revealed a firm, non-moveable fixed mass. **(A)** Abdominal contrast-enhanced CT examination shows diffuse bowel wall thickening in the anterolateral rectal region. **(B)** Fat-suppressed sagittal **(C)** and axial T2W images reveal borders and extent of the tumoral mass. **(D)** On high b value (b800) diffusion weighted images, the tumor appears hyperintense when adjacent structures become hypointense. **(E)** ADC map shows a very low ADC value within the tumor (mean: 0.69±28 mm2/s). **(F)** Fusion of high b-value diffusion-weighted and T2W fat-suppressed image clearly shows the lesion.

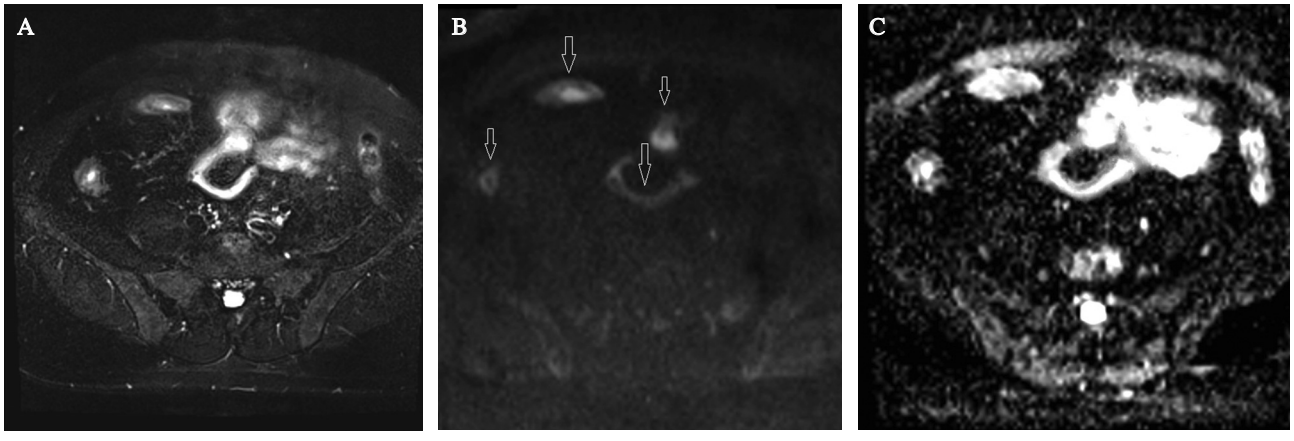

Figure 3. A 33-year-old male patient had intermittent colicky abdominal pain and diarrhea for 3 months. **(A)** T2W axial image shows narrowed, rigid sigmoid loop and thickening of the cecum wall. **(B)** On high b value DW-MRI, multiple segments are involved (arrows). **(C)** ADC map shows intermediate and low ADC values (mean: 1.59±0.61 mm^2/s). Endoscopic biopsy confirmed Crohn's disease.

dant with the severity of the disease. DW-MRI has also been used in the evaluation of liver fibrosis and the assessment of Crohn's disease activity (13,14). In addition, several studies have reported that DWI was successful in evaluating the efficacy of the treatment in CRC. Hosonuma et al. (15) demonstrated that both low (400 s/mm^2) and high (800 s/mm^2) b-value DWIs could detect malig-

nancy and that DWI was a potentially useful screening tool. Although a mean ADC value of 1.194 mm^2/s was obtained for colorectal carcinomas, the sensitivity of this technique was decreased by the presence of patients with false-positive results. We found a mean ADC in group A (92% of malignant) of 1.19±0.51 mm^2/s, which is very close to that reported in the study of Hosonumo et al. Nasu et al. (16) reported that DWI with a b value of 1000 s/mm^2 effectively decreased the false-positivity rate. Thus, we used a high b-value DWI to minimize false-positivity in this study.

Inflammatory bowel disease (IBD) is an idiopathic disease, which probably involves an immune reaction of the body against its own intestinal tract. The two major types of IBDs are ulcerative colitis, which is limited to the colon, and Crohn's disease, which can involve any segment of the gastrointestinal tract from the mouth to anus. An unknown factor/agent (or a combination of factors) triggers the immune system to produce an inflammatory reaction in the intestinal tract. Increased cell volume on the intestinal tract wall may also contribute to the restricted diffusion in the active stage of the disease. Therefore, ADC values do decrease, but the lowest reported ADC values in the thickened bowel wall belong to colorectal carcinoma (17, 18). This point was further emphasized by Kılıçkesmez et al. (14). They found statistically significant differences between the ADC values of IBD and malignancy. In our study, the mean ADC value of inflammatory disease (1.39±0.53) was higher than of the malignant group (1.19±0.51). DW-MRI can also be used to determine the IBD activity. Oto et al. (19) reported that DWI provides quantitative measures of bowel inflammation that can differentiate actively inflamed bowel segments from normal bowel in Crohn's disease. In our study, we found multiple involved intestinal segments that could not be seen on CT images in a patient with Crohn's disease.

To our knowledge, this is the first study that compares the ADC values of benign and malignant diffuse wall thickening. Because DW-MRI is completely non-invasive, does not require ionizing radiation or injection of contrast material, and does not cause patient discomfort, it is a potentially powerful tool in the detection of rectosigmoid cancer. In addition, this technique can be easily added to an MR examination protocol because it requires only a minimal prolongation of the examination time (20-23). It would be a useful adjunct to conventional sequences.

Our study has several limitations, including its retrospective design and small sample size. Thus, our results need to be confirmed in larger clinical studies. In this study, we had to combine patients with ulcerative colitis and Crohn's disease. Appearances of DW-MRI, depending on histopathological features, may be completely different according to the stage and activity of IBDs. A malignant neoplasm that overlaps an inflammatory lesion also adversely affects the assessment of quantitative measurements.

In conclusion, our preliminary data suggest that DWI with quantitative measurement of ADC value seems to be a useful method in the diagnosis of diffuse colorectal malignancy and its discrimination from other benign colorectal diseases. However, radiologists should be aware of possible overlaps that may lead to misdiagnoses when DWI is used alone, and these findings should be validated with larger studies.

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