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ORIGINAL ARTICLE

Magnetic Resonance Enterography: Safe and Effective Imaging for Stricturing Crohn's Disease

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Abstract
Background Symptomatic Crohn's disease (CD) patients often undergo diagnostic imaging studies for evaluation of disease activity or complications including bowel strictures and obstruction. Magnetic resonance enterography (MRE) provides information regarding disease activity, chronicity, and stricture formation without using ionizing radiation.
Aim Examine the use of MRE among CD patients presenting with symptoms suggesting obstruction in a tertiary care practice setting.
Methods We performed a retrospective study of all CD patients undergoing MRE at a tertiary IBD referral center over a 3-year study period including a subgroup analysis of patients presenting obstructive symptoms. Positive and negative findings from MRE were correlated with medical and surgical decision outcomes over the subsequent 90-day period.
Results In the study, 119 CD patients underwent 133 MRE scans, including 40 scans on individuals presenting with obstructive symptoms. Positive findings of CD including active inflammation, stricturing, and penetrating disease were more frequent in MREs ordered to evaluate obstructive symptoms (87.5%) compared other indications (58.1%, $p = 0.001$). In patients presenting with obstructive symptoms, MRE findings assisted in directing a change of clinical management towards escalation of medical therapy in 55% and surgery in 32.5%. Review of surgical resection specimens corroborated MRE findings of disease activity and fibrosis in 92% of cases going to surgery.
Conclusions In practice-based use at a tertiary IBD referral center, MRE provided an effective, radiation-free alternative to computed tomography by providing valuable diagnostic information for evaluating and directing care in Crohn's disease, particularly for patients presenting with obstructive symptoms.

Keywords Crohn's disease · Magnetic resonance enterography · Obstructive symptoms · Ionizing radiation

Abbreviations

CD	Crohn's disease
CT	Computed tomography
MRE	Magnetic resonance enterography
MR	Magnetic resonance
SBFT	Small bowel follow-through
SEM	Standard error of the mean
CTE	Computed tomography enterography
ACR	American College of Radiology
UC	Ulcerative colitis

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Introduction

Crohn's disease (CD) is a chronic inflammatory condition that can affect any part of the alimentary tract, most commonly the distal ileum. CD of the small bowel typically begins with inflammation, but can progress to fibrosis complicated by stricturing and obstruction as well as penetrating disease with resultant fistulae and abscesses [1]. Since the distal small bowel is less accessible to endoscopic evaluation, radiographic imaging is commonly employed as part of the diagnostic work-up of CD patients presenting with new abdominal symptoms. An ideal imaging study provides an accurate assessment of disease extent and activity while identifying complications of stricturing or penetrating disease [2]. The presence or absence of these findings impacts subsequent CD management decisions particularly when deciding between escalating medical therapy and surgical resection.

Computed tomography (CT) of the abdomen and pelvis has been the cross-sectional imaging modality of choice when evaluating CD patients presenting with new abdominal complaints or a change in their pre-existing condition. Advantages of helical CT scanning are its wide availability and its ability to provide a rapid and accurate means of evaluating the abdomen and pelvis for both the intestinal and extraintestinal complications of CD [3]. However, recent recognition of the potential long-term effects of repeated exposure to ionizing radiation from CT scans has led to increased interest in the application of other non-ionizing radiation based cross-sectional imaging modalities for patients with chronic diseases [4, 5].

Magnetic resonance enterography (MRE) is a newer imaging technique that has been utilized to aid in the diagnosis of CD patients without exposure to ionizing radiation. Multiplanar cross-sectional imaging sequences obtained during MRE allow for simultaneous visualization of luminal pathology as well as extraintestinal complications of CD in virtually any orientation, independent of their location within the abdominal cavity [6]. MRE can assess the features of a pathologically altered bowel segment through characteristic patterns of attenuation, degrees of enhancement, and length of involvement. Additionally, areas of stricturing with prestenotic dilatation, fistulae, abscess, and other intraperitoneal or extraintestinal complications can all be identified in three dimensions [7].

MRE has significant advantages as a diagnostic tool for CD patients. Importantly, MRE eliminates ionizing radiation exposure, and therefore may be a more appropriate alternative to CT scanning, especially in CD patients who undergo repeated imaging studies over time [8]. Also, with a quality MRE exam, some reports suggest that an experienced radiologist can differentiate findings consistent with active inflammation from the chronic changes of fibrosis based on different enhancement patterns [8–10]. This feature of the MRE examination has the potential to be especially useful when considering surgical verses medical management options, particularly among patients presenting with obstructive symptoms. In this study, we aimed to examine, from a practice-based viewpoint, the diagnostic value of MRE among symptomatic patients with IBD with a focus on patients presenting with suspected obstructing CD.

Methods

Patient Population and Study Database

All adult patients with an established diagnosis of Crohn's disease who underwent an MRE examination at a high-volume tertiary IBD referral center over the 3-year period from 2006 to 2008 were identified for inclusion into this retrospective study. Relevant patient demographic information and CD-related clinical histories were collected in addition to the indications for magnetic resonance (MR) imaging and pertinent radiographic findings. The Human Research Protection Office (Institutional Review Board) at the Washington University in St. Louis School of Medicine approved this study and the informed consent requirement was waived.

The subset of patients presenting for MRE due to suspected intestinal obstruction were identified using pre-specified criteria for suspected obstruction including symptoms of nausea and/or vomiting with associated abdominal distention and/or decreased flatus and bowel movements representing a change from their baseline symptoms. MRE requisitions listing suspected obstruction as the indication for the study in patients with known CD were also included if clinical history by secondary chart review corroborated the requested indication. MRE findings were taken directly from the transcribed report generated by the abdominal MR radiologists at Mallinckrodt Institute of Radiology of the Washington University in St. Louis School of Medicine. Additional data collected included CD medications prescribed within the 30-day period following the MRE study as well as CD surgeries performed during the 90-day period following the MRE exam.

Diagnostic Studies

All MRE studies were performed using the standardized protocol of the Mallinckrodt Institute of Radiology of the Washington University in St. Louis School of Medicine. Patients fasted for a minimum of 4 h followed by oral ingestion of 750–1,350 ml of VoLumen (E-Z-EM Inc.,

New York, NY, USA), a sorbitol-based biphasic contrast agent given 45 min prior to scanning. Intravenous glucagon [(1 mg), Eli Lilly & Co, Indianapolis, Indiana, USA] was given immediately prior to scanning the noncontrast sequences. The standard MRE protocol utilizes pre-contrast HASTE and 2D Gradient Recalled Echo (GRE) fat-saturated (FS) sequences followed by post-contrast 3D-FLASH Coronal, 2D GRE FS, and Tru-FISP (BSSF) sequences. A single dose (0.1 mmol/kg) of a standard gadolinium contrast agent (Gadobenate Dimeglumine (Multihance) or Gadoversetamide (Optimark)) is injected at 3 cc/s prior to the post-contrast sequences. The post-contrast 3D-FLASH sequences are timed at 25 s (arterial phase) and 55 s (enteric phase). The 2D GRE FS sequence is then done in succession (delayed phase). The total in-room time for an MRE exam was typically 30 min or less.

Findings of stricture, active inflammation, and fibrosis were extracted from the transcribed radiology summaries and interpretations from each reviewing MR abdominal radiologist. Criteria used for classifying disease activity on MRE are described as based on the interpreting radiologist's final read and as detailed by abdominal MR specialist (CAR and VRN): MRE findings of luminal narrowing and wall thickening were classified as stricture. An obstruction was identified when there was dilated bowel proximal to a transition point or stricture. The presence of early post-contrast bowel wall enhancement and thickening in the setting of intermediate to increased T2 signal intensity bowel wall thickening was classified as active inflammation (Fig. 1). Other frequently listed features associated to the description of active inflammation included fat proliferation, serosal hypervascularity, and enlargement of associated lymph nodes. Changes suggestive of fibrosis were defined by the presence of delayed or absent contrast enhancement with intermediate to decreased T2 signal intensity bowel wall thickening (Fig. 2). Compound lesions were identified when components of both early and delayed enhancement were present (Fig. 3) [8].

In recognition that a benefit of MRE imaging is avoidance of ionizing radiation, data were also extracted from patient charts to calculate the number of prior CT and small bowel follow-through (SBFT) examinations performed for each study patient over the prior 48 months before the initial MRE exam. Estimated cumulative radiation exposure per patient over the 48 months was also calculated using standard estimates of radiation for CT (12.0–15.8 mSv/study) and SBFT (2.2 mSv/study) [11].

Pathology

Pathology reports for the subset of patients who underwent surgery during the 90-day period following their MRE exams were reviewed. Notable findings of interest included extent of bowel involvement, inflammatory changes, extent of fibrosis and muscular hypertrophy, and presence of strictures or fistulae. Lesions were classified by the reviewing pathologist as predominantly inflammatory, predominantly fibrostenotic, or compound lesions based on the attending pathologist's review and final report.

Statistical Analysis

Descriptive statistics were reported as percentages, means, and standard errors of the mean (SEM). Continuous variables were compared using unpaired Student's t test and categorical data were compared using two-sided Fisher's exact test. In all instances, p values ≤ 0.05 were considered to be significant.

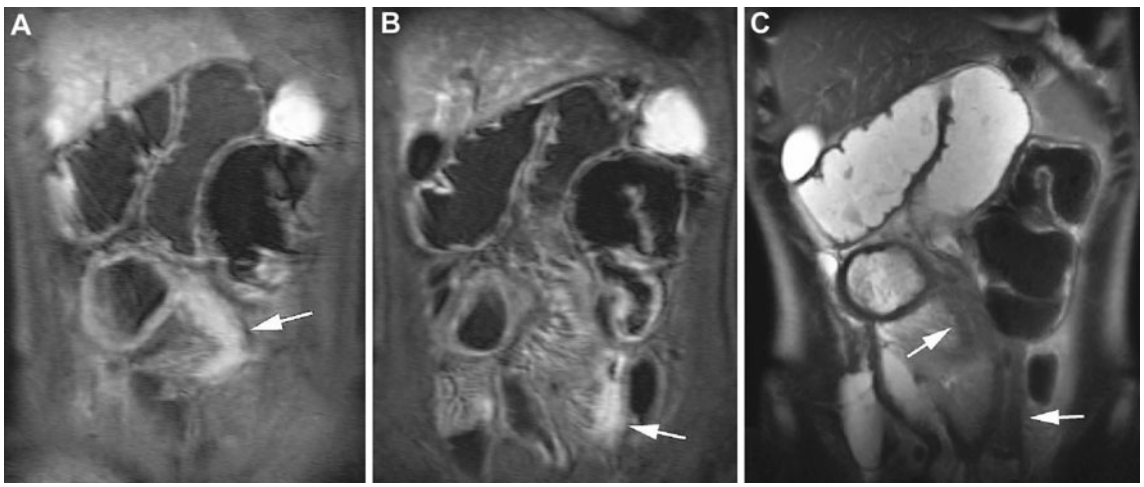

Fig. 1 Images consistent with active inflammatory disease of a narrowed distal ileum showing mucosal enhancement on early post-contrast coronal VIBE sequences (**a** and **b**). Intermediate signal intensity wall thickening of the same segment is shown by a coronal T2 HASTE image (**c**)

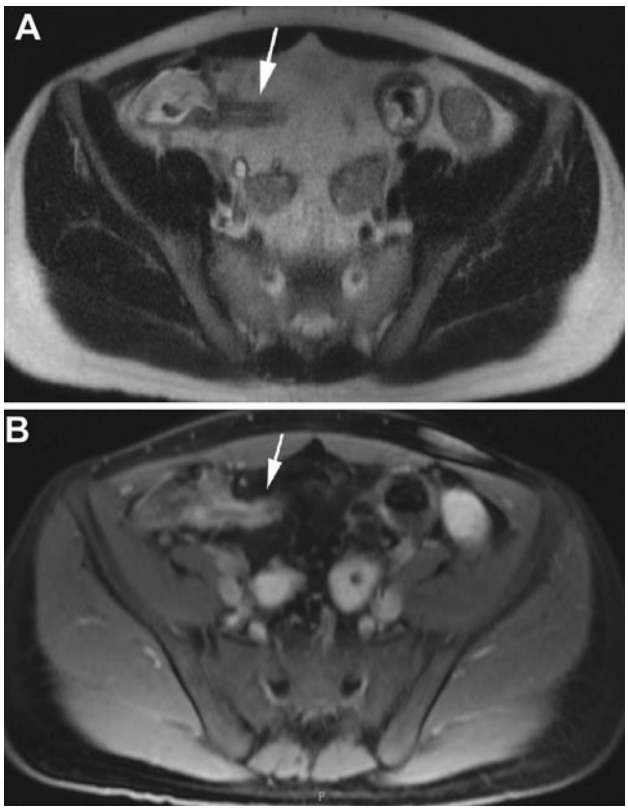

Fig. 2 Findings suggestive of chronic fibrosing disease showing low signal intensity thickening of the terminal ileum on an axial T2 HASTE sequence (**a**) and corresponding delayed enhancement on axial VIBE sequence (**b**)

Results

Study Population

A total of 119 patients with established Crohn's disease underwent 133 MRE scans during the 3-year study period including 40 scans performed on 36 patients presenting with suspected obstruction. Primary indications for the remaining 93 studies included new or unexplained abdominal symptoms (e.g., pain, diarrhea), evaluation of disease activity and exclusion of abscesses or fistulae. The characteristics of these patients are listed in Table 1. None of the exams had to be terminated prematurely due to patient intolerance.

The key radiographic findings of active inflammatory, stricturing, or penetrating CD features as described in the MRE studies are summarized in Table 2. The overall rate of these positive findings on MRE was higher when the indication for ordering MRE was evaluation of obstructive symptoms (87.5%) compared to scans ordered for other indications (58.1%, $p = 0.001$). The presence of active inflammation, strictures, and obstruction were more common in the cohort with obstructive symptoms. Patients underwent an average of 2.8 ± 0.5 CT scans and 1.0 ± 0.2 SBFT studies during the preceding 48 months prior to their MR exams. Mean radiation exposure per patient was 38.0 ± 7.0 mSv for CT scans and 2.2 ± 0.4 mSv for SBFTs with cumulative radiation exposure due to imaging of 40.2 ± 7.3 mSv over the 2-year study period.

MRE Studies for Suspected Obstruction

Of the 40 MRE exams performed among the CD patients presenting with suspected obstruction, partial or complete bowel obstruction was identified in 40% ($n = 16$) of patients (Table 2). All patients with radiographically confirmed obstruction had associated inflammatory ($n = 9$ of 16, 56.2%), fibrostenotic ($n = 3$ of 16, 18.8%), or compound strictures ($n = 4$ of 16, 25%) diagnosed on MRE. No patient presenting with obstructive symptoms went for surgery in the absence of stricture formation on MRE.

Active inflammatory disease was present in 32 (80.0%) of the scans performed on CD patients with suspected obstruction compared to 49.5% ($n = 46$ of 93) for CD patients having an MRE for other indications ($p = 0.001$, Table 2). Among the 32 studies showing active inflammatory disease, 20 (62.5%) also included a stricture: 14 inflammatory and six fibrostenotic. All 20 patients with MRE findings of both active inflammation and stricture underwent subsequent surgery (50.0%) or change in medication (50.0%) (Fig. 4). Medication changes included initiation of steroids (40.0%) or immunomodulators or biologic therapies (60.0%) within the 30-day period following the exams. The remaining 12 patients had active inflammation and no associated stricture on MRE. All of these patients underwent subsequent changes in their medical regimen primarily with the initiation of biologic therapy alone (66.7%), in combination with immunomodulators (16.7%) or steroids with antibiotics (16.7%). Patients with active inflammation plus stricturing disease were more likely to be referred for surgery than patients with active inflammation only on MRE (10/20 vs. 0/12, $p = 0.004$).

Eight patients presenting with obstructive symptoms had no active inflammation identified on MRE; however, three of these patients had evidence of fibrostenotic strictures and were directed to surgery (Fig. 4). The remaining scans lacked any finding suggestive of active CD and thus the management strategy in these patients was symptom-focused and did not include escalation or change anti-inflammatory-based therapy. At 90 days of follow-up, none of these patients had gone to surgery, nor had the new anti-inflammatory therapy been initiated.

Pathology

Review of pathology reports revealed that findings on surgical specimens correlated well with pre-operative MRE

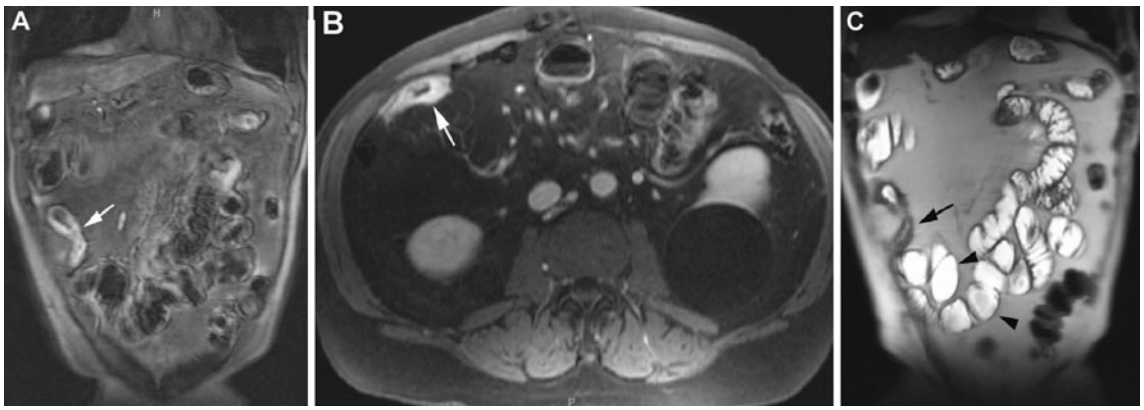

Fig. 3 Early postcontrast VIBE sequence (**a**) demonstrates mucosal enhancement of a narrowed terminal ileum (*arrow*) with persistent enhancement of the wall on a delayed phase (**b**). Multiple upstream loops of small bowel (*arrowheads*) in the right lower quadrant are dilated on coronal T2 HASTE sequence (**c**). This pattern suggests a compound stricture displaying changes of both active inflammatory disease and those suggestive of fibrotic change. Image **b** also shows extensive proliferation of mesenteric fat, a finding that is associated with inflammation

Table 1 Demographics and characteristics of CD patients with MRE examinations

	Suspected obstruction	Other indications
Number	36	83
Gender (M:F)	18:18	31:52
Mean age (years)	40.0 ± 2.4	36.1 ± 1.4
Range (years)	18–77	17–67
Ethnicity		
Caucasian	30 (83.3%)	78 (94.0%)
African American	5 (13.9%)	4 (4.8%)
Hispanic	1 (2.8%)	1 (1.2%)
Smoking history		
Current	12 (33.3%)	23 (27.7%)
Former	5 (13.9%)	11 (13.3%)
Never	19 (52.8%)	49 (59.0%)
History of prior surgical resection	23 (63.9%)	49 (59.0%)
Multiple prior resections	8 (22.2%)	19 (22.9%)

No differences between groups were found to be statistically significant

findings in 92% of patients with obstructive symptoms. While absolute confirmation of spatial involvement could not be performed, all seven patients with inflammatory strictures on MRE had severe active inflammation associated with stricture on pathology. All three patients with compound strictures were found to have active inflammatory and fibrostenotic elements of stricturing disease. One of the three patients who had an MRE-identified fibrostenotic stricture was found to have an adhesive band with no associated stricture during surgery.

Discussion

Magnetic resonance enterography is a newer cross-sectional imaging technique used in Crohn's disease, which provides detailed evaluation of both luminal and extraluminal abdominal pathology without exposing the patient to ionizing radiation. In this retrospective study, we examined the use of MRE in patients with established Crohn's at a tertiary IBD referral center and report it to be a well-tolerated exam providing meaningful information to assess disease activity, chronicity, and complications. MRE was particularly useful in the subset of CD patients with suspected obstruction where an identifiable cause was identified 87.5% of the time. The ability of MRE to identify stricturing CD impacted subsequent management decisions for the majority of these symptomatic patients. The identification of strictures, particularly those determined to have a fibrostenotic component, often prompted referrals for surgery in lieu of escalating medical therapy. Review of surgical pathology reports showed correlation to MRE findings in the majority of operative cases further supporting the accuracy of MRE as a diagnostic modality for IBD. Active disease on MRE corroborated clinical assessment leading to subsequent medical therapeutic changes among all CD patients with suspected obstruction. Conversely, the absence of active inflammatory CD on MRE prevented premature escalation of medical therapy in the majority of patients whose symptoms may not have been directly attributable to their underlying Crohn's disease.

Due to the chronic, progressive nature of CD, patients frequently undergo multiple CT exams over the course of their disease. In particular, computed tomographic enterography (CTE) has been increasingly ordered during the

Table 2 Radiographic findings on MRE evaluation

	Suspected obstruction	Other indications	*p* value
Number of studies	40	93	
Active inflammation	32 (80.0%)	46 (49.5%)	0.001
Obstruction[a]	16 (40.0%)	0 (0.0%)	<0.0001
Stricture	23 (57.5%)	5 (5.4%)	<0.0001
Inflammatory	14 (60.8%)	1 (20.0%)	0.15
Fibrostenotic	3 (13.0%)	4 (80.0%)	0.008
Compound[b]	6 (26.1%)	0 (0.0%)	0.55
Abscesses	1 (2.5%)	9 (9.7%)	0.28
Fistulae	2 (5.0%)	7 (7.5%)	0.72
No findings	5 (12.5%)	39 (41.9%)	0.001

[a] Partial or complete

[b] Inflammatory and fibrostenotic features

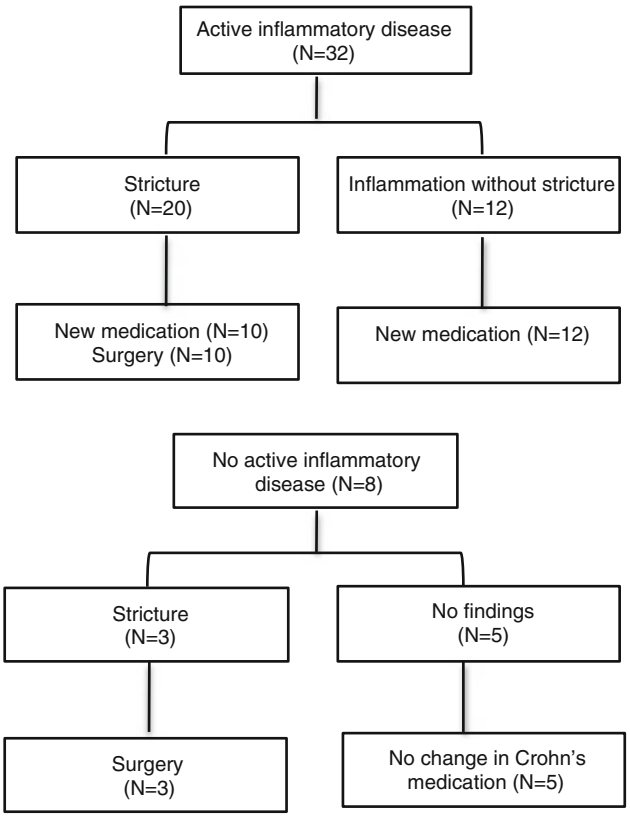

Fig. 4 Medical and surgical management decisions based on MRE radiographic findings in CD patients presenting with suspected obstruction

evaluation of CD due to the high-resolution multiplanar imaging sequences, which provide greater detail of the small bowel and extraluminal complications of CD [12]. CTE findings have been demonstrated to correlate with other makers of active disease such as elevated C-reactive protein (CRP). Recent studies also suggest that CTE impact patient management with respect to surgical decision-making or medical therapies [13, 14]. Because of these more disease-specific features, the overall number of CTEs ordered has been increasing in the past few years [11]. However, in order to visualize these subtle soft tissue attenuation differences in the small bowel, CTE exposes patients to as much as 1.5–2 times the dose of radiation compared to conventional CT. The increasing cumulative radiation exposure parallels a potential increased risk of radiation-associated malignancy, with the number of cancers attributable to CT-related radiation ranging from 1.5 to 2.0% [4]. The median lifetime-associated risk of cancer with multiphase abdominal CT is estimated to be 4 per 1,000 patients [15].

Despite the growing concerns regarding increasing radiation exposure with repeated CT scans and the potential associated risks, the American College of Radiology (ACR) Appropriateness Criteria lists conventional CT or CTE as the diagnostic studies of choice in the initial evaluation of adults and children with suspected Crohn's disease. The ACR criteria also recommend CT as the first line study for patients that have known CD and present with stable, mild symptoms or systemic symptoms of fever, abdominal pain, and leukocytosis [16]. Due to the nature and location of acute IBD-related symptoms, CD patients are at greater risk for higher cumulative volumes of ionizing radiation exposure than the general population. Compared to ulcerative colitis patients, CD patients are exposed to 2.5 times more cumulative radiation during the course of their disease [11]. Risk factors for increased radiation exposure in CD patients include early age of diagnosis, upper gastrointestinal tract involvement, penetrating disease, more intense immunosuppressive regimens, or multiple surgeries [17]. Many of our study patients had multiple previous CT exams prior to the MR examination. The cumulative radiation dose of our patient population was 40.2 ± 7.3 mSv during the prior 2 years before their first MRE study. In comparison, the average annual exposure to environmental ionizing radiation in the United States is approximately 3 mSv/year [18]. Utilization of MRE eliminates additional exposure to ionizing radiation associated with CT exams, which had been the routine imaging study of choice for symptomatic CD patients presenting to our emergency department or clinic. The importance of this feature is underscored by recent work suggesting that the risk of cancer development from even a single CT scan may be as high as 1 in 80 [19].

There is increasing interest in application of magnetic resonance imaging techniques for CD patients both for its unique imaging qualities and its avoidance of radiation exposure. Though debate exists, some reports suggest that MRE has higher sensitivity and specificity to identify subtle

features of mural enhancement or thickening than conventional single-phase CT and comparable diagnostic accuracy as CTE [3, 20–22]. MRE findings have also demonstrated high correlation with endoscopic indices of disease activity for patients with known ileocolonic disease [23]. One recent study showed MRE findings correlated well with surgical findings [9]. These investigators also suggested a scoring system predictive for patient management. However, a scoring system with significant numerical overlap between groups and one in which intermediate scores directed patients to surgery verses no management change or escalation of medical therapy may be challenging to adopt. A significant challenge is that on pathology examination, many strictures include both fibrosis and active inflammatory infiltrate. Overall however, these studies suggest that though it is a newer imaging modality, MRE is steadily gaining acceptance among physicians taking care of CD patients. Ultimately, an ideal scoring system for MRE would direct the clinician as to likelihood of response to anti-inflammatory treatment by defining whether lesions were predominantly inflammatory or fibrotic.

Limitations exist both for this study and to the feasibility of widespread adoption of MRE as a first-line cross-sectional imaging technique in Crohn's disease. MRE exams are static, leading to potential difficulty in differentiating luminal stenosis from normal collapsed bowel; however, the administration of oral Volumen and IV glucagon promote bowel distention are used to minimize this as a confounder. This study was retrospective and the MRE readings were not read by the same MR radiologist, nor was the clinical decision-making team the same for each patient. However, each patient with CD seen at our institution is consulted on by a physician specializing in IBD and through review of electronic medical records facilitated a high degree of consistency in collected data. All radiologists interpreting the MRE images were abdominal MR radiology specialists. Furthermore, the analysis represents a real-time representation of how MRE was employed, interpreted, and used to direct decision-making in a large academic medical center. Barriers to routine adoption of MRE into clinical practice include the lack of standardized MRE protocols, additional cost compared to conventional CT, slower study turnaround, lack of insurance coverage, and lack of experienced MR radiologists [8, 10]. Additionally, there may be concerns regarding patients' ability to tolerate the longer scanner time with MRE compared to CT as well as the potential for motion artifact that can interfere with the quality of the study. These factors may impact clinicians' decisions on whether to order an MRE over a CT scan. However, newer imaging sequences are being developed to optimize exam time while minimizing patient discomfort and motion artifact resulting from bowel peristalsis [8].

The most common indications for cross-sectional imaging in CD patients include abdominal pain, obstruction, or evaluation of disease activity [24]. In this study, we found that MRE identifies findings that complement clinical assessment, as well as provides meaningful information to help direct subsequent management decisions for symptomatic CD patients. Therapeutic decisions may also be impacted by the identification of unsuspected lesions in patients with vague symptoms or low clinical suspicion of disease. When stricturing or active disease was present, patients had a change in their CD regimen based on the results.

MRE can provide meaningful information to aid in the management of these complicated patients without subjecting them to ionizing radiation exposure. With rising awareness of the cumulative radiation exposure experienced by this predominantly younger patient population, gastroenterologists caring for IBD patients should increasingly consider use of cross-sectional imaging studies other than CT. Our study suggests that MRE is an attractive and viable alternative. Further studies utilizing standardized protocols for performing the MR exams and interpretation of active and chronic inflammatory changes among CD patients are needed.

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