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Incoherent-motion magnetic resonance imaging and pediatric Crohn disease

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ABSTRACT

Crohn disease is a chronic inflammatory bowel disease of unknown etiology with approximately one-third of patients being children and adolescents. Long-standing inflammation can result in fibrostenosing disease, usually of the terminal ileum. However, distinguishing between inflammation and fibrosis on conventional imaging is difficult. Incoherent motion magnetic resonance imaging is a novel imaging modality that evaluates the speed of water diffusion, and therefore may distinguish between inflammation and fibrosis. We report our preliminary experience with a 12-year-old patient who underwent intravoxel incoherent motion (IVIM) as an attempt to identify perioperative, as well as IVIM features, suggestive of fibrosis; this, in order to better-delineate timing between continued medical management and transition to an operative intervention through non-invasive adjuncts.

Key words: Incoherent-motion magnetic resonance imaging, Crohn disease

Introduction

Crohn disease (CD) is a chronic inflammatory bowel disease (IBD) of unknown etiology. Approximately one-third of patients with CD are children and/or adolescents. CD may involve any part of the gastrointestinal tract (GI) with chronic, relapsing, and potentially unremitting clinical course [1]. If left untreated, long-standing inflammation may result in bowel obstruction, stricture, fistula, and/or abscess; in addition, there is an increased risk for small and large bowel malignancy in areas of chronic inflammation [2]. In current practice, magnetic resonance enterography (MRE) has largely replaced computed tomography (CT) enterography as the imaging reference standard in assessing bowel inflammation at most pediatric institutions. A major advantage of MRE is that it does not require ionizing radiation, which is a major consideration when imaging children. However, the accuracy of MRE in distinguishing between inflamed and fibrotic segments in CD patients is less than optimal, which has limited its widespread utilization as the sole assessment tool for IBD [3-4].

Incoherent-motion magnetic resonance imaging (MRI) intravoxel incoherent motion (IVIM) is a novel

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imaging and analysis technique that allows for quantification of tissue cellularity and microcirculation using diffusion-weighted MRI (DW-MRI) with multiple b values [5-9]. Overall, DW-MRI is a non-invasive imaging technique that is sensitive to the thermally-driven, random motion of water molecules, modified in living tissue by the interaction between cell membranes and macromolecules [5,6]. This microscopic motion is most commonly characterized by the decay of the water signal with b-factor [5-9]. The signal decay is commonly modeled as a mono-exponential function associated with apparent diffusion coefficient (ADC) as the decay rate parameter [5-9].

Previously, Freiman et al [7, 8] demonstrated the important role of the microcirculation as measured by IVIM in distinguishing normal from abnormal bowel regions in pediatric CD utilizing these multiple b values; reduction in b values signifies potential stenosis [7,10]. Restricted diffusion previously observed by our group is primarily also associated with changes in blood flow that are reflected by a reduction in the perfusion parameter F of the IVIM model in the cases of chronic inflammation and stenosis; on the other hand, active inflammation will show an increase in the perfusion parameter F of the IVIM model [9]. The non-enhancing F values have been reported to be 0.59 ± 0.26 versus enhancing F values of 0.27 ± 0.2; the former indicating inflammation versus the latter signifying reduction in microvascular volume and potential chronic nature of the disease process [9]. Therefore, we report our experience with a patient who underwent IVIM in an attempt to identify features suggestive of fibrosis versus active inflammation, as well as the overall qualitative agreement between radiographic, endoscopic, and surgical evaluations of a CD patient.

Case Report

Demographics

The patient was 12 years of age at the time of surgery; however, he was initially diagnosed at 9 years of age. The duration of his symptoms was 2.5 years prior to surgery. These symptoms had increased in intensity and had included an increased aversion to certain foods, as well as increased abdominal discomfort, frequent bloody bowel movements, and poor weight gain. He was otherwise not obstructed, nor did he have anemia related to bloody bowel movements. Body mass index (BMI) was 16 kg/m2 and, at the time of the surgery, he was only on low-dose steroids. The indications for surgery were failure of medical management and limiting overall exposure to steroids, improving his BMI and limiting overall morbidity.

Histologic Detection of Active Bowel Inflammation or Fibrosis

The simple endoscopic score for CD (SES-CD) scale/score was employed to validate preoperative endoscopic studies; Moskovitz et al. defined the cutoffs for each disease severity as follows: 0-2 suggested inactive; 3-6 mildly inactive; 7-15 moderately active; and, >16 severely active diseases [4,11]. Endoscopy and colonoscopy were performed prior to operative intervention and MRE on this patient. The SES-CD for this case was 11 while the ileocecal valve appeared stenotic at the time of the preoperative colonoscopy as seen in Figure 1.

Radiographic Findings

Three different imaging modalities were utilized in this patient including DW-MRI, ADC mapping calculated from the DWI-MRI data, and IVIM modeling. This patient had restricted diffusion on IM-MRI, as well as on DWI-axial images as evidenced by increased signal intensity on diffusion imaging, lower b values (signal decay), and reduced F-value component of the mathematical model generated by the scan. Figures 2a and 2b, in combination with qualitative findings above, are suggestive of fibrostenotic disease. The calculated b value for this patient's segment was 1.44911 um2/ms. As compared to normal ADC values for the terminal ileum that have previously been reported, including 3.116 ± 0.56 um2/ms, and 3.3 ± 0.9 um2/ms respectively, this b value was significantly reduced [9,10]. Increased signal intensity on DW-MRI imaging and corresponding decreased signal intensity on ADC imaging may be seen when potential fibrostenosing disease is present. Figure 3 depicts a representative fast-diffusion fraction map obtained by IVIM with the ileum annotated by green. The ileum was noted to have a reduced fast-diffusion fraction (F) compared to the surrounding regions on IVIM modeling. The calculated F-value was 0.19, which was significantly lower than previously reported F-values [9]. This is consistent with the clinical findings of chronic inflammation.

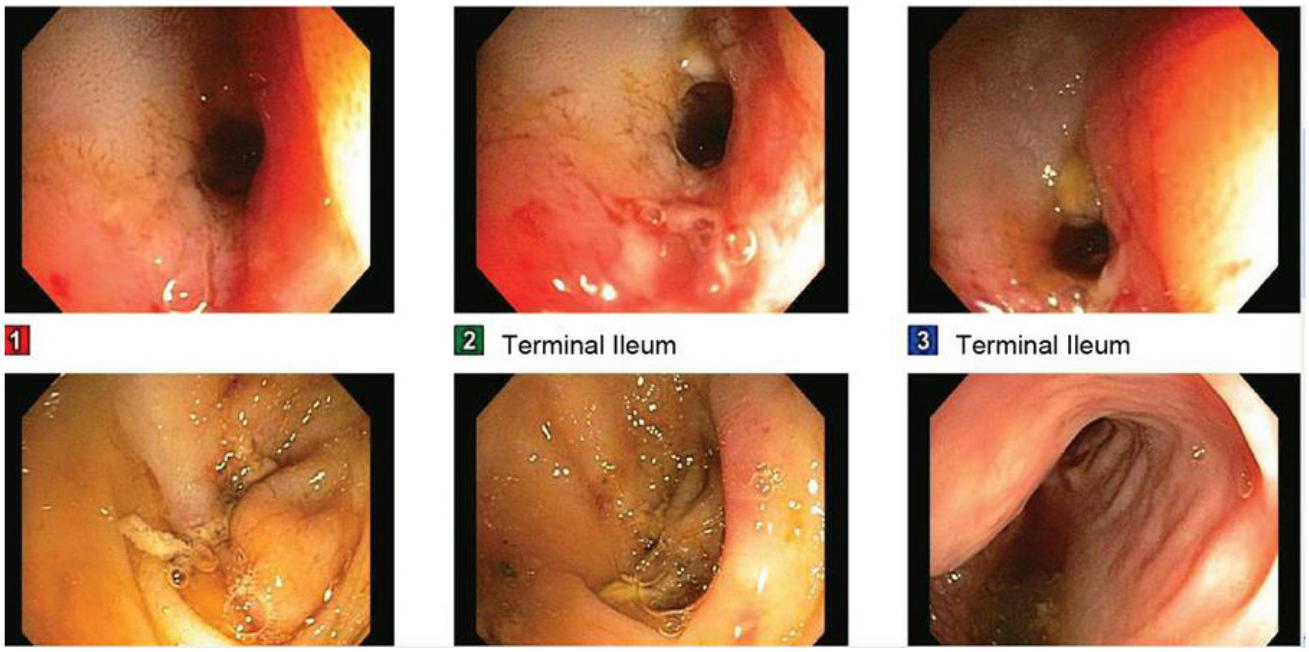

Figure 1. At this patient's preoperative colonoscopy, patient's disease was moderately active by the simple endoscopic-Crohn disease score, and the ileocecal valve appeared stenotic at the time.

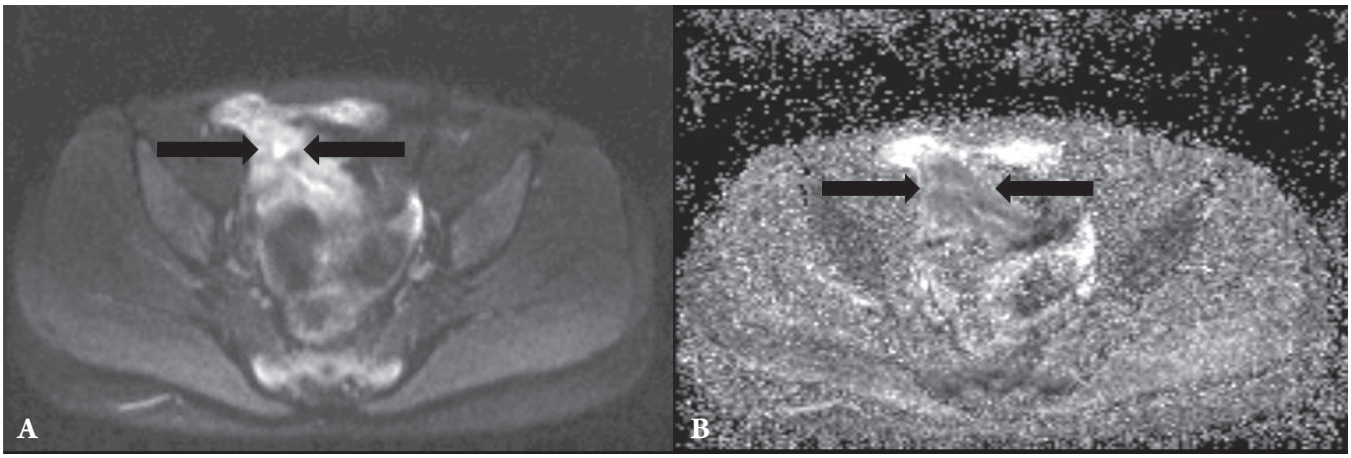

Figure 2. (A) Portrays hyperintensity (black arrows) on DW-MRI diffusion imaging, **(B)** Portrays decreased signal intensity (black arrows) on apparent diffusion coefficient (ADC) imaging corresponding to reduced calculated b values. Increased signal intensity on diffusion-weighted magnetic resonance imaging and corresponding decreased signal intensity on ADC imaging may be seen when potential fibrostenosing disease is present.

Surgical Bowel Resection Histological Reference

A single incision laparoscopic ileocecectomy with 12 cm stapled side-to-side functional end-to-end ileocolostomy was performed. Approximately 10 cm of the small bowel were resected. The histopathological specimens showed significant inflammatory changes and marked stricturing of the terminal ileum consistent with the preoperative imaging data.

Discussion

MRE has largely replaced CT enterography as the cross-sectional imaging reference standard for the assessment of bowel inflammation at most pediatric institutions. MRE does not require ionizing radiation, a major consideration when imaging children. However, the ability of MRE to distinguish between acute, inflamed and fibrotic segments in CD patients was limited, which prevented widespread utilization as the sole assessment tool for IBD. The early results from our case show qualitative and quantitative agreement between a non-invasive tool (IVIM) and other forms of preoperative and perioperative evaluation of a patient with CD, who had progressed from medical management to operative intervention for chronic, fibrostenotic sequelae.

Overall, our patient is similar to other patient cohorts included in other larger studies [12]. Longitudinal registry data show that children diagnosed between the ages of 13 and 16 years have an increased probability of needing bowel surgery compared with younger

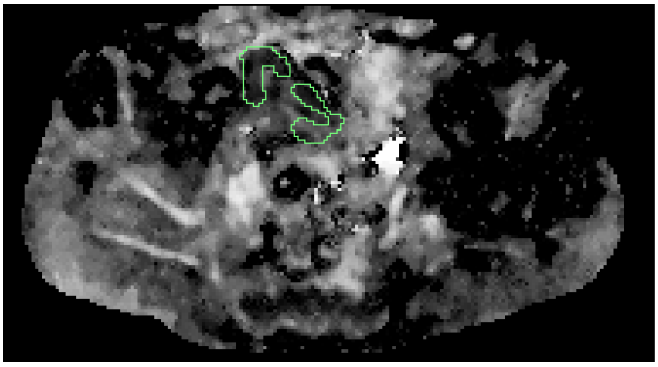

Figure 3. Representative fast-diffusion fraction map obtained by the IVIM method with the ileum annotated by green. The ileum presents with a reduced fast-diffusion fraction compared to the surrounding regions. This is consistent with the clinical findings of chronic inflammation.

children [13,14]. The presence of active inflammation or fibrosis is still a conundrum that is not reliably distinguished preoperatively by traditional clinical methods; however, diagnostic imaging has evolved to better delineate those aforementioned conditions. CD is characterized by segmental, asynchronous lesions with varying degrees of severity [15]. There is no single gold standard as far as endoscopic description and diagnostic evaluation; diagnostic imaging evaluations include conventional enteroclysis, ultrasonography with and without contrast, Doppler evaluation, and CT enteroclysis [15]. This radiographic evaluation has progressed to MRI and subsequently MRE. At our institution, the standard of care has become the utilization of MRE.

Earlier detection of non-responders is of utmost importance and should be supported by both histopathological changes, as well as reliable imaging findings, in order to embark upon surgical interventions. Previous guidelines have recommended evaluating the whole GI with upper endoscopy, ileocolonoscopy, and small bowel imaging [16]. More recent studies have elucidated that pediatric patients with IBD, specifically CD, may have stricturing as well as penetrating disease at the same time and are not necessarily mutually exclusive; thus overall knowledge of this allows the entire healthcare team to provide more holistic care for these children [17-19]. In fact, more recent classification scales propose to include this subgroup of pediatric patients in order to better prognosticate their outcomes; yet, consensus has not been achieved as of now [19]. Patients with isolated terminal ileal disease or ileocolonic disease, like our case, have the highest risk (6-9 folds) of developing stricturing or penetrating disease, which will eventually require operative intervention [20].

Thus, many pediatric CD patients will, by definition, have a long and unfortunately unrelenting course that is balanced by both conventional and novel treatment measures; the quagmire ensues when those treatments fail, and the need for surgery arises. When looking at this imaging technique thus far, we have noticed similarities regarding the qualitative description that IVIM provides, which may predict a non-invasive treatment algorithm. For example, chronic cases (like our case) have the following characteristics: (1) failure of non-operative management; (2) endoscopic exams consistent with stenosis or fibrosis; (3) reduction in ADC calculated b values; and, (4) a more significant and sensitive reduction in the F-component of perfusion on the IVIM model. Furthermore, the choice of multiple b values used to acquire the images, and the improved analysis model may continue to have a substantial impact on the diagnostic accuracy of quantitative biomarkers for CD in this patient population [9].

Conclusion

IVIM is a novel imaging modality that evaluates the speed of water diffusion, and therefore may distinguish between inflammation and fibrosis. We continue to employ this technique in the evaluation of our pediatric CD patients, so that healthcare professionals may have a rapid and non-invasive imaging modality of CD activity. Furthermore, building on this case patient, our hope is that there will be continued overall agreement between these radiographic, endoscopic and surgical evaluations of CD patients to limit excessive invasive tests and predict future need for operative interventions earlier.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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