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Accuracy and interobserver agreement of diffusion-weighted imaging in pediatric inflammatory bowel disease☆

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ABSTRACT

Purpose: To determine interobserver agreement (IOA) and accuracy of conventional MR enterography (MRE), qualitative diffusion, and apparent diffusion coefficient (ADC) values for detecting clinically active inflammation.
Methods: MREs in 57 consecutive children with suspected inflammatory bowel disease were retrospectively reviewed.
Results: Substantial IOA for conventional MRE (kappa=0.65) and qualitative diffusion (kappa=0.64), but fair to good IOA for ADC, (intra-class coefficient=0.63) were seen. Conventional MRE detected active clinical inflammation well (area under curve [AUC] 0.725), while qualitative diffusion and ADC did not perform well (AUC=0.572 and 0.461, respectively).
Conclusion: DWI can be helpful in diagnosing inflammatory bowel disease but does not perform well in identifying those with active inflammation.

1. Introduction

Magnetic resonance enterography (MRE) has rapidly emerged as the modality of choice for imaging evaluation of inflammatory bowel disease (IBD) and has become part of the European Society for Paediatric Gastroenterology Hepatology and Nutrition diagnostic criteria [1–3]. Lack of radiation, superior soft tissue contrast, and the ability to evaluate peristalsis by cine sequences are key advantages of MRE.

Diffusion-weighted imaging (DWI) is an Magnetic Resonance Imaging sequence that provides information about water molecule mobility and cellularity of a tissue. It helps to detect or characterize pathology. Recent studies in adults [4–10] as well as in children [11,12] have shown that an inflamed bowel wall is restricted on DWI. In a pediatric series, DWI has been shown to be equal or superior to conventional MRE sequences in detection of Crohn's disease (CD) lesions and has the potential to replace contrast-enhanced sequences [11]. In another pediatric study, restricted diffusion within the bowel wall on DWI has been shown to be associated with signs of active inflammation seen on conventional MRE sequences [12]. Interobserver agreement and association of DWI features including qualitative diffusion restriction and apparent diffusion coefficient (ADC) values with clinical markers of inflammation have not been reported. Although it may be desirable to avoid gadolinium-based contrast media (GBCM) injection, especially in patients with impaired renal function and to reduce cost, imaging time, and need of intravenous access, more data are needed before DWI becomes the stand-alone technique to detect actively inflamed bowel segments.

The objectives of this study were:

1. To determine the interobserver agreement for qualitative restricted diffusion, quantitative ADC values, and radiologist global assessment of inflammation based on conventional MRE sequences.
2. To determine the diagnostic performance of conventional MRE findings of inflammation, qualitative restricted diffusion of the bowel wall on DWI, and ADC values in:
   a. Distinguishing patient with IBD from patients without IBD, and
   b. Detecting clinically active inflammation in children with IBD.
3. To compare the mean ADC values in the qualitatively restricted and nonrestricted bowel segments.

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2. Patients and methods

2.1. Patients

A retrospective review of MRE examinations in children performed at our institution from March 1, 2011 to May 30, 2011 was done. Indications for MRE examinations included known or suspected IBD. Consecutive MREs done at 1.5 T on a Siemens MRI scanner (Avanto, Siemens Medical system, Erlangen, Germany) were included. Exclusion criteria included MRE without DWI and incomplete MRE.

2.2. MRI technique

MREs were performed using our standard institutional protocol: oral ingestion of intraluminal contrast (3% sorbitol) at a dose of 20 ml/kg, up to maximum of 1350 ml; intravenous injection of two doses of the antiperistaltic agent hyoscine butyl bromide (Buscopan; Boehringer Ingelheim, Ingelheim, Germany) at a dose of 0.3 mg/kg with maximum dose of 20 mg; and intravenous injection of a standard dose of GBCM (Magnevist, Bayer Schering Pharma) (0.1 mmol/kg). Oral contrast ingestion was started 1 h prior to the start of the scan. The first dose of Buscopan was administered after the initial evaluation sequence and cine sequence while the second dose was administered at the time of GBCM injection. Sequences acquired included precontrast axial and coronal HASTE (single-shot T2-weighted images) and TrueFISP, axial diffusion-weighted images, precontrast coronal T1-weighted VIBE, and post contrast axial and coronal VIBE sequences.

Axial diffusion-weighted images were acquired using three b-values: 50, 400, and 800 s/mm^2. Other parameters for DWI included TR-7943 ms, TE-76 ms, FOV-250-380 mm, number of signal averages-4, matrix 160×192, and slice thickness of 5 mm with 1-mm gap. Total scan time for DWI sequence was 4 min and 31 s. Coverage for DWI included lower abdomen from the level of mid-kidneys to the pubic symphysis. The study period falls in the initial phase of inclusion of DWI in the MRE protocol at our institution during which time only the lower abdomen was covered. This often meant that the transverse colon and splenic flexure were not included.

2.3. Image analysis

The bowel was divided into nine segments for review: jejunum, ileum, terminal ileum (approximately 10 cm from ileo-cecal valve), cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum. The anatomic bowel segments were selected by each reviewer based on their knowledge and experience. All radiologists were blinded to the clinical details and diagnosis.

2.3.1. Conventional imaging review

Two experienced radiologists (OMN and MLG, with 4 and 8 years' experience reading pediatric MREs, respectively) independently reviewed MRE images for signs of active inflammation. They based their gestalt on recognized MRE findings of inflammation (wall thickening>3 mm, prominent mucosal and/or stratified enhancement, enhancing lymph nodes, mural ulcerations, and surrounding inflammatory signs such as fibrofatty proliferation) [1]. They classified segments as actively inflamed, normal, or indeterminate. When long segments were involved or when multiple lesions were present in a segment, the most severe lesion was taken to represent that segment. DWI images were not referenced during this review.

2.3.2. Qualitative DWI analysis

The radiologists (OMN, MLG) also independently reviewed DWI on a separate occasion, at least 6 weeks after reviewing the conventional imaging. Conventional MRE images were not referenced during this review. Each segment was labeled as *restricted* or *not restricted*. "Restricted" segments were defined as those with bright signal on the b-value 800 images and low signal on the ADC map (Fig. 1). Sometimes the bowel wall could not be visualized on the ADC map because of poor signal-to-noise ratio (SNR). In this case, bowel wall segments that were as bright as lymph nodes (which normally show restricted diffusion) on the b-value 800 images were labeled *restricted*. Segments that were nonevaluable because of noncoverage or significant artifacts were labeled *nonavailable*.

2.3.3. Consensus review

Disagreements on conventional imaging and qualitative DWI were resolved by a third radiologist (GBC, 4 years' experience in reading MRE). The third reviewer independently reviewed imaging only in cases with disagreement and was blinded to the original reviews. Two of three agreements were considered final. The overall findings after consensus review were used for further analysis.

2.3.4. Quantitative DWI analysis

ADC maps were calculated using mono-exponential model. ADC measurements (unit = mm^2/s) were performed by two radiologists (GBC and ZA, with 4 and 1 years' experience in reading MREs, respectively) with the Syngo software platform provided by the vendor (Siemens Medical System, Erlangen, Germany). The ADC images were magnified, and a single largest possible free-hand region of interest (ROI) was drawn covering bowel wall that was brightest on DWI and darkest on the ADC map (Fig. 1). ROI was drawn directly on ADC images. The ADC value for each segment was noted, and the mean of the values reported by both radiologists was used in the analysis. In normal segments without any diffusion restriction, the ADC value was measured in the area of bowel wall that was most easily visible, that is, the best SNR. The mean ADC value from all segments measured was used for patient-level analysis. The ADC values of the lower pole of the right kidney and right psoas muscle at the level of the aortic bifurcation were also measured using a round ROI for reference.

2.4. Patient charts

Patient charts were reviewed, blinded to imaging findings, by an experienced pediatric gastroenterologist with expertise in IBD (PC) to establish the clinical diagnosis. A diagnosis of IBD was based on established criteria agreed upon in Porto [13]. Clinic forms, dictated physician letters, and laboratory values were reviewed to determine the presence of inflammatory disease activity as close in time as possible to the MRE. For patients with CD, the weighted pediatric CD activity index (wPCDAI) was calculated [14]. For patients with ulcerative colitis (UC) and inflammatory bowel disease unspecified (IBD-U), the pediatric ulcerative colitis activity index (PUCAI) was calculated [15]. Patients were deemed to have active clinical inflammation with wPCDAI≥12.5 [14] or Pediatric Ulcerative Colitis Disease Activity Index ≥10 [15].

2.5. Statistical analysis

Interreader agreement for conventional MRE findings and qualitative DWI analysis was performed using kappa statistics. Kappa values of <0.20 were considered poor agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement, and >0.80 almost perfect agreement [16]. Interreader agreement for the measurement of ADC values was assessed by calculating the interclass correlation coefficient (ICC). ICC values of <0.4 represented poor agreement, 0.4 to 0.75 indicated fair to good agreement, and >0.75 indicated excellent agreement [17]. Overall agreement was then reported separately for each of the nine segments of the gastrointestinal tract.

Kappa statistics were also used to assess the agreement between conventional MRE findings of inflammation and diffusion restriction on qualitative DWI analysis. Differences in mean ADC values with and without inflammation as assessed by either qualitative diffusion restriction or physician global assessment (PGA) of inflammation were analyzed using Student's *t* test.