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Observations and Research

CT or MR Enterography to Assess Response During Vedolizumab Therapy for Small Bowel Crohn's Disease

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Background: To describe response to therapy of small bowel (SB) Crohn's disease (CD) at CT or MR enterography (CTE/MRE) in patients on vedolizumab.

Methods: Patients with SB CD who underwent CTE/MRE exams greater than 12 months apart on vedolizumab therapy were included. Length (in cm) and inflammation severity (EMBARK score) of inflamed SB segments were assessed. Changes in inflammation length of 3.4 cm or greater or inflammation severity of 2 EMBARK points or greater was categorized as response or progression, as appropriate, with development of newly inflamed segments, strictures, or penetrating complications also indicating progression. Patients not meeting the criteria for response or progression were categorized as having stable disease.

Results: Of 36 SB CD patients, the large majority had prior surgery (86%; 31), anti-TNF use (92%; 33), and internal penetrating (78%; 28) disease. Thirty-two patients had paired baseline and follow-up CTE/MRE exams without interval surgery, with clinical response observed in 24/32 (75%). Based on imaging response criteria, 22% (7/32; 95% CI: 9%–40%) had response, 50% (16/32; 95% CI: 32%–68%) were stable, and 28% (9/32; 95% CI: 14%–47%) had disease progression. Fifty-six percent of (18/32; 95% CI: 38%–74%) patients had clinical improvement with response or stable disease by imaging. Patients with stable disease had shorter median baseline lengths of SB inflammation ($P = .012$). Proportion of patients with colonic inflammation, perianal disease, or penetrating complications did not change.

Conclusions: Most patients on vedolizumab for over 12 months demonstrated response or stable SB disease when using objective cross-sectional radiologic imaging criteria using CTE/MRE.

Lay Summary

Most Crohn's disease patients who stayed on vedolizumab for over 12 months demonstrated improved or stable small bowel disease when evaluating follow-up CT or MR enterography exams for changes in small bowel inflammation, or newly developed strictures or penetrating complications.

Key Words: Crohn's disease, enterography, vedolizumab, stricture, response

Introduction

Crohn's disease (CD) affects the small bowel (SB) in the majority of patients.[1] Colonoscopy, while accurate for the detection of colorectal inflammation, fails to identify up to 50% of patients with active small intestinal disease due to limited ileal assessment, proximal SB CD, penetrating complications, or intramural inflammation despite normal-appearing mucosa.[2,3] Computed tomography enterography (CTE) and magnetic resonance enterography (MRE) complement endoscopic evaluation and are accurate in detecting intramural disease, strictures, enteric fistulas, and proximal small intestinal inflammation.[4,5]

Symptoms correlate poorly with the presence of active inflammation in CD.[6] Radiologic response to treatment portends better outcomes, and sustained remission by CTE or MRE nearly eliminates surgical risk.[7,8] Close monitoring of SB disease with the appropriate escalation of therapy for worsening disease improves outcomes (treat-to-target).[9] In clinical practice, periodic assessment by cross-sectional enterography allows clinicians to assess response to therapy, determine disease progression, and monitor treatment response.[8,9] In addition, emerging imaging data have demonstrated increased rates of radiologic improvement and transmural healing after 12 months of biologic therapy compared to 3- and 6-month intervals.[10]

Vedolizumab, a gut-specific inhibitor of α4β7 integrin, blocks leukocyte trafficking and has been approved in the medical management of moderate to severe CD.[11,12] Vedolizumab is safe and effective resulting in clinical and deep remission in up to 1/3 of patients in routine clinical practice, but descriptions

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of radiologic response in the SB are limited.[13] Kotzke et al[14] reported radiologic remission using a variety of cross-sectional imaging methods but did not describe imaging endpoints. CTE and MRE are highly accurate for the detection of moderate to severe SB CD and estimates of length as well as severity of SB inflammation have shown to be highly reproducible.[15–17] Studies looking at the imaging response of SB CD to vedolizumab are sparse and in early phases.[14,18] Our purpose was to describe radiologic response to therapy of SB CD using CTE/MRE in patients on vedolizumab for at least 12 months.

Methods

Study Design and Population

After institutional review board approval, this HIPAA-compliant retrospective study was performed. Inclusion criteria included patients (1) with SB CD established by a gastroenterologist, (2) who underwent serial ($n \geq 2$) CTE and/or MRE exams separated by greater than 12 months while being treated with vedolizumab between 2014 and 2018 with archived images available for review, and (3) both CTE/MRE exams performed while on vedolizumab therapy or vedolizumab therapy initiated following the first exam. Patients with strictures, penetrating complications, colorectal inflammation, and perianal disease were included. Exclusion criteria included patients with CTE or MRE exams not performed with intravenous contrast. Patients who underwent interval surgery between imaging exams were included and considered to have progression of SB CD.

Data Collection and Image Interpretation

Clinical characteristics were abstracted by a gastroenterologist from the laboratory, endoscopic as well as radiology reports, and included date of first vedolizumab infusion, interval between vedolizumab infusions, history of penetrating disease/surgical resection, previous exposure to therapy (biologics, immunomodulators, and corticosteroids), age, vedolizumab drug and antibody levels, laboratory parameters (albumin, hemoglobin), Harvey-Bradshaw index, endoscopic (SES-CD) scores, and disease duration. Clinical response was assessed retrospectively from chart review using the parameters of CD patient-reported outcome signs and symptoms (CD-PRO/SS). Two domains were analyzed, "Bowel Signs and Symptoms" (including number of bowel movements, bowel movements mostly or completely liquid, and urge to have bowel movements right away), and "Abdominal Symptoms" (including pain in the belly, bloating, and passing gas).[19] Improvement in either of these domains was considered a clinical response.

Two experienced radiologists (with 3 and 22 years as staff GI radiologists) reading in consensus, blinded to clinical information and previous imaging results, analyzed each CTE/MRE for the presence of active inflammatory SB CD, colorectal inflammation, perianal disease, penetrating complications (fistula, abscess, inflammatory mass), and lymphadenopathy using a specialized computer workstation. Active inflammatory SB CD was defined by segmental mural hyperenhancement and wall thickening.[5] The length of SB inflammation was measured using a 3D spline tool. Inflammation severity was assessed using the EMBARK score. EMBARK scoring is a visual scoring system that has been used to compare enteric inflammation at CTE to the SES-CD and grades SB inflammation on a scale from 0 to 3 (Table 1).[20] Strictures were defined according to the Society of Abdominal Radiology/AGA and CONSTRICT criteria and demonstrated imaging findings of luminal narrowing, wall thickening, and proximal SB dilation of 3 cm or greater.[5,21] Length and

Table 1. Imaging information recorded from CTE/MRE datasets using the specialized computer workstation for each patient.

Imaging parameter	Scale or measurement
SB inflammation	
Length	In cm, using spline tool delineating centerline of SB
Inflammation—EMBARK score[20]	0 = no imaging findings of inflammation 1 = mural hyperenhancement with absent or equivocal wall thickening of 3.0–4.9 mm 2 = mural hyperenhancement with wall thickening between 5 and 9.9 mm 3 = findings of severity score 2 with perienteric stranding, luminal ulcerations, or mural thickness of 10 mm or more in thickness
Other imaging findings of inflammation (perienteric stranding/fluid, ulcers, comb sign)	Present or absent
Lymphadenopathy	All <1 cm short axis, less than 3 with short axis >1 cm, greater than 3 with short axis greater than 1 cm
Penetrating disease	
Fistula(s)[5]	None, simple, complex; associated with inflamed segment/stricture or anastomosis
Abscess	Present or absent; associated with inflamed segment/stricture or anastomosis
Stricturing disease	
Length and inflammation	As above
Proximal SB dilation	In cm, using spline tool delineating centerline of SB
Colorectal inflammation (cecum/ascending, transverse, descending/sigmoid, rectum)	
Inflammation	4-point scale (absent, mild/equivocal, moderate, severe) based on mural T2 hyperintensity
Length	0%–24%, 25%–49%, 50%–74%, 75%–100% of segment
Perianal disease	Absent, present—simple, present—complex (branching or multiple fistulas; horseshoe ramifications, or abscess)
Chronic mesenteric venous occlusion	Present or absent

inflammation severity (defined as EMBARK) were also measured for strictures.

Table 1 summarizes imaging information recorded from CTE/MRE datasets for each patient and included assessment of penetrating complications, colonic inflammation, and perianal disease. Patient-level response of SB CD inflammation on follow-up CTE or MRE is summarized in Table 2 and is similar to those proposed by Deepak et al,[8] which corresponded to lower risk of surgery, steroid dependence, and hospitalization (see "Statistical Analysis"), and which takes into account the development of newly inflamed SB segments, unequivocal changes in inflammation length (in cm) and severity (by EMBARK score), and newly developed strictures or penetrating complications.[22] Based on previously reported minimum detectability of change in lengths of SB inflammation of 3.4 cm,[22] an inflamed SB segment was considered unequivocally progressing if length increased by 3.4 cm or greater and responding if length decreased by 3.4 cm or greater. Segments with changes between –3.4 and 3.4 cm were considered as no definitive change. This minimum detectability of change of 3.4 cm reflects a previously estimated 1 standard deviation estimate of the radiologist to radiologist variation in measurements lengths of inflammation using a 3D spline tool in a computer workstation. A change in EMBARK score of 2 or more was considered to represent an unequivocal change in inflammation severity. For per-patient assessments, the highest EMBARK score associated with any inflamed segment was assigned.

Statistical Analysis

The primary outcome measure for this study is the change response to vedolizumab therapy, which was categorized as response, stable SB disease, or disease progression per patient based on CTE/MRE findings. The precision in the response rate was estimated using a 95% exact confidence interval for a proportion (ie, number meeting response definition/total patients). For the purposes of this study, changes in actively inflamed SB segments and SB strictures were grouped together; however, development of a new stricture is an imaging criterion indicating disease progression. Patients without inflammation at baseline and follow-up were considered to have one bowel segment with stable disease (ie, neither progression nor response).

Per-patient categorization of progression of SB CD was defined by an increase in length of any inflamed segment by 3.4 cm or greater or an increase in inflammation severity by 2 points on the EMBARK scale (even if another improved), or development of new stricturing or penetrating complications, or development of newly inflamed bowel segments. Imaging-based response criteria for response and stable disease follow an analogous pattern (Table 2). Patients undergoing surgery between the 2 CTE/MRE exams were considered to have disease progression. The proportion of patients with clinical improvement coupled with treatment response or stable SB CD is also reported.

Fisher's exact test was used to test if the changes in the categorized SB inflammation length (decreased, stable, or lengthened) were associated with changes in inflammation severity by EMBARK score (increased vs stable or decreased) and the per-patient categorization of progression, with additional analysis performed using the Kruskal–Wallis test to examine the relationship between imaging response and baseline EMBARK score.

Secondary analysis included associating changes in patient symptoms with patient demographic and historical factors, as well as changes in SB inflammation on CTE/MRE. Descriptive statistics were used to describe changes in colorectal inflammation, penetrating complications, and perianal disease, to ensure that there were no large changes in CD activity outside the SB in the cohort.

Table 2. Per-patient response assessment of small bowel Crohn's disease by response category, taking into account small bowel inflammation, and stricturing and penetrating complications.

Response category	Change in inflammation (by length [cm] and severity [EMBARK])	Change in stricturing disease	Change in penetrating disease
Response	• Decrease in length by 3.4 cm or greater without increase in EMBARK by 2 points • Decrease in EMBARK by 2 points without increase in length by 3.4 cm or greater • No new inflamed segments	No new stricture development	No new fistula/abscess development
Transmural healing[a]	No visible inflammatory lesions (EMBARK = 0)	No strictures	No penetrating disease
Stable disease	• Change in total length of small bowel disease is <3.4 cm • Change in inflammation severity is 0 or 1 point on EMBARK scale • No new inflamed segments	No new stricture development	No new fistula/abscess development
Progression	• Increase in length by 3.4 cm or greater • Increase in EMBARK by 2 points • Newly inflamed segments	Development of a new stricture	Development of a new fistula/abscess

[a]Transmural healing is a subset of response, as described in the table (ie, all patients with transmural healing are also considered responders).

All authors had access to the study data and both reviewed and approved the final manuscript.

Results

Seventy-two patients with SB CD underwent at least 2 CTE/MRE exams while on vedolizumab therapy or began vedolizumab therapy after the first imaging exam; however, in 22 patients, the time interval between imaging exams was 12 months or less, and another 13 patients had at least one of the imaging exams that was not available for review. One patient was excluded as vedolizumab was given only intermittently. Therefore, 36 patients were identified as suitable for assessment of clinical follow-up. Four of these patients had surgical intervention between the baseline and 12-month follow-up CTE/MRE exam and were considered to have progressed clinically. Table 3 summarizes demographic and historical features of these patients. The 32 patients with imaging response criteria are the focus of this work, but we also report overall response including those with interval surgery.

Primary Analysis—Per-Patient Assessment of Imaging Response to Vedolizumab (n = 32)

Baseline and follow-up CTEs were performed in 11 patients, with another 11 patients having MRE for baseline and follow-up exams. Baseline CTE with follow-up MRE was performed in 6 patients, and baseline MRE with follow-up CTE was performed in 4 patients. Determination of per-patient response based on changes in SB CD by CTE/MRE was performed in 32 patients. Of these, 27/32 (84%) patients began vedolizumab therapy after baseline CTE/MRE, while 5/32 underwent both enterography exams on maintenance therapy. Table 3 presents demographic and historical features of these patients, with 28/32 (88%) patients having had 44 prior IBD-related surgeries. The large majority had a history of penetrating disease 26/32 (81%), perianal disease in 16/32 (50%), and prior antitumor necrosis factor (TNF) antagonist use 29/32 (91%). The median vedolizumab drug level was 14.65 μg mL^{-1} (range 3–60), with no patients (0/17) developing antibodies to vedolizumab. The median time between index and second enterography scan included in the analysis was 737 days (range 469–1856), and the median time between the first baseline CTE/MRE and initiation or subsequent vedolizumab dose was 44 days. Clinical indications for the second CTE/MRE included routine surveillance to assess response (n = 21), symptoms (eg, pain, nausea, vomiting; n = 9), preoperative assessment (n = 1), and assess upper tract inflammation (n = 1).

Regarding patient-level responses to vedolizumab treatment, 7 patients, 22% (7/32; 95% CI: 9%–40%) had response to therapy by imaging criteria (decrease in inflammation severity and length [n = 1], decrease in length only [n = 5], decrease in severity only [n = 1]; without new inflamed segments, strictures, or penetrating complications; Figures 1 and 2). One patient had a stricture that resolved. Half of the

Table 3. Summary of clinical characteristics of examined patients undergoing serial CTE/MRE on vedolizumab therapy.

	N = 32	N = 36
Age	42 (19–80)	41 (19–80)
Sex, female %	23/32 (72%)	22/36 (61%)
Median duration of disease	15.5 years (range 5–44)	11.5 years (range 5–44)
Surgical history	28/32 (88%), 44 total surgeries	31/36 (86%), 47 total surgeries
Penetrating disease	26/32 (81%)	28/38 (78%)
Perianal disease	16/32 (50%)	18/36 (50%)
Prior TNF antagonist use	29/32 (91%)	33/36 (92%)
Combination with IM	23/32 (72%)	27/36 (75%)
Smoking	4	4
Harvey-Bradshaw—median	12 (3–20)	12 (3–20)
VDZ drug levels	14.65 (3–60)	14.7 (3–60)
Antibody to VDZ	0 of 17	0 of 19

Abbreviations: TNF, tumor necrosis factor; IM, immunomodulatory; VDZ, vedolizumab.
Thirty-two patients underwent imaging-based response assessment and are the focus of this work. An additional 4 patients underwent interval surgery between the 2 cross-sectional imaging exams, and their additional data are included in the second column.

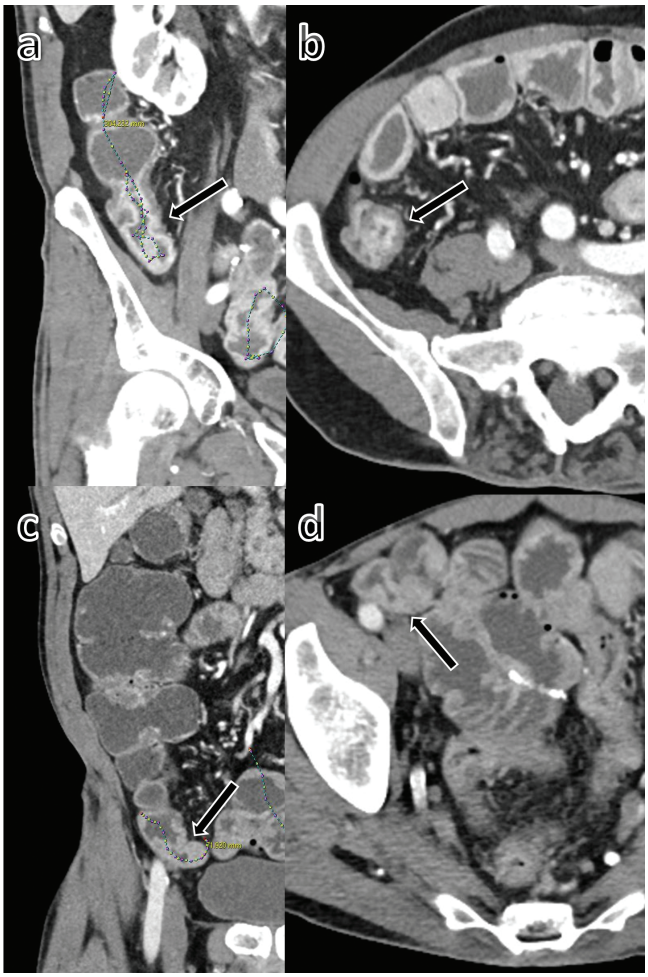

Figure 1. A 67-year-old male underwent baseline CT enterography with a follow-up exam 22 months later. Baseline CT enterography exam demonstrates an ileocecal resection with 21.4 cm of neo-terminal ileal inflammation and an EMBARK score of 3 (A, B: arrows). Follow-up CT enterography exam demonstrated a decrease in length of subtle segmental hyperenhancement to 7.2 cm with a decrease in the EMBARK inflammation severity score to 1 (C, D: arrows).

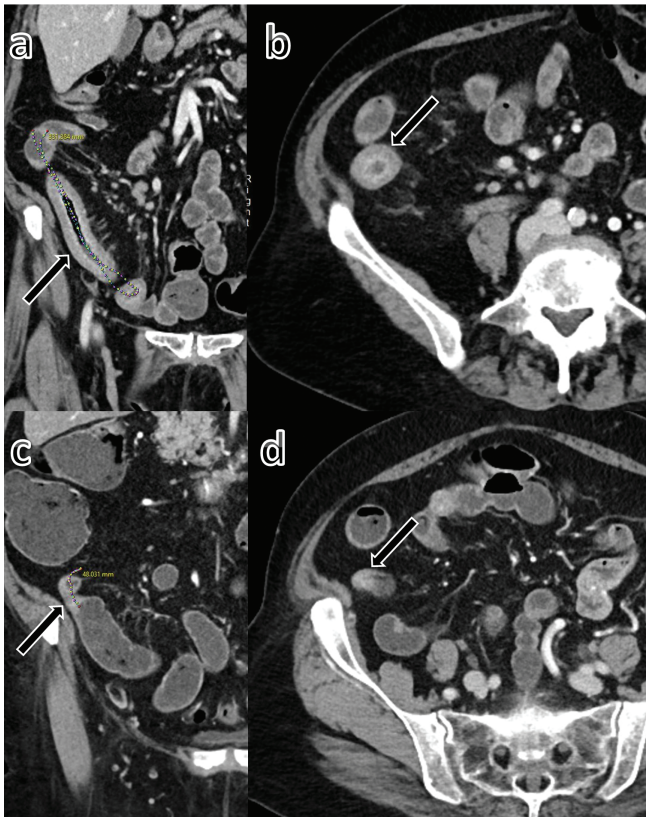

Figure 2. A 76-year-old male underwent baseline CT enterography followed by CT enterography 19 months later. Baseline CT enterography exam demonstrates an ileocecal resection with 33.1 cm of neo-terminal ileal inflammation and an EMBARK score of 3 (A, B: arrows). Follow-up CT enterography exam demonstrated decreased length to 4.8 cm and reduction in the EMBARK score to 1 (C, D: arrows).

imaged patients (50%; 16/32; 95% CI: 32%–68%) had stable disease (Figure 3), with 3 of these patients (3/32; 9%) having persistence of radiologic remission on baseline and follow-up. Nine patients (28%; 9/32; 95% CI: 14%–47%) had progression of SB disease (5 lengthening of inflammation, 2 new penetrating complications, 3 newly developed strictures, 2 new inflamed SB segments). We examined for factors that may be associated with imaging response to vedolizumab. The total length of inflamed SB at baseline imaging was associated with response (mean length in response = 41 cm; mean length in stable patients = 5 cm; mean length in progression = 19 cm; $P = .016$). Imaging response tended to be associated with EMBARK score (with higher scores tending to be associated with imaging response; $P = .10$). No other imaging or demographic features were associated with imaging response. Obviously, changes in total length of SB inflammation were different between response categories owing to the response criteria we employed (mean change in inflammation length for responders = −19 cm; mean change in length for patients with stable disease = 0 cm; mean change in length for patients with progression = +10 cm; $P < .001$).

While the focus of our work is on the 32 patients with response to vedolizumab therapy based on imaging response, considering the 4 patients with interval surgery as treatment failures, 19% (7/36; 95% CI: 8%–36%) had response, 36% (16/36; 95% CI: 21%–53%) had stable disease, and 36% (13/36; 95% CI: 21%-–54%) had disease progression.

In the primary analysis cohort with assessment of SB response by imaging, 75% (24/32; 95% CI: 56%–89%) patients had a clinical improvement in the 2 domains assessed in CD-PRO/SS while on vedolizumab therapy, 9% (3/32; 95% CI: 2%–25%) had no change, and 16% (5/32; 95% CI: 16%–53%) patients worsened. Clinical worsening was associated with an increased number of inflamed bowel segments (mean number of segments if clinically improved and stable = 1.4 and 1.3, respectively; mean number of segments for clinically worsened = 3.2; $P < .001$), total length of inflamed SB per patient at baseline imaging (mean length for clinical improvement = 11 cm; for clinical stability = 54 cm; for clinical worsening = 24 cm; $P = .033$), and tended to be associated with changes in length of inflammation ($P = .055$). Clinical worsening was not significantly associated with prior SB resection ($P = .204$), prior ileocolonic resection ($P = .091$), or any prior medical therapy or combination of medical therapies, or other clinical and historical parameters.

Taking both imaging response criteria and clinical improvement into account, 56% (18/32; 95% CI: 38%–74%) patients had clinical improvement in addition to response or stable disease at CTE/MRE.

Analysis of Inflamed SB Segments

At baseline CTE/MRE, there were 49 inflamed SB segments (including 9 strictures with inflammation) in 29 patients, with 3 patients with prior enteric resections having no SB inflammation. There were no strictures without inflammation. At baseline, the mean length of small intestinal disease was 11.1 ± 20.1 cm (25th and 75th percentile: 2.9 cm, 13.3 cm) and the mean EMBARK score was 1.7 ± 1.7.

Of the 49 inflamed SB segments, 12 (24.5%) decreased in length by 3.4 cm or greater (13.7 ± 13.1 cm; median 8.8 cm), indicating response; and 29 (59.2%) did not change significantly in length (0.2 ± 1.5 cm, median 0.3 cm), indicating stable disease; and 8 (16.3%) increased in length by 3.4. cm or greater (13.4 ± 8.4 cm, median 10.4 cm), indicating progression. The EMBARK inflammation severity score decreased in 37% (18/49) inflamed segments (14 segments by 1 point; 4 segments by 2 points), remained unchanged in 45% (22/49) segments, and increased in 18% (9/49) segments (8 segments by 1 point; 1 segment by 2 points). Approximately 6% (3/49) of inflamed SB segments underwent complete transmural healing on follow-up. Relating to the relationship of inflammation severity to changes in inflammation length, the baseline inflammation severity (EMBARK score) was associated with the change in per lesion length assessment (ie, improved, stable, or worsened length, $P = .07$).

Summary of Colorectal and Perianal Disease

Categorizing colorectal segments as absent/mild versus moderate to severe, at follow-up CTE/MRE, 24 patients had unchanged findings of colorectal inflammation, 5 patients had a decrease in colorectal inflammation, and 3 patients had an increase in colorectal inflammation.

Regarding perianal disease, 4 (12.5%) patients had simple perianal disease, and 3 (9%) had a complex disease with multiple fistulas, horseshoe ramifications, or abscess at baseline imaging; in follow-up, 2 (6%) patients had simple and 4 (12.5%) had complex perianal disease, respectively. Five patients (16%) had penetrating disease at baseline imaging

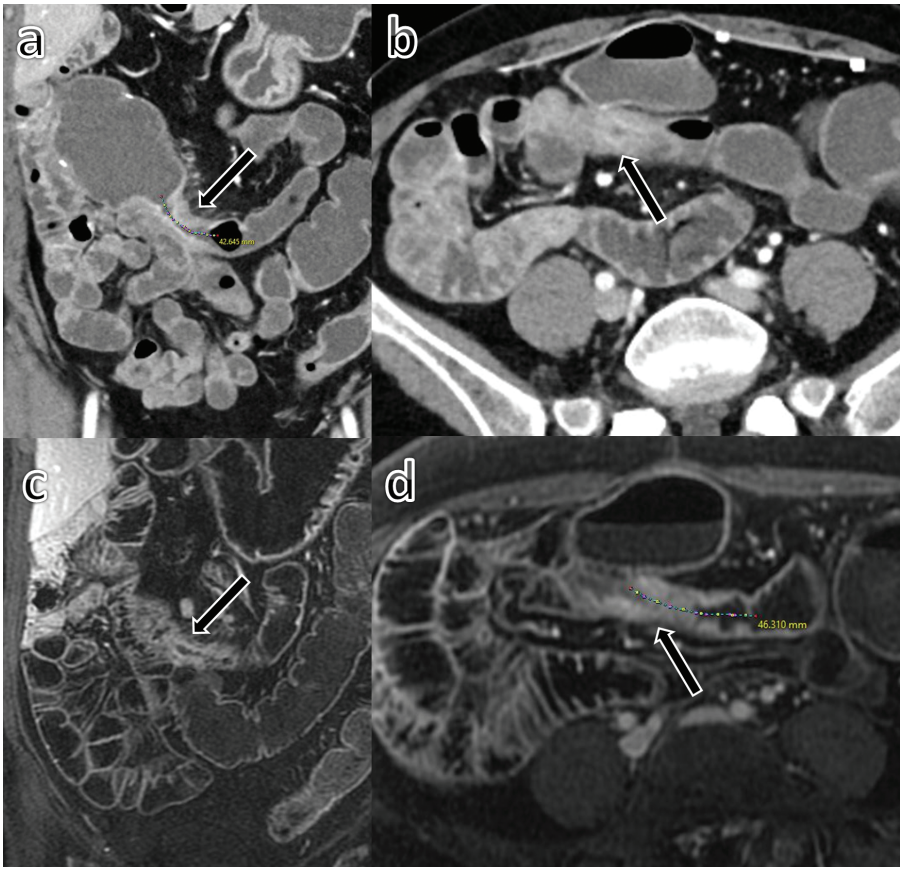

Figure 3. A 56-year-old female underwent baseline CT enterography followed by MR enterography 5 years later. Baseline CT enterography exam demonstrates an ileocecal resection with 4.3 cm of neo-terminal ileal inflammation and an EMBARK score of 2 (A, B: arrows). Follow-up MR enterography exam demonstrates similar length and severity of inflammation (4.6 cm, EMBARK score 2, C, D: arrows), indicating stable disease by predefined response criteria.

exam, and 4 (13%) had penetrating disease at follow-up. Five (16%) patients had numerous enlarged mesenteric lymph nodes greater than 1.0 cm at baseline, with 3 (9%) patients having enlarged lymph nodes at follow-up. Two patients (6%) had imaging findings of chronic mesenteric venous occlusion at baseline and follow-up.

Discussion

We examined patients with SB CD on vedolizumab therapy with 2 CTE/MRE exams at least 12 months apart. In these high-risk patients with SB CD, the large majority of our patients had prior intestinal surgery, internal penetrating disease, and prior anti-TNF exposure. Surprisingly, only approximately one-third of patients had progression of SB disease with either increasing lengths or severity of SB inflammation, new strictures or penetrating complications, or newly inflamed loops. About one-fifth of patients had response to therapy with shortening of inflamed segments without other findings of progression. Half of the patients (16/32; 95% CI: 32%–68%) had stable SB inflammation, with these patients having shorter lengths of SB inflammation at baseline imaging and follow-up. Taking both clinical improvement and imaging response into account, 56% (18/32; 95% CI: 38%–74%) patients had clinical improvement in addition to response or stable disease at CTE/MRE. SB segments that responded to vedolizumab therapy were shortened by a median of 8.8 cm, while progressing lesions increased in length by a median of 10.4 cm. No appreciable changes in non-SB CD-related inflammation (changes in perianal disease, colorectal inflammation, or other penetrating complications) were detected.

Broadly speaking, the goal of therapy in CD is to induce control of active inflammation and prevent long-term consequences. Objective markers including endoscopic or cross-sectional imaging are used to monitor response and substantiate clinical symptoms. The GEMINI 2 study showed a modest vedolizumab effect inducing clinical remission at week 6 but a significant improvement at 52 weeks.[11] While about 2/3 of the GEMINI patients had SB disease, there was no anatomic assessment of the SB. Two therapeutic studies do report some imaging results in CD patients undergoing vedolizumab treatment, but do not describe or differentiate SB inflammation apart from colorectal inflammation or penetrating complications. The VERSIFY trial demonstrated increased rates of radiologic remission at 52 weeks (38.1% of patients) compared to 26 weeks (21.9% of patients), but reported the terminal ileal results along with colonic results, so the overall degree and response of SB inflammation is unknown.[18] Kotzke et al,[14] utilizing a combination of both ileocolonoscopy and cross-sectional imaging (CTE, MRE, or contrast-enhanced bowel ultrasound), found an imaging-based, objective remission rate of 18.9% in 122 CD patients with SB CD. Radiographic remission was defined as complete normalization of inflammatory parameters on cross-sectional imaging, but the authors did not use standardized definitions or descriptions

for radiographic outcomes. Not only did we examine for changes in inflammation length and severity as measured from CTE/MRE, we also incorporated the development of new strictures, penetrating complications, and newly inflamed segments into our response assessment categories, reflecting clinical practice and long-term outcome measures. Twenty-two percent of our patients demonstrated imaging response, while 9% maintained an imaging-based absence of inflammation.

While radiologists and gastroenterologists agree on imaging criteria for detecting SB inflammation,[5] and MR severity indices reproducibly estimate inflammation severity, agreed-upon criteria for response assessment remain lacking. Clinical guidelines state that length of disease should be reported.[5] Length of disease can be measured using a spline tool using most PACS workstations and is highly reproducible (ICC of 0.8 or greater).[23] Length represents a simple index that can be employed in clinical practice for response assessment: when the length of an inflamed segment becomes zero, transmural healing by cross-sectional imaging is reached. MR inflammation severity scores only reflect burden and length of SB inflammation when multiple segments are added together, but do not directly measure the length and this limitation makes calculation impractical in a clinical setting.[24]

There are several limitations of our study including the small number of patients and lack of generalizability to TNF naïve (and surgically naïve) patients. We hope to address these issues with a prospective multicenter study. The dosing frequency was dependent on the prescribing gastroenterologist. The interval selected (greater than 12 months) was based on emerging radiologic imaging data, suggesting increased rates of improvement and transmural healing at 12 months compared to 3 or 6 months.[10] The standardized interval in this study was meant to maximize therapeutic benefit at a consistent time interval. Our results likely overestimate stable disease and response given that only patients who remained on vedolizumab for 1 year were analyzed, but we utilized standard objective endpoints. A minority of patients had endoscopy within 30 days of CTE/MRE. Correlating endoscopic and histologic data with imaging characteristics of CTE/MRE would be beneficial and brings to light the need for future prospective studies with larger numbers. Further work is also needed to understand the relationship between imaging inflammation severity and the length of inflamed bowel segments.

Approximately one-third of patients with small intestinal CD on vedolizumab therapy for over 1 year showed progression of SB disease on follow-up CTE/MRE after baseline exam. Approximately 20% had response to therapy of SB inflammation, and slightly over half had stable, short-segment inflammation. Slightly over half of patients had clinical improvement combined with response or stable disease by imaging assessment. These observations occurred despite the large majority of patients having poor prognostic features of intestinal surgery, internal penetrating disease, and anti-TNF exposure. Response and stable disease were examined using the length and severity of SB inflammation without the development of penetrating complications, strictures, or new SB lesions—response criteria that have been linked with improved long-term outcomes. Over this interval, the proportion of patients with colonic inflammation, internal penetrating, and perianal disease remained stable. This study leverages data obtained in routine clinical care and highlights the importance of cross-sectional enterography as a complementary modality in the evaluation and management of CD of the small intestine.

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Conflicts of Interest

L.K. is an employee of Baylor College of Medicine and has no other conflicts to disclose. A.I., Y.S.L., P.K.E., D.R.H., and R.E.C. are employees of the Mayo Clinic and have no other conflicts to disclose. D.H.B. and J.G.F. are employees of Mayo Clinic and receive a grant from and consult for Takeda Pharmaceuticals Inc., with funds provided to the institution. J.S. is an employee of Takeda Pharmaceuticals Inc. and receives stock or stock options.

Data Availability

Data are available upon request to the corresponding author.

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