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Impact of Small Bowel MRI in Routine Clinical Practice on Staging of Crohn's Disease

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Abstract

Background and Aims: Small bowel visualisation is a complex diagnostic approach, but mandatory for risk stratification and stage-adjusted therapy in Crohn's disease. Current guidelines favour transabdominal ultrasound and small bowel MRI as methods of choice, although their clinical impact in daily practice remains controversial. The aim of this study was to evaluate the diagnostic benefit of small bowel MRI in Crohn's disease according to Montreal Classification, in routine practice.
Methods: Patients who underwent MR-enterography [MRE] or MR-enteroclysis [MRY] were included in a retrospective single-centre study. MRI findings were correlated with results from clinical work-up and evaluated in terms of [1] diagnostic yield, [2] significant additional information, and [3] alterations in the assessment of disease behaviour and location according to Montreal Classification.
Results: A total of 347 small bowel MRI examinations were analysed [MRE: 49 / MRY: 298]. MRI had an average sensitivity/specificity of 82.5% and 99.9% [positive predictive value: 99.8% / negative predictive value: 91.1%] respectively. In every second patient, new relevant diagnostic information was provided. Incorporation of the MRI results caused significant shifts in Montreal Classification, specifically higher L-levels [+21.2%; $p < 0.05$] and higher B-levels: [+24.6%; $p < 0.05$].
Conclusions: Even in routine practice, small bowel MRI is a powerful and reliable technique in small bowel work-up. Since MRE and MRY presented high diagnostic yields, often detected significant additional information, and significantly caused shifts in Montreal Classification, both techniques are confirmed to be excellent tools in diagnosing and monitoring Crohn's disease in its daily course.

Keywords: Inflammatory bowel disease; Crohn's disease; small bowel MRI

1. Introduction

Detailed knowledge about disease location, extent, and severity is mandatory for risk stratification and stage-adjusted therapy in Crohn's disease [CD]. Entire small bowel visualisation has prognostic value as the small bowel is most frequently affected by inflammation [more than 80% prevalence in CD], which commonly correlates with complications such as stenosis, fistula, abscess [up to 9-fold] and therefore more severe course of disease.[1]

Since small bowel imaging is still a challenge, MRI plays a pivotal role and is implemented in current consensus guidelines for

small bowel investigation in CD.[2] Delineation of extraintestinal and transmural inflammation and freely selectable multiplanar imaging with high intrinsic soft-tissue resolution are the significant advantages of MRI. Particularly young patients, who require numerous follow-up examinations, profit from this marginally invasive method without radiation exposure, in view of the relapsing pattern of CD.[3] Restricted availability, difficult examination conditions and the typical contraindications of MRI [claustrophobia, non-MRI-certified implants, adiposity *per magna*, etc] hinder its application. Furthermore, small bowel MRI is relatively costly and time consuming and owns limited potential to depict superficial mucosal lesions. Adequate luminal distension is crucial for small bowel MRI.

Whereas in magnetic resonance enterography [MRE] the contrast agent is applied by oral ingestion, magnetic resonance enteroclysis [MRY] is performed within a fluid distribution through a nasojejunal tube placed in the distal duodenum. Current literature describes sensitivities and specificities for MRY and MRE concerning the diagnosis of CD as from 87% to 100% [MRY] / 78% to 100% [MRE]; for the detection of fistulas from 57% to 100% / 75% to 94%; and for identification of stenoses from 55% to 100% / 96%, respectively.[4,5,6,7,8,9]

Although small bowel disease in CD and its diagnosis by MRI imply exceptional relevance, the evidence base is minor, mostly deriving from small single-centre studies which represent the routine course deficiently; and comparative studies regarding alternative methods are rare and in parts less convincing. The Montreal Classification [MC] of inflammatory bowel disease is an easy, assessable and widely accepted prognostic and therapeutic parameter including the age at diagnosis and the location and behaviour of disease.[10] To our knowledge, only one publication investigated the clinical benefit of small bowel MRI and only one study assessed disease behaviour according to MC.[11,12] Since we judge small bowel MRI an accurate technique, providing additional intramural and peri-intestinal information, the present study aimed to evaluate the diagnostic impact of small bowel MRI in CD patients in routine clinical course in an extended retrospective analysis. We therefore sought to determine: the diagnostic effect on disease behaviour and location according to MC [1], whether small bowel MRI is reliable in routine practice [2] in context of compliance and diagnostic yield; and if it offers significant additional diagnostic information [3]. Additionally we investigated whether MRE or MRY should be the preferred method for small bowel assessment in CD [4] since both techniques were performed in this study.

2. Materials and Methods

2.1. Study population

We conducted a retrospective single-centre study of patients undergoing small bowel MRI [MRE / MRY] between 2003 and 2010, referred by the Department of Gastroenterology and Hepatology of the University Hospital Bergmannsheil Bochum, Germany. From 2003 to 2008 only MRY was performed, and from 2009 on the protocol was changed and only patients who did not tolerate MRE [regarding drinking large amounts of contrast agent for bowel distension] underwented an MRY. Patients with lacking MRI reports [no documentation in our database] were excluded; no patient was excluded because of insufficient image quality, abortion, or an incomplete study. Patients with multiple MRI examinations within the study period were also included. Patients had been referred for small bowel MRI for various clinical indications including Crohn's disease, ulcerative colitis, coeliac disease, abdominal pain, etc. Only patients with confirmed or highly suspected inflammatory bowel disease [Crohn's disease, ulcerative colitis, or inflammatory bowel disease type unclassified] were selected for assessment of Montreal Classification.

2.2. Reference standard

Before attending small bowel MRI, patients underwent a standardised diagnostic algorithm for suspected or verified Crohn's disease at the local department of gastroenterology and hepatology according to the ECCO guideline which contained:[2] [1] clinical evaluation [history, symptomatology, clinical examination, complaints, clinical course]; [2] laboratory parameters; [3] endoscopy including histopathology [oesophagogastroduodenoscopy, ileocolonoscopy, eventually capsule endoscopy/enteroscopy]; and [4] transabdominal ultrasound. The reference standard was based on the synopsis of all diagnostic findings from the standardised diagnostic algorithm and finally correlated with the MRI findings. Briefly, the reference standard of the bowel segment between anorectum and ileum was ileocolonoscopy including histopathology. The reference standard of bowel segments between terminal ileum and duodenum was ultrasound, enteroscopy and capsule endoscopy if possible. Proximal to the distal duodenum, oesophagogastroduodenoscopy functioned as reference standard. In case endoscopy or ultrasound had not been performed but symptoms, laboratory parameters, clinical course, or succeeding investigations made proximal small bowel disease most likely [ie clinical sign of ileus as hint for bowel obstruction], this status was accepted as reference. All MRI examinations were performed within 14 days after executing the standardised diagnostic algorithm. Significant additional diagnostic information was defined as newly diagnosed pathologies by small bowel MRI, which led to a change in Montreal Classification. The diagnoses Crohn's disease [CD], ulcerative colitis [UC], or inflammatory bowel disease type unclassified [IBDU] were based on clinical evaluation, endoscopy with histopathology, ultrasound, and MRI, as stated in the ECCO guideline.[2]

2.3. Montreal Classification

Assessment of the Montreal Classification [MC] was carried out using the reference standard as baseline control. Thereafter MRI findings were compared with the baseline control and all changes regarding disease behaviour and location were represented as absolute and relative values [as shown in Tables 1 and 2]. Statistical significance was determined by using the chi-square test [X^2-test]. *p*-Values of less than 0.05 were considered statistically significant. For patients presenting both a stricturing [B2] and a penetrating [B3] pattern of disease simultaneously, MC was modified and the opportunity to combine and classify, 'stricturing' and 'penetrating' [B2 + B3 ± *p*] with or without perianal affection was established, in order to assess the current status of behaviour properly and avoid bias or loss of information, since MC in the original form does not offer the opportunity to represent both patterns simultaneously [see Supplementary Table 10, available as Supplementary data at *ECCOJCC* online].[10]

2.4. Small bowel MRI

MRY and MRE examinations were performed according to standardised protocols of the Institute of Diagnostic Radiology, Interventional Radiology and Nuclear Medicine of the University Hospital Bergmannsheil Bochum, Germany.

Before MRI examination, patients were instructed to have low fibre and light meals on the day before and to fast for 8 h before examination. Whereas in magnetic resonance enterography [MRE] the contrast

Table 1. Location of disease according to Montreal Classification.

Location		MRY [*n* = 144]				MRE [*n* = 35]				MRI [*n* = 179]		Significance
	Code	Δ *n*	Δ %	Δ *n*	Δ %	Δ *n*	Δ %	Δ *n*	Δ %	Δ *n*	Δ %	X^2
Terminal ileum pre/post	L1	-1	-0.7%	DIT: - 11/144	DIT: - 7.6%	0	0%	DIT: - 5/35	DIT: - 14.3%	DIT: - 16/179	DIT: - 8.9%	
Colon pre/post	L2	-5	-3.5%			-2	-5.7%					
Ileocolon pre/post	L3	-5	-3.5%			-3	-8.6%					
Proximal to TI pre/post	L4	+1	+0.7%	IIT: + 31/144	IIT: + 21.5%	0	0%	IIT: + 7/35	IIT: + 20%	IIT: + 38/179	IIT: + 21.2%	$p < 0.05$
Proximal to TI + ileocolon pre/post	L3 + L4	+25	+17.4%			+5	+14.3%					
Proximal to TI + colon pre/post	L2 + L4	0	0%			0	0%					
Proximal to TI + TI pre/post	L1 + L4	+5	+3.5%			+2	+5.7%					

IBD patients were assessed according to Montreal Classification before and after MRI examination. Location [L] of disease after performing the standardised diagnostic algorithm was compared with the location of disease after MRI examination for all [*n* = 179] IBD patients [MRY: *n* = 144 / MRE: *n* = 35]. Chi-square test before and after MRY [L-levels]: X^2: $p < 0.05$, 95% CI; chi-square test before and after MRE [L-levels]: X^2: $p < 0.05$, 95% CI; chi-square test between MRY and MRE [L-levels]: pre and post: X^2: $p > 0.05$, 95% CI.

MRY: MR-enteroclysis; MRE, MR-enterography; MRI, sum of all MRY and MRE examinations; X^2, chi-square test; pre / post, difference before and after small bowel MRI examination; proximal to TI, affected gastrointestinal segments proximal to terminal ileum; TI, terminal ileitis; stricturing, stricturing pattern of disease; penetrating, penetrating pattern of disease; code, code according to Montreal Classification; Δ, difference between pre and post examination; *n*, absolute number of patients; %, relative number of patients in percent; DIT, decrease in total; IIT, increase in total; IBD, inflammatory bowel disease.

agent was applied by oral ingestion, magnetic resonance enteroclysis [MRY] was performed within a fluid distribution through a nasojejunal tube placed in the distal duodenum. Radioscopy was performed to confirm the correct position of the tube, and Klean-Prep [Norgine, Hamburg, Germany] was prepared according to manufacturer's instructions at room temperature; 1000 ml Klean-Prep was supplied at 100 ml/min and another 1000 ml was administered at 120–130 ml/min. Before MRE, small bowel distension was achieved by drinking 2000 ml of Moviprep [Norgine, Hamburg, Germany]. The MRI scanner Magnetom Symphony Quantum [Siemens Healthcare, Erlangen, Germany] with spine- and body-array coils was used for image acquisition. Supplementary Tables 8 and 9, available as Supplementary data at *ECCOJCC* online, illustrate the different sequences performed in this study. In order to reduce breathing artefacts and facilitate bowel distension and bowel loop separation, patients were examined in the prone position if possible.[13] The MRI's field of interest should contain the whole abdomen between diaphragm and symphysis including anorectum; 2040 mg N-butylscopolaminiumbromid [Buscopan, Boehringer Ingelheim, Germany] was injected intravenously to reduce intestinal peristalsis. If necessary another 20 mg of N-butylscopolaminiumbromid could be applied at a later time point.Thereafter 0.1 mmol/kg bodyweight of the contrast agent Gadopentetat-Dimeglumin [Magnevist / Gadovist, Bayer Schering Pharma, Bergkamen, Germany] was injected intravenously at 2.0 ml/s according to manufacturer's instruction. Directly after injection, the second image acquisition was performed representing the arterial phase, and after 30 s the third measurement was executed characterising the venous phase. Total scan time lasted between 30 to 40 min.

2.5. Analysis of MRI examinations

After image acquisition, all MRI studies were evaluated by two resident radiologists on a PACS workstation in a consensus decision. Image quality was classified as 'good', 'constricted', and 'bad' according to certain parameters [degree of wall distension, visualisation of intramural and extraintestinal configurations, contrast agent flow, minimisation of breathing artefacts, and adequate selection of slice thickness] though without implementation of a standardised score. As demonstrated in Table 3, pathological alterations caused by CD and assessed by small bowel MRI were evaluated according to certain parameters: inflammation [mural thickening of at least 3 mm in MRI measured by using digital calliper], bowel wall hyperenhancement [considered pathologically when it had an increased intensity towards adjacent bowel wall segments after injection of contrast agent], bowel wall oedema with or without mural stratification, comb sign, mesenteric fibrofatty proliferation, and lymphadenopathy as illustrated in Figure 2. Stenosis was defined as luminal narrowing of more than 80% compared with unaffected adjacent bowel segments, and diameter and length of stricturing segments were measured by means of digital callipers [see Table 3]. Characteristics of stenoses were defined as inflammatory or fibrotic according to the presence/absence of signal intensity in T2 weighted sequences and contrast enhancement, as shown in Table 3. Severities of stenoses were evaluated into low-grade, high-grade, and high-grade with prestenotic dilatation. Lesion distribution was defined into the following segments: duodenum, jejunum, ileum [proximal to the terminal ileum], terminal ileum, colon ascendens, colon transversum, colon descendens, and anorectum. The results of the pre-imaging studies [endoscopy, ultrasound, etc] were available for review when the MRI examinations were analysed. Finally both MRI techniques were compared according to an inter-individual comparison. Some patients had MRI examinations with both techniques due to intolerance of one technique as mentioned above.

2.6. Diagnostic yield

In order to determine the diagnostic yield of small bowel MRI, MRI findings were evaluated in terms of sensitivity, specificity, positive and negative predictive values according to the above mentioned reference standard, and significant additional diagnostic information. Calculation of diagnostic yield was initially performed for the whole study population [MRY: *n* = 298 / MRE: *n* = 49] and secondly only for confirmed or highly suspected IBD patients [MRY:

Table 2. Behaviour of disease according to Montreal Classification.

Behaviour		MRY [*n* = 144]				MRE [*n* = 35]				MRI [*n* = 179]		Significance
	Code	Δ *n*	Δ %	Δ *n*	Δ %	Δ *n*	Δ %	Δ *n*	Δ %	Δ *n*	Δ %	X^2
Non-stricturing + non-penetrating pre/post	B1	-13	-9.0%	DIT:- 19/144	DIT:- 13.2%	-4	-11.4%	DIT:	DIT:- 20%	DIT:- 26/179	DIT:- 14.5%	$p < 0.05$
Stricturing pre/post	B2	+23	+16%	IIT:+ 36/144	IIT:+ 25%	+3	+8.6%	- 7/35	IIT:+ 22.9%	IIT:+ 44/179	IIT:+ 24.6%	
Penetrating pre/post	B3	+1	+0.7%			-1	-2.9%	IIT:+ 8/35				
Non-stricturing + non-penetrating + perianal pre/post	B1p	-6	-4.2%			-2	-5.7%					
Stricturing + perianal pre/post	B2p	+6	+4.2%			+1	+2.9%					
Penetrating + perianal pre/post	B3p	+2	+1.4%			0	0%					
Stricturing + penetrating pre/post	B2 + B3	+2	+1.4%			+1	+2.9%					
Stricturing + penetrating + perianal pre/post	B2p + B3	+2	+1.4%			+3	+8.6%					

IBD patients were assessed according to Montreal Classification before and after MRI examination. Behaviour of disease after performing the standardised diagnostic algorithm was compared with behaviour after MRI examination for all [*n* = 179] IBD patients [MRY: *n* = 144 / MRE: *n* = 35]. Chi-square test before and after MRY [B-levels]: X^2: $p < 0.05$, 95% CI; chi-square test before and after MRE [B-levels]: X^2: $p < 0.05$, 95% CI; chi-square test between MRY and MRE [B-levels]: pre and post: X^2: $p > 0.05$, 95% CI.

MRY, MR-enteroclysis; MRE, MR-enterography; MRI, sum of all MRY and MRE examinations; X^2, chi-square-test; pre / post, difference before and after small bowel MRI examination; proximal to TI, affected gastrointestinal segments proximal to terminal ileum; TI, terminal ileitis; stricturing, stricturing pattern of disease; penetrating, penetrating pattern of disease; perianal, perianal inflammation within IBD; code, code according to Montreal Classification; IBD, inflammatory bowel disease; Δ, difference between pre and post examination; *n*, absolute number of patients; %, relative number of patients in percent; DIT, decrease in total; IIT, increase in total.

Table 3. Small bowel MRI parameters for the assessment of Crohn's disease: definition of pathological alterations in Crohn's disease assessed by small bowel MRI.[8,27,28,29,30,31]

Pathology	MRI parameter	Definition
Active inflammation	Mural thickening	BW thickening > 3 mm
	Mural hyperenhancement	Segmental increased intensity of the BW compared with normal appearance after intravenous Gd-DTPA administration
	Bowel wall oedema	Increased signal of the BW compared with normal BW evaluated on T2-weighted sequences
	Mural stratification	Visualisation of two [or three] layers within the BW ['target' or 'double halo' appearance]
	Comb sign	Increased vascularity [prominence / dilatation] of the vasa recta supplying the small bowel or colon perpendicularly to the bowel lumen
	Mesenteric fibrofatty proliferation / adjacent fat stranding	Streaky decreased signal within the mesenteric fat on nonfat suppressed T2-weighted images around the inflamed bowel leading to increased separation of bowel loops
	Lymphoid nodes enlargement	Lymphoid node enlargement of more than 5mm measured in the shortest diameter
Chronic inflammation	Regenatory / reparative changes	Regenerative polyps, mucosal atrophy ± segmental BW thickening, ± luminal narrowing, ± heterogeneous mild to moderate wall enhancement, ± fibrofatty proliferation, ± lymphadenopathy, ± low to moderate T2 signal intensity
	Pseudopolyps / cobblestone pattern	Mucosal atrophy and denudation, network of high signal intensity intersecting longitudinal, transverse, and/or oblique linear ulcerations, surrounding residual islands of mucosa
	Pseudodiverticules / small bowel retraction	Asymmetrical bowel fibrosis and shortening secondary to ulceration of the mesenteric side of the bowel
Stricturing disease	Stenosis	Luminal narrowing of more than 80% compared with unaffected adjacent bowel segments
	Fibrotic stenosis	Fixed narrowing, low to moderate T2-weighted signal intensity; minor nonhomogeneous contrast enhancement without any oedema / surrounding mesenteric inflammation
	Inflammatory stenosis	Stenosis associated with a segment of thick-walled bowel, high signal intensity on T2-weighted images
	Functionally significant stenosis	Prestenotic dilatation of bowel lumen proximal to the stenosis measured > 3 cm in diameter.
	Functionally not significant stenosis	Stenosis > 10% narrowing of the bowel lumen compared with normal adjacent bowel in the absence of dilatation
Penetrating disease	Superficial ulcerations	Small dots of high signal intensity surrounded by a low-signal-intensity rim < 1 cm in diameter
	Sinus tract	Blind-ending tract arising from the BW but not reaching another epithelium-lined surface; high-signal-intensity tracts on T2-weighted images
	Deep transmural ulceration / fistulation	Thin linear structures / protrusions with high signal intensity on T2-weighted images surrounded by a zone of lower signal intensity exceeding the mucosal layer, and/or penetrating the thickened BW
	Abscess / phlegmon / local fluid collection	Well-defined, encapsulated collection of pus, high signal-intensity on T2-weighted images, low signal intensity on T1-weighted images, strong rim enhancement

Gd-DTPA, gadopentetat-dimeglumin [small bowel MRI contrast agent]; BW, bowel wall.

n = 144 / MRE: *n* = 35]. For this, MRE and MRY were analysed separately and 'terminal ileitis', 'small bowel disease', and 'stenosis' [small bowel] served as comparative parameters. Thereafter overall diagnostic yield of both MRI techniques was determined as average.

2.7. Statistics

Statistical analysis was performed with SPSS 18-21 [IBM, Armonk, USA]. T-tests and chi-square tests were used to determine statistical significance. Analysis was considered statistically significant with a *p*-value in t-tests or X^2-tests ≤ 0.05. Patients were included in our analysis regardless of MRI quality and even if they did not fully adhere to the MRI protocol.

2.8. Ethical considerations

The study was approved by the institutional review board [registry number 4194-11] and informed consent was obtained from all patients before the examinations.

3. Results

3.1. Baseline characteristics

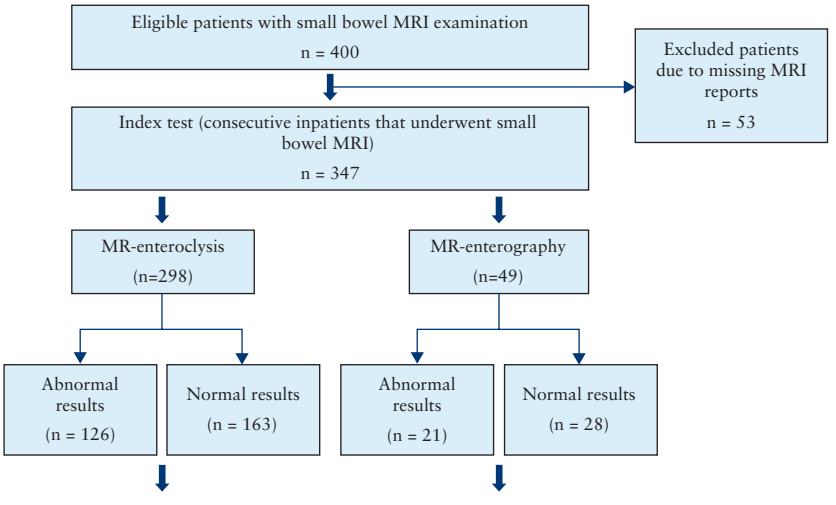
In the cohort of 400 patients who underwent small bowel MRI examination, 53 were excluded due to missing MRI reports, so that in summary our study population contained a total of 347 patients [mean age 45 ± 16 years, range 15–81 years, 54% female / 46% male] which is shown in Figure 1. Overall patient's baseline characteristics were equally balanced between MRI subgroups as displayed in Table 4. Our representative study population contained a slight excess of women (54% vs 46%, t-test: $p < 0.01$, 95% confidence interval [CI]), though significant differences in age, body mass index [BMI], medication, duration of disease, comorbidities, or incidence of complications among the different MRI subgroups [see Tables 4 and 5] were not found [t-test: $p > 0.05$, 95% CI].

3.2. Indication for small bowel MRI

In all, 36.6% of patients applied for small bowel MRI with verified CD, 48.7% with suspected CD [verified within diagnostic work-up in 18%], and 1.7% with UC [see Supplementary Table 11, available as Supplementary data at *ECCOJCC* online]. No significant difference occurred between MRI subgroups according to indication chi-square test: $p > 0.05$, 95% CI].

3.3. Diagnostic findings through small bowel MRI

Figure 1 demonstrates that MRY was performed in 86% [298/347] and MRE in 14% [49/347], and 11% [37/347] of our patients had more than one small bowel MRI examination. MRY resulted more often in good quality of imaging and complete bowel distension than MRE [72% / 60% vs 53% / 35%, chi-square test: $p < 0.05$, 95% CI], [see Supplementary Table 13, available as Supplementary data at *ECCOJCC* online]. Incomplete small bowel visualisation occurred more often with MRE than with MRY [65% vs. 35%, chi-square test: $p < 0.05$, 95% CI]. Jejunum was the most common anatomical segment with incomplete bowel visualisation in both methods [MRY: 19% / MRE: 45%, chi-square-test: $p < 0.05$, 95% CI]. Complaints during small bowel MRI [6%, 22/347], ie nausea and/or emesis, claustrophobia, pain and diarrhoea were more often detected in MRE compared twith MRY [MRY: 4.7% vs MRE: 16.3%, t-test: $p < 0.05$, 95% CI, see Supplementary Table 13]. A total of 2% of MRY examinations had to be aborted due to patient's discomfort [chi-square-test: $p > 0.05$, 95% CI]. In all, 60% [207/347] of our study population presented active inflammation in MRI [MRY / MRE: 57% vs 74%, t-test: $p < 0.05$, 95% CI]. Multiple statements in terms of location of disease were possible [ie colon and small bowel]. CD and UC were recorded in 48.1% [167/347; MRY / MRE: 45% vs 69%, chi-square test: $p < 0.05$, 95% CI] and 2.3%, respectively, [8/347; MRY / MRE: 2.3%



Parameter	MRY findings / reference standard (n=298)		MRE findings / reference standard (n=49)		Significance MRY / MRE
	N	%	N	%	Chi-square-test
SB affection	95/109	32% / 37%	6/27	12% / 55%	p < 0.05
Terminal ileitis	45/121	15% / 41%	24/28	49% / 57%	p < 0.05
Fistula	9/22	3% / 7%	6/10	12% / 20%	p < 0.05
Stenosis	66/88	22% / 30%	12/16	24% / 33%	p > 0.05
CD	87/133	29% / 45%	22/34	45% / 69%	p > 0.05

Figure 1. Study flow chart: 400 patients underwent small bowel MRI examination, 53 were excluded due to missing MRI reports. 347 inpatients were included in our study [MRY: 298 / MRE: 49]. MRI findings were evaluated in terms of diagnostic yield against reference standard and 'terminal ileitis', 'small bowel disease', and 'stenosis' [small bowel] served as comparative parameters. Significance: chi-square test between the two MRI subgroups to determine significant differences with 95% CI; *n*: absolute number of patients; %: number of patients percent; CD: Crohn's disease; SB affected: small bowel affected. Significant differences regarding the reference standard of the MRI subgroups [MRY/MRE] have been determined for the parameters: small bowel affected, terminal ileitis, fistula, and Crohn's disease, with $p < 0.05$, 95% CI.

Table 4. Demographic characteristics.

Parameter	MRY [*n* = 298]		MRE [*n* = 49]		MRI total [*n* = 347]		Significance
	n	%	*n*	%	*n*	%	
Age in years	45.3 ± 16	-	43.8 ± 17	-	45.1 ± 16	-	t > 0.05
Sex [female]	157	52.7%	31	63.3%	188	54.2%	t < 0.05
BMI in kg m^{-2}	23.8 ± 5.8	-	24.2 ± 5.2	-	23.9 ± 5.7	-	t > 0.05

MRY, MR-enteroclysis; MRE, MR-enterography; MRI total, sum of MRY and MRE examinations; *n*, absolute number of patients; %, relative number of patients in percent; t, t-test; age in years, age in years on the day of examination; BMI, body-mass-index.

Significance: t-test between parameters of MRY- and MRE-subgroups to determine significant differences with 95% CI.

Table 5. Age at diagnosis according to Montreal Classification.

Age at diagnosis	MRY [*n* = 129]		MRE [*n* = 33]		MRI total [*n* = 162]	
code	*n*	%	*n*	%	*n*	%
A1	12	9.3%	4	12.1%	16	9.9%
A2	89	69%	19	57.6%	108	66.7%
A3	28	21.7%	10	30.3.%	38	23.5%

Confirmed or highly suspected IBD patients were assessed according to Montreal Classification before and after MRI examination. Age at diagnoses was documented for 162/179 IBD patients [MRY: n=129 / MRE: n=33]. A1, onset of disease before the age of 16; A2, onset of disease between 17 and 40 years of age; A3, onset of disease at above 40 years of age; IBD, inflammatory bowel disease; MRY, MR-enteroclysis; MRE, MR-enterography.

vs 2%; chi-square-test: $p < 0.05$, 95% CI]. It was found that 30% [104/347] suffered from stenoses, 9% [32/347] had fistulas, 44.1% [153/347] presented colitis, and 39.2% [136/347] had an active small bowel inflammation. In the terminal ileum, we determined inflammation in 43% [149/347] of our cohort [see Figure 1].

Peri-intestinal inflammation was detected in 19% [65/347] through small bowel MRI [11% lymphadenopathy, 14% inflamed mesenteric fat, and 2% intraabdominal abscesses]. Table 6 illustrates that in 49%, MRI findings led to a relevant diagnostic improvement [additional diagnostic information] in the context of disease, ie detecting a new inflammation in 22.5%, new stenosis in 14.1%, and new fistula in 3.5%.

3.4. Test criteria for small bowel MRI

3.4.1. Overall diagnostic yield

Calculated on the basis of all study patients [*n* = 347], small bowel MRI had an overall sensitivity and specificity of 82.5% and 99.9% [positive predictive value [PPV]: 99.8% / negative predictive value [NPV]: 91.1%], respectively [see Table 7]. Average sensitivity and specificity for the diagnosis of terminal ileitis were 77.5% and 99.7%, respectively [PPV: 99.4% / NPV: 84.6%]. The highest accuracy was seen in the diagnosis of small bowel inflammation [small bowel proximal to terminal ileum], with average sensitivity and specificity of 91.7% and 100%, respectively, [PPV: 100% / NPV: 94.4%]. For the detection of stenoses, MRI presented average sensitivity and specificity of 78.2% and 100% [PPV: 100% / NPV: 94.3%], respectively. We did not identify any significant difference between MRY and MRE in terms of diagnostic yield, although MRE achieved slightly higher sensitivities on average and in each subgroup analysis, and we did not perform an intra-individual comparison between both techniques; chi-square test: $p > 0.05$, 95% CI, see Table 7].

3.4.2. Diagnostic yield including IBD patients only

After including only confirmed or highly suspected IBD patients, small bowel MRI had average sensitivity and specificity of 83.4% and 99.7%, respectively [PPV: 99.8% / NPV: 80.6%] as shown in Supplementary Tables 15–20, available as Supplementary data at *ECCOJCC* online. Average sensitivity and specificity for the diagnosis of terminal ileitis were 79.6% and 99%, respectively [PPV: 99.3% / NPV: 66%]. The highest accuracy was also seen in the diagnosis of small bowel inflammation [small bowel proximal to terminal ileum] with average sensitivity and specificity of 91.9% and 100%, respectively [PPV: 100% / NPV: 86.7%]. According to the results above, a significant difference between MRY and MRE in terms of diagnostic yield had not been determined; chi-square test: $p > 0.05$].

3.5. Montreal Classification of inflammatory bowel disease

3.5.1. Age at diagnosis

In all, 52% of our study population [179/347] had inflammatory bowel disease [IBD]. In 91% [162/179] we were able to determine the age at onset [see Table 5]: 67% [108/162] of IBD patients had an onset of disease between 17 and 40 years of age [A2], 23.5% at above 40 [A3; 38/162], and 9.9% before the age of 16 [A1; 16/162]. There was no significant difference between the two subgroups [MRY and MRE] according to the parameter age at diagnosis [chi-square test: $p > 0.05$, 95% CI].

3.5.2. Location [L]

Comparing Montreal Classification before and after MRI examination, small bowel MRI led to a significant shift towards a larger extent of disease [higher L-levels: +21.2%, chi-square test: $p < 0.05$, 95% CI [see Table 1]. In MRY, cases of limited extent of disease decreased [-7.6%] and numbers of larger extent increased significantly [L-levels: +21.5%, chi-square test: $p < 0.05$, 95% CI]. Analogously, MRE presented similar tendencies with a decrease of limited extents [L-levels: -14.3%] and an increase of larger extents of disease [L-levels: +20%, chi-square test: $p < 0.05$, 95% CI]. We did not identify a significant difference between the two MRI subgroups according to the parameter location [chi-square test: $p > 0.05$, 95% CI

3.5.3. Behaviour [B]

Small bowel MRI led to a significant shift of behaviour [B] to more severe types of disease [higher B-levels: +24.6%, chi-square-test: $p < 0.05$, 95% CI, see Table 2]. In MRY, cases of milder disease decreased [-13.2%] whereas the numbers of more severe types of disease increased [higher B-levels: +25%, chi-square test: $p < 0.05$, 95% CI]. Analogously, we detected a decrease of milder cases of disease in MRE [-20%] in favour of an increase of more severe types of disease [higher B-levels: +22.9%, chi-square test: $p < 0.05$, 95%

Table 6. Additional diagnostic information determined by small bowel MRI

Additional diagnostic information	MRY [*n* = 289]		MRE [*n* = 49]		MRI total [*n* = 347]		Significance
	• *n*	• %	• *n*	• %	• *n*	• %	• Chi-square test
New information / diagnosis in total	142	47.7%	28	57.1%	170	49%	$X^2 > 0.05$
New inflammation	64	21.5%	14	28.6%	78	22.5%	$X^2 > 0.05$
New inflammation PTI	53	17.8%	12	24.5%	65	18.7%	$X^2 > 0.05$
New backwash-ileitis	3	1.0%	0	0%	3	0.9%	$X^2 > 0.05$
New neoplasm	16	5.4%	2	4.1%	18	5.2%	$X^2 < 0.05$
New fistula	6	2.1%	6	12.2%	12	3.5%	$X^2 < 0.05$
New stenosis	41	13.8%	8	16.3%	49	14.1%	$X^2 > 0.05$
New length of stenosis	26	8.7%	5	10.2%	31	8.9%	$X^2 > 0.05$
New length of inflammation	38	12.8%	9	18.4%	47	13.5%	$X^2 > 0.05$
New peri-intestinal inflammation	52	17.4%	11	22.4%	63	18.2%	$X^2 > 0.05$
Extension of diagnosis in total	129	43.3%	23	47%	152	43.8%	$X^2 > 0.05$

New information / diagnosis: pathology had to be relevant [ie larger extent of inflammation, stenosis, etc] within the course of disease; new inflammation PTI, any inflammation of the small bowel which was located proximal to terminal ileum; new backwash-ileitis, terminal ileitis affecting an ulcerative colitis patient; new neoplasm, previously unknown neoplasm of any location; extension of diagnosis, inflammation was detected by endoscopy but relevant additional pathologies [ie fistulas] were detected by small bowel MRI; MRY, MR-enteroclysis; MRE, MR-enterography; MRI total, sum of MRY and MRE examinations.

Significance: chi-square test between parameters of MRY- and MRE-subgroups to determine significant differences; *n*, absolute number of patients; %, number of patients in percent; X^2, chi-square test.

Table 7. Overall diagnostic yield of MR-enteroclysis and MR-enterography [n = 347].

Parameter	MRY [*n* = 298]				MRE [*n* = 49]				**Significance**
	Sens.	Spec.	PPV	NPV	Sens.	Spec.	PPV	NPV	
Diagnostic yield	75.96%	99.81%	99.6%	89.28%	89%	100%	100%	92.88%	$X^2 > 0{,}05$
TI	66.12%	99.44%	98.8%	81.1%	88.9%	100%	100%	88%	$X^2 > 0.05$
Stenosis	74.6%	100%	100%	93.63%	81.8%	100%	100%	95%	$X^2 > 0.05$
SB affected	87.16%	100%	100%	93.1%	96.3%	100%	100%	95.65%	$X^2 > 0.05$

Diagnostic yield, average value of the respective comparative parameters; TI, terminal ileitis; stenosis, small bowel stenosis; SB affected, affected small bowel; Sens., sensitivity; Spec., specificity; PPV, positive predictive value; NPV, negative predictive value; MRY, MR-enteroclysis; MRE, MR-enterography; MRI total, sum of MRY and MRE examinations.

Significance: chi-square test between parameters of MRY- and MRE-subgroups; X^2, chi-square-test.

Average sensitivity of small bowel MRI [MRY + MRE]: 82.48%.

Average specificity of small bowel MRI [MRY + MRE]: 99.91%.

Average positive predictive value of small bowel MRI [MRY + MRE]: 99.8%.

Average negative predictive value of small bowel MRI [MRY+ MRE]: 91.08%.

CI]. Altogether we did not identify a significant difference between the two MRI subgroups [chi-square test: $p > 0.05$, 95% CI].

4. Discussion

Despite recent innovations of direct and indirect imaging methods as well as further development of existing techniques, small bowel imaging is still a complex diagnostic approach, but useful due to high prevalence of disease, prognostic relevance, and potential complications of small bowel CD, as Thia *et al*. could prove in a comparable study population of 306 patients.[1] Under study conditions, MRI showed reasonable results, but data from larger cohorts and daily routine practice are missing. To our knowledge this is the first study evaluating small bowel MRI's diagnostic impact on CD patients by assessment of the Montreal Classification before and after examination in routine clinical course with an extended study population. We sought to analyse 400 small bowel MRI examinations, but failed to collect 53 reports of MRI studies. Most indications were known [37%] or suspected [50%] CD, so that in the end 87% of our study patients were examined due to CD [verified in 48%, 167/347]. The cohort is comparable to other CD populations, so that our data seem to be representative in terms of baseline characteristics.

4.1. Diagnostic yield

Altogether, high diagnostic accuracies were determined for small bowel MRI, with an overall [*n* = 347] average sensitivity and specificity of 82.5% and 99.9% [PPV: 99.8% / NPV: 91.1%], respectively, which is consistent with current literature [see Table 7].[8,13,14,15,16,17,18,19] Additionally, our sub-analysis including only IBD patients [*n* = 179], which is shown in Supplementary Tables 15–20, available as Supplementary data at *ECCOJCC* online, present an almost similar diagnostic yield, with an overall average sensitivity and specificity for small bowel MRI of 83.4% and 99.7%, respectively [PPV: 99.8% / NPV: 80.6%]. Since small bowel MRI has been primarily developed for the assessment of localisation between the ligament of Treitz and the ileocecal valve, in the present study the highest diagnostic accuracies were recorded in this segment, with an average sensitivity and specificity of 91.7%

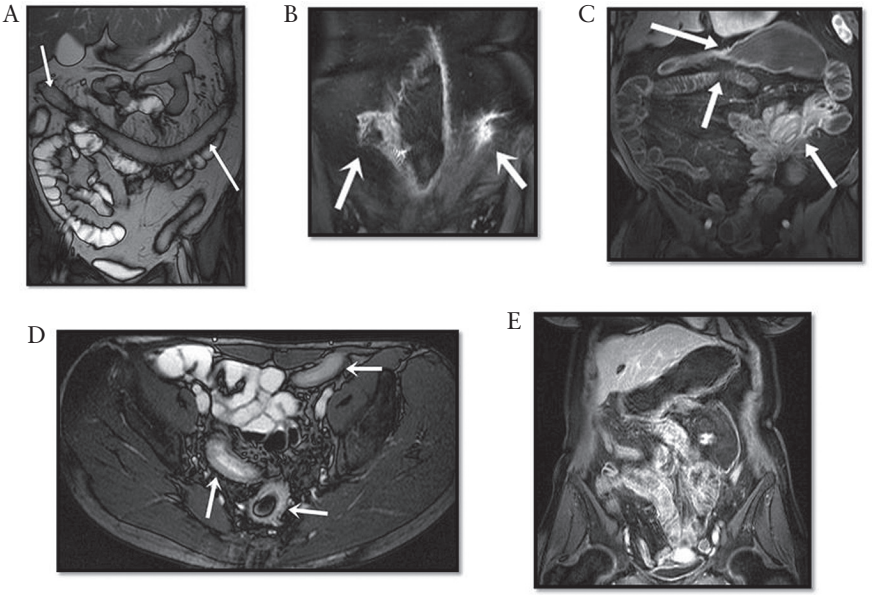


Figure 2. Representative small bowel MRI sequences. [A] TRUFI-sequence small bowel MRI; Crohn's disease with inflammatory colon transversum. [B] T2 weighted small bowel MRI; penetrating Crohn's disease presenting enterocutaneus fistulas. [C] Contrast-enhanced T1-weighted small bowel MRI; Crohn's disease indicating severe inflammation including stenosis and prestenotic dilatation. [D] TRUFI-sequence small bowel MRI; Crohn's disease with segmental inflammation of the jejunum, terminal ileum, and anorectum. [E] Contrast-enhanced T1-weighted small bowel MRI. Sequence with poor image quality due to breathing artefacts and intestine peristalsis.

and 100%, respectively [PPV: 100% / NPV: 94.4%]. Additionally, small bowel MRI presented high values for the detection of terminal ileitis, with average values of 77.5% and 99.7%, respectively [PPV: 99.4% / NPV: 84.6%]. Though specificity seems to be very high for the entire small bowel, we assume the values to be substantially accurate. However, whereas the jejunum and proximal ileum lack a simple and robust endoscopic reference standard, conventional ileocolonoscopy confirms inflammation of the terminal ileum particularly reliably. Therefore, MRI does not demonstratee every slight inflammation, but if it once displays a lesion, the result is reliably correct. Furthermore, both techniques presented as powerful and precise in the diagnosis of stenoses, in the specification of length, localisation, clinical relevance [eg ileus], and subtype [fibrotic or inflammatory], with a combination of high average sensitivities and specificities of 78.2% and 100%, respectively [PPV: 100% / NPV: 94.3%, see Table 7]. Finally, small bowel MRI detected previously unknown peri-intestinal inflammation regularly [18%], providing important information regarding inflammation of mesenteric fat [14%], lymphadenopathy [11%], and abscesses [2%], which could be a hint of an active inflammation in CD which even correlates to C-reactive protein [CRP] and the Crohn's Disease Activity Index [CDAI].[20]

Supplementary Table 13, available as Supplementary data at *ECCOJCC* online, demonstrates that both MRY and MRE proved to be reliable and powerful in terms of image quality in daily course of disease, as good quality of imaging [70%, 241/347] and complete bowel distension [56.5%, 196/347] were achieved frequently. Impaired visualisation of the jejunum was found relatively often [22.2%, 77/347], for which no conclusive explanation can be found as yet; but our results confirm the problem, which was already mentioned by Schreyer *et al*.[19] Probably gastrointestinal motility leads to a premature decrease of distension of proximal bowel loops [depending on contrast agent's flow rate / timing of application of contrast agent and timing of imaging]. Regarding compliance, MRY and MRE seem to be patient-friendly, well tolerated and safely performable in routine practice, due to low rates of abortion [2% of all MRY] and complaints [6%], which agrees with current literature [see Supplementary Table 13].[13]

4.2. Additional information and Montreal Classification

An important result of this study small bowel MRI was that it caused a significant shift in the Montreal Classification towards more severe patterns of disease. In summary, it led to an increase in the extent of inflammation [higher L-levels; chi-squaretest: $p < 0.05$, 95% CI] and disease behaviour, ie increase of stricturing/penetrating patterns to more complicated clinical courses [higher B-levels; chi-square test: $p < 0.05$, 95% CI, see Tables 1 and 2].

Therefore, MRI reveals relevant additional diagnostic information related to inflammatory processes [ie new inflammation: 22.5%, new stenosis: 14.1%, new fistula: 3.5%, new neoplasm: 5.2%, new peri-intestinal inflammation: 18.2%, etc] in every second patient [see Table 6]. Without performing small bowel MRI, disease activity and extent would have been underestimated regardinging risks of complications [stenosis, fistula]. Thia *et al*. proved the presence of small bowel inflammation to be an important predictor of more severe course of CD [stricturing/penetrating pattern].[1] This fact, together with the above outlined shift of Montreal Classification, underlines the particular significance of small bowel MRI in terms of risk stratification of CD patients. Hafeez *et al*. investigated the impact of MRE on clinician's diagnostic confidence and choice of therapeutic strategy for CD patients: after MRI examination, therapy was adjusted in 61% [31/51], in 27% [14/51] therapy was reduced, and in 33% [17/51] therapy was intensified.[11] Whether small bowel MRI really serves as a prognostic tool and therefore justifies intensification of therapy remains unclear and should be addressed in future studies.

4.3. MR-enterography or MR-enteroclysis

Being aware that evaluating two diagnostic techniques without performing an intra-individual analysis lacks methodical significance, we nevertheless think that this inter-individual analysis represents the diagnostic performance of MRE/MRY sufficiently. Although image quality is better in MRY, this does not lead to a significant relevance in terms of diagnostic yield. In the present study, both MRY and MRE obtained high diagnostic accuracies across all issues. Certainly, in view of the small number of MRE examinations [n = 49] and limited and equal numbers, an intra-individual analysis would be preferable for comparison. However our hypothesis, that MRY in general achieves a more efficient bowel distension and thus possibly offers the opportunity for a more accurate diagnosis, coincides with prior studies.[7,8,19,21,22,23,24,25,26] Nevertheless, MRE achieved a slightly, even though not significantly, higher sensitivity compared with MRY [chi-square test: $p > 0.05$, 95% CI]. Furthermore, with no nasoduodenal tube, MRE does not require radiation exposure and is less invasive; but the rapid ingestion of large amounts of liquid can be perceived as burden and might cause nausea, particularly in children.[23] Due to the fact that MRE obtained equivalent diagnostic accuracy compared with MRY, but with less time, cost and resourceseffort, higher patient compliance, less invasiveness, no radiation exposure, and less patient burden, we preferentially recommend MRE as other authors do.[7,8,19,23,24] Future studies, to investigate whether small bowel MRI causes changes in therapy and standardised inflammation activity scores [including thresholds for bowel enhancement], have to be developed for routine practice.

4.4. Limitations

The retrospective study design is associated with certain limitations, such as loss of information [missing reports, missing age at onset of disease], unequal group power between MRY [n = 289] and MRE [n = 49], and lack of a standard MRI report protocol and assessment of disease activity, which partly led to difficulties in interpretation. However, to our knowledge, there is no previous study focusing on small bowel MRI's diagnostic impact in daily course of the disease that includes such a large number of patients, which probably represents daily routine practice more accurately than earlier investigations. Furthermore, due to patient selection, consultations between radiologists and gastroenterologists, and the partially non-standardised diagnostic algorithm [small numbers of VCE / enteroscopy] there might be possible causes of statistical bias. Finally, a reference standard consisting of various modalities in small bowel MRI offers considerable, but well-known problems which, in the present study, were solved by determining a reference based on all diagnostic findings as widely used in earlier studies.

5. Conclusion

As far as we are aware, this study investigated for the first time the diagnostic benefit of small bowel MRI on Crohn's disease phenotype by assessment of Montreal Classification in routine clinical course. MRY and MRE obtained comparably high diagnostic accuracies even in routine practice, affirming their role as powerful and reliable techniques in small bowel investigation of CD patients. MRE should be the favoured technique in small bowel diagnostics of CD patients because of minimal invasiveness. MRI is important in staging and prognostic evaluation of Crohn's disease, since it alters Montreal Classification significantly towards more severe stages of disease. Without performing small bowel MRI, disease behaviour and extent would have been underestimated frequently, thus resulting in false risk stratification, which might be relevant to prognosis of complications and choice of therapy.

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Conflict of Interest

The authors declare that there is no actual or potential conflict of interest.

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Author Contributions

GL: conducting the study, acquisition of data, analysis and interpretation, drafting the manuscript, approving the final manuscript. TB: conception and design of the study, data analysis and interpretation, supervision, drafting the manuscript, approving the final manuscript. VN: supervision, revision of the manuscript, support in terms of radiology approving the final manuscript. WS: supervision, revision of the manuscript, support in terms of gastroenterology, approving the final manuscript.

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