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Research Article

The Prediction of Active Crohn's Disease on Diffusion-Weighted Imaging

Fatma Kulali[1]* and Kamil Ozdil[2]

[1]*Associate Professor of Radiology Department, University of Health Sciences Umraniye Training and Research Hospital, Turkey*

[2]*Professor of Gastroenterology Department, University of Health Sciences Umraniye Training and Research Hospital, Turkey*

***Corresponding Author:** Fatma Kulali, Associate Professor of Radiology Department, University of Health Sciences Umraniye Training and Research Hospital, Turkey.

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Abstract

Purpose: We aimed to investigate the diagnostic performance of diffusion-weighted imaging (DWI) and normalized apparent diffusion coefficient (nADC) in the prediction of active Crohn's disease.

Methods: A total of 47 patients (21 [45%] women and 26 [55%] men) with a mean age of 40 years were included in this study. Magnetic resonance imaging (MR) and DWI examinations of patients with Crohn's disease were reviewed. Five intestinal segments were evaluated for simplified MR index of activity (sMaRIA). The estimations of sMaRIA and nADC values were performed for each segment. The diagnostic performances of nADC values and sMaRIA were evaluated for the detection of active Chron's disease. The relationship between radiological findings and colonoscopy results was analyzed statistically.

Results: Among 235 intestinal segments of 47 patients, there were 76 active inflammatory segments. The nADC values of active inflammatory intestinal segments were lower compared to inactive group's ($p < 0.05$). Active disease had lower nADC value. For all segments (n = 235), with a cut off value of nADC ≤ 0.75, the sensitivity, specificity and accuracy ratio was 89.2%, 98.8%, and 95.7%, respectively (AUROC: 0.981). Higher sMaRIA scores were significantly related to lower nADC values ($p < 0.05$).

Conclusions: The estimation of nADC value-with a cut off value ≤ 0.75 is an important predictor for active Crohn's disease. Especially in patients at high risk for contrast agent administration, nADC value is useful for the detection of disease activity.

Keywords: Crohn's Disease; Disease Activity; Magnetic Resonance Enterography; Diffusion-Weighted Imaging; Apparent Diffusion Coefficient

Introduction

Crohn's disease is a chronic inflammatory bowel disease with recurrent acute attacks. It takes place in any part of gastrointestinal tract from mouth to anus. The most common involvement site is terminal ileum (80%). Full thickness involvement of intestinal wall and skip lesions are the characteristics of Crohn's disease. It can be presenting with erosions and aphthous ulcers. Active disease can be treated conservatively whereas chronic disease can lead to irreversible damage and the requirement of surgery. Therefore, the early diagnosis of active Crohn's disease is necessary for planning appropriate treatment and avoiding complications such as fistula, abscess, stricture and ileus [1-4].

For diagnosis and activity assessment of Chron's disease, endoscopy is the gold standard. However, it is an invasive method. The evaluation of extramural structures and small intestine except for distal part of terminal ileum is impossible with endoscopy. Alternative imaging modalities are needed such as computed tomography

(CT) with administration of intravenous, oral and rectal contrast agent, CT enterography, contrast enhanced magnetic resonance imaging (MR) and MR enterography. CT has ionizing radiation risk and repetitive scans can cause high radiation dose. MR is superior to CT because of lack radiation risk and increased soft tissue resolution. MR enterography provides more detailed information about the wall of small intestine as a result of luminal expansion. Contrast-enhanced sequences are helpful for activity evaluation [1-5]. There are several indices for activity evaluation [5-7]. Recently, the use of simplified MR index of activity (sMaRIA) has been gradually increased [8,9]. Another adjunctive imaging modality is diffusion-weighted imaging (DWI) which can also be helpful for the assessment of disease activity [1-4,10]. Diffusion restriction indicates active inflammation. Normalized apparent diffusion coefficient (nADC) is quantitative measurement of diffusion restriction on ADC map. ADC map is obtained from DWI [11,12].

DWI has advantages of no need for contrast-agent and short scan time. Therefore, we aimed to investigate the diagnostic performance of diffusion-weighted imaging (DWI) and normalized apparent diffusion coefficient (nADC) in the prediction of active Crohn's disease.

Materials and Methods

Between January 2020 and July 2020, at a single institution, MR enterography and DWI examinations of patients with Chron's disease were reviewed retrospectively from hospital information system.

The patients with insufficient imaging (n = 2), patients underwent intestinal operation (n = 5), patients with more than two weeks of interval between MR and colonoscopy (n = 10) and patients < 18 years-old (n = 7) were excluded.

A total of 47 patients (21 [45%] women and 26 [55%] men) with a mean age of 40 ± 14 (SD) years) with MR enterography and DWI examinations were included in this retrospective study. All patients had colonoscopy which is the reference modality in our study. The maximum interval between MR examinations and colonscopy was two weeks in all patients.

MR Protocol

All MRIs were performed on 1.5 Tesla system (Magnetom Aera®, Siemens Healthineers, Erlangen, Germany). Liquid diet in the previous day of examination and pre-procedural eight hours fasting were recommended to patients. For expansion of lumen, at 60 minutes before examination, oral ingestion of 1500 ml water solution with 3% mannitol were started. Intravenous glucagon was applied for reducing peristalsis. The parameters of upper abdominal MRI sequences were as follows: Coronal T2-weighted half-Fourier acquisition single-shot turbo spin-echo (HASTE) [TR/TE: 2000/130, field of view (FOV): 420 mm, slice thickness 7 mm], axial T2-weighted HASTE (TR/TE: 2000/162, FOV: 440 mm, flip angle 90°,slice thickness 6 mm) with and without fat saturation, spoiled dual gradient echo T1-weighted in- and opposed-phase MR imaging (TR/TE: 209-209/2.3-4.8,slice thickness 7 mm), axial pre-contrast and post-contrast dynamic T1 3D VIBE (TR/TE: 800/22, FOV: 440 mm,slice thickness 5 mm) sequences. The parameters of lower abdominal MRI sequences were as follows: Sagittal T2-weighted HASTE [TR/TE: 5000/112 ms, FOV: 350 mm, matrix: 256 x 256, slice thickness 7 mm], Coronal fat saturated T2-weighted HASTE (TR/TE: 4000/84 ms, FOV: 320mm, matrix: 256 x 320, slice thickness: 5 mm), axial T2-weighted HASTE (TR/TE: 3700/88 ms, FOV: 320 mm, matrix: 182x320, slice thickness 5 mm), axial pre-contrast and post-contrast dynamic T1 3D VIBE (TR/TE: 4.5/2.1 ms, FOV: 380 mm, image matrix size: 195 x 320, flip angle: 15°, slice thickness 5 mm) sequences. The parameters of MR enterography was coronal T2-weighted steady-state gradient echo sequence (TRUFI) (TR:570ms, TE:1.68 ms, FOV:420 mm, slice thickness:5 mm, matrix:256 x 256) and axial TRUFI (FOV:420mm, slice thickness:5 mm). In upper and lower abdomen, axial diffusion weighted single shot echo-planar imagings were performed with b values 0 and 1000 s/mm^2 (TR/TE: 5200/58 ms, NEX: 3, FOV: 430, image matrix size: 115 x 192; slice thickness: 5 mm).

Image analysis

MR findings of five intestinal segments (terminal ileum, right colon, transverse colon, left colon and rectum) were analyzed by an experienced radiologist in abdominal imaging-blinded to clinical and endoscopic results. For active disease, sMARIA ≥1 and for severe disease sMARIA ≥ 2 were defined [8]. Therefore, for each segment, sMaRIA score was estimated by a formula: 1×wall thickening > 3 mm + 1 × edema + 1 × fat stranding + 2 × ulcers. Score changes from 0 to 5 based on the criteria in the formula [7,8]. Additionally, nADC value (ADC value of intestinal wall/ ADC value of psoas muscle) was calculated (Figure 1). ROI measurements were performed at intestinal wall and psoas muscle in the dedicated workstation (Leonardo, Siemens Healthcare). The correlation between sMARIA

and nADC values for each segment and the relationship between sMARIA and colonoscopy results was statistically analyzed.

Figure 1: Diffusion restriction of thick rectal wall (arrow) with hyperintensity on DWI (a) and hypointensity on ADC map (b) is seen. The ROI measurement of ADC value in rectal wall is demonstrated on ADC map (b).

Statistical analysis

Statistical analysis was performed using the MedCalc Statistical Software 12.7.7 (MedCalc Software bvba, Ostend, Belgium) package program. Parameters with normal distribution were analyzed using Shapiro–Wilk test. For statistical analysis, Mann-Whitney U test were used, where appropriate, and $p < 0.05$ was used to determine statistical significance. Receiver operating characteristic (ROC) analysis was performed to calculate the sensitivity, specificity, and accuracy ratios The receiver operating characteristic (ROC) analysis was performed for nADC values. Cut off values were obtained. Area under the receiver operating characteristics curve (AUROC) was estimated.

Results

In 47 patients with Chron's disease, 235 intestinal segments were investigated. Of 235, 76 (32%) were active inflammatory segments. Of 47, 39 patients (83%) had terminal ileum involvement (Figure 2). The most common second site was rectum (25%) (Figure 3). Left colon (n = 10), transvers colon (n = 8) and right colon (n = 5) involvements were also observed in our study.

The mean nADC value of active inflammatory segments (n = 74) and inactive segments (n = 161) was 0.66 ± 0.12 and 1.01 ± 0.09, respectively. There was statistically significant difference between two groups ($p < 0.05$). Active disease had lower nADC value. The best of cut off value of nADC was ≤ 0.75 to detect active terminal ileum involvement with sensitivity of 89.7%, specificity of 87.5% and accuracy of 89.4% (AUROC: 0.958). Among patients with terminal ileitis, there were one false positive and four false negative results with a cut off value of nADC ≤ 0.75**.** For all segments (n = 235), with a cut off value of nADC ≤ 0.75, the sensitivity, specificity and accuracy ratio was 89.2%, 98.8%, and 95.7%, respectively (AUROC: 0.981). There were two false-positive and eight false-negative results.

Figure 2: Coronal contrast enhanced VIBE sequence (a) and coronal TRUFI-MR enterography (b) of 25-year-old woman shows increased contrast enhancement in the thick walls of terminal ileum (arrows) with skip lesions and luminal stenosis.

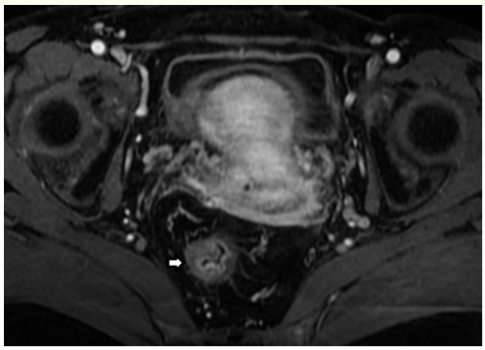

Figure 3: Axial contrast enhanced VIBE sequence of 36-year-old woman with contrast enhancement of rectal wall (arrow) and fat stranding.

Among 47 patients, according to sMaRIA score, there were eight normal, eight active, and 31 severe terminal ileum involvement. Increased disease activity with higher sMaRIA scores were significantly related with lower nADC values ($p < 0.05$).

Discussion

MR enterography associated with contrast enhanced sequences is an important modality in the diagnosis and activity assessment of Crohn's disease. The increased wall thickness, intramural edema, increased contrast enhancement of wall, fat stranding, engorgement of vasa recta, association with adjacent fluid and lympadenopathy are indicators of active disease. DWI also predicts the activation of disease with diffusion restriction [1-5]. Diffusion restriction is hyperintense on DWI and hypointense on ADC map. Acute inflammation shows diffusion restriction and lower ADC values compared to normal tissue [11-12].

In literature, several studies have been investigated the role of DWI in Crohn's disease. Seo., *et al*. [13] compared the diagnostic efficacy of contrast-enhanced MR enterography and DWI MR enterography in 44 patients for assessment of active terminal ileitis. They found that DWI MR enterography showed similar sensitivity and specificity ratios to contrast enhanced MR enterography [13]. Cansu., *et al*. [1] reported that MR enterography had high sensitivity (97.9%), specificity (95.5%) and accuracy (94.8%) ratios in all intestinal segments for evaluation of active Crohn's disease in 43 patients. They reviewed DWI findings qualitatively regardless of ADC value [1]. Barat., *et al*. [3] found that the sensitivity of DWI MR enterography (80-100%) was similar to contrast-enhanced MR enterography's (88-100%) for demonstration of Crohn's complications by the experienced radiologist.

Some previous studies demonstrated that the misleading DWI findings were mostly observed in colorectal segments due to insufficient luminal distension [14-16]. In our study, the false-positive results were due to inadequate luminal expansion.

Some studies have been conducted on the role of ADC values on the activity of Chron's disease. Pendse., *et al*. [17] suggested that there was weak intraobserver reliability and did not offer the estimation of ADC value in routine. They recommended qualitative DWI findings but not quantitative measurements. In contrast, Straksyte., *et al*. [10] found that ADC value had a negative relationship with activity index of disease. Similarly, in our study lower nADC values indicated increased activity.

Ninivaggi., *et al*. [18] demonstrated that there was significant difference between ADC values of pathological and normal intestinal segments ($1.48 \pm 0.058 \times 10^{-3}$ mm^2/s versus $3.525 \pm 0.07 \times 10^{-3}$ mm^2/s; $p < 0.05$). They found a cut off ADC value of 2.416×10^{-3} mm^2/s that showed high sensitivity (100%) and specificity (100%) in the differential diagnosis of normal and pathological intestinal segments [18]. Our findings were similar. Additionally, nADC values were estimated for standardization.

We searched the diagnostic performance of nADC in active Chron's disease. There was a strong correlation between sMaRIA scores and nADC values in our study. Increasing activity demonstrated lower nADC. The best cut off value of nADC ≤ 0.75 depicted high accuracy ratio (95.7%) in the prediction of disease activity. Previous studies have been mentioned that the standardization of ADC value was difficult and there were conflicting results due to different b values and protocols [1,17]. In previous studies, only ADC value was performed instead of nADC value [5,13,17]. In contrast to other studies, for standardization of ADC value, nADC value was estimated in our study. We recommended the estimation of nADC value to reduce the measurement differences.

There are some limitations in our study. First, the sample size of our study was small. Second, radiological findings were reviewed by an experienced radiologist in abdominal imaging so, interobserver variability couldn't be analyzed. Third, because of retrospective nature of this study, the correlation with Crohn's disease endoscopic index of severity and laboratory findings didn't investigated in this study.

Conclusions

The estimation of nADC value is an important predictor for active Crohn's disease. In the prediction of disease activity, the best cut off nADC value was ≤ 0.75 with accuracy ratio of 95.7%. Especially in patients at high risk for contrast agent administration, nADC value is useful for the detection of disease activity. We recommended nADC value estimation instead of ADC value for standardization.

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Conflict of Interest

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