Magnetic resonance enteroclysis in patients with Crohn’s disease: Fat saturated T2-weighted sequences for evaluation of inflammatory activity

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KEYWORDS
Crohn’s Disease; MRI; MR enteroclysis; Inflammatory activity

Abstract

Background and aims: To evaluate fat saturated (fs) T2-weighted (w) fast relaxation fast spin echo (FRFSE)-sequences compared to the standard protocol with contrast agent for the evaluation of inflammatory activity in patients with Crohn’s Disease (CD).

Methods: Forty-eight patients (male, 17; female, 33; mean age, 37 years) with suspicion of inflammatory activity in proven CD who underwent MR enteroclysis (MRE) at 1.5 T (GE Healthcare) were retrospectively included. Two blinded radiologists analyzed MRE images for presence and extent of CD lesions and degree of local inflammation for fs T2-w FRFSE and contrast enhanced T1-w images (T2-activity; T1-activity; score, 1–4) in consensus. Furthermore, mural signal

Abbreviations: fs, fat saturated; w, weighted; FRFSE, fast relaxation fast spin echo; CD, Crohn’s Disease; MRE, magnetic resonance enteroclysis; CDAI, Crohn’s Disease Activity Index; MRI, magnetic resonance imaging; SSFP, steady-state free precession sequences; FIESTA, fast imaging employing steady state acquisition; 2D, two-dimensional; FOV, field of view (FOV); SPGR, spoiled gradient echo; FRFSE, fast relaxation fast spin echo; ROI, region of interest; SI, signal intensity; ROC, receiver operator characteristic; WBC, white blood cells


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1. Introduction

Crohn’s Disease (CD) is a chronic relapsing inflammatory disease of the gastrointestinal tract involving all the layers of the bowel wall. Possible complications are fibrostenotic strictures, fistulas and abscesses. The course of the disease is characterized by remitting and relapsing episodes. For optimizing the therapeutic strategy, evaluation of CD activity is essential. Patients with active inflammation should receive different medical therapy as patients with chronic disease without active inflammation. Also, the localization of the inflammatory activity is important to allow an optimized treatment of the patients. Assessment of disease activity is based on a variety of clinical and inflammation parameters and scores, e.g. the Crohn’s Disease Activity Index (CDAI), as well as endoscopic findings. However, upper and lower endoscopy are not always complete and do not sufficiently allow the evaluation of the small bowel as well as the full transmural extent of the disease. Furthermore, biochemical markers may be normal in patients with acute inflammation. Different types of radiological investigations are used to study the small bowel in CD; however, Magnetic Resonance Enteroclysis (MRE) has developed into the method of choice. Various Magnetic Resonance Imaging (MRI) findings such as contrast enhancement of the bowel wall have been proposed as accurate markers of disease activity, however, in acute and chronic disease an overestimation of disease activity based on contrast enhancement is possible. A promising alternative is the assessment of bowel wall edema by evaluating T2-w images. Therefore, the purpose of the present study was to evaluate fat saturated (fs) T2-weighted (w) Fast Relaxation Fast Spin Echo (FRFSE)-sequences compared to the standard protocol with contrast agents for the evaluation of inflammatory activity in patients with CD.

2. Material and methods

2.1. Patients

For retrospective enrolment it was required that patients had an either by endoscopy or surgery histologically proven CD and had undergone MRE for evaluation of inflammatory activity. In total, 48 consecutive patients (female, 32; male, 16; mean age, 37±11 years) in a time interval of 2.5 years were enrolled. A complete digital MRE-dataset and a comprehensive clinical documentation including histopathologic data had to be present. In 45 of 48 eligible patients, ileocolonoscopy within 3 days after the MRE was performed. Furthermore, in a subset of patients surgical exploration was performed within a maximum of 10 days (n=6; including the 3 patients with missing ileocolonoscopy). In all patients, evaluation of CDAI on the day of MRE was performed. The institutional review board approved this retrospective study.

The scan protocol used in all patients was the following:

1. Steady-state free precession sequences (SSFP) and Fast Imaging Employing Steady State Acquisition (FIESTA), two-dimensional (2D) coronal: TR, 6.4 ms; TE, 1.7 ms; flip angle, 55°; BW, 125 kHz; field of view (FOV), 48 cm; matrix, 256×192 pixels; slice thickness, 4.5 mm; acquisition time, 40 slices in 1 min 50 s.
2. SSFP and FIESTA, 2D axial: TR, 6.9 ms; TE, 1.7 ms; flip angle, 55°; BW, 125 kHz; FOV, 40 cm; matrix, 256×256 pixels; slice thickness, 4.5 mm; acquisition time, 60 slices in 3 min.
3. T1-w fs spoiled gradient echo (SPGR) coronal: TR, 3.9; TE, 1.7; flip angle, 12°; BW, 62.5 kHz; FOV, 48 cm; matrix, 256×160 pixels; slice thickness, 4 mm; gap = 2 mm; acquisition time, 40 slices in 28 s.
4. T1-w FS SPGR axial: TR, 3.9; TE, 1.8; flip angle, 12°; BW, 62.5 kHz; FOV, 40 cm; matrix, 256×160 pixels; slice thickness, 4 mm; gap = 2 mm; acquisition time, 60 slices in 41 s.
5. Axial Fast Relaxation Fast Spin Echo (FRFSE)-2D: TRS, 3.4 ms; TE, 1.5 ms; flip angle, 45°; BW, 125 Hz; FOV, 48 cm; matrix, 224×224 pixels; slice thickness, 3 mm; gap, 20 mm; acquisition time, 1 min 42 s.

The T1-w sequences listed as point 3 and 4 were performed 60–70 s after intravenous application of a paramagnetic intensity (SI) ratios (T2-ratio; T1-ratio) were recorded. Patient based MRE findings were correlated with endoscopic (45 patients), surgical (6 patients), histopathological, and clinical data (CDAI) as a surrogate reference standard.

Results: In total, 24 of 48 eligible patients presented with acute inflammatory activity with 123 affected bowel segments. ROC analysis of the total inflammatory score presented an AUC of 0.93 (p<0.001) for T2-activity (T1-activity, AUC 0.63; p=0.019). ROC analysis revealed an AUC of 0.76 (p<0.001) for the T2-ratio (T1-ratio, AUC 0.51; p=0.93). General linear regression model revealed T2-activity (p=0.001) and age (p=0.024) as predictive factors of acute bowel inflammation.

Conclusions: T2-w FRFSE-sequences can depict CD lesions and help to assess the inflammation activity, even with improved accuracy as compared to contrast-enhanced T1-w sequences.
contrast medium (0.2 ml Gd-DTPA/kg body weight; Magnevist, Bayer Schering Pharma, Leverkusen, Germany).

In total, preparation and examination time varied between 45 and 60 min.

2.3. Image quality

For MRE analysis, a dedicated MRI-viewing workstation (Advantage Windows 4.3; GE Healthcare) was used. Two experienced radiologists (6 and 12 years of experience in abdominal MRI reading) evaluated all MRE data blinded to clinical data in consensus reading.

Quality of scans was evaluated concerning contrast filling of the bowel and artifacts for three different MRE sequences (transverse and coronal FIESTA-2D pre-contrast and T1-w-Sequence post-contrast).

For bowel filling, a non-quantitative 5-point scale was used: (1) very good (hydro-distension throughout the entire small bowel proximal to a possible stenosis), (2) good (almost complete distension), (3) moderate (partial distension reaching the pathologic segments), (4) poor (incomplete filling and pathologic segments not reached but diagnosis still possible), (5) non-diagnostic (small bowel distension absent or insufficient for reliable diagnosis).

For artifacts, a 4-point scale was used: (1) no relevant artifacts, (2) discrete artifacts without impairing image interpretation, (3) heavy artifacts disturbing image interpretation, (4) non-diagnostic (images insufficient for reliable diagnosis due to artifacts). Furthermore, the cause of the artifacts was assessed (patient movements, peristalsis, breathing artifacts, others (including technical artifacts)). The overall image quality was finally assessed as good (hydro-distension=3 and artifacts<3), moderate (hydro-distension=3 and artifacts<3), or poor (hydro-distension>3 and/or artifacts>2).

2.4. Diagnostic image analysis

Eight bowel segments were evaluated per patient: duodenum/jejunum, proximal ileum, distal ileum, ileocaecal transition, ascending colon, transverse colon, descending colon, sigmoid, and rectum. The following parameters were recorded for each segment: maximum wall thickness (mm) and length of CD segment (affectation; short, <5 cm; intermediate, 5–15 cm; long, >15 cm).

The presence of mural edema (hypointensity on T2-w fs FRFSE-sequences) was graded with a 4-point scale (1, none; 2, mild; 3, intense; 4, super bright; referred to T2-activity) in correlation to the signal intensity (SI) of the cerebral spinal fluid. Contrast enhancement of the bowel wall after intravenous contrast administration (referred to T1-activity) was graded with a 4-point scale (1, none; 2, mild; 3, intense; 4, strong) in correlation to the SI of the aorta. For statistical comparison of the T1- and T2-activity with the CDAI, the values of the most prominently affected segment were correlated. Furthermore, contrast enhancement patterns of the affected bowel wall were evaluated (homogeneous vs. layered). SI measurements were performed on most representative axial images of the T2-w and contrast enhanced T1-w images by placement of a single oval ROI fitted to the brightest part of bowel wall in the affected segment. The ROIs were designed oval as long (up to 1.5 cm) and as wide (depending on wall thickness) as possible in order to include the brightest region of the involved segment along the bowel wall and to exclude adjacent tissue and lumen for minimization of partial volume effects. On the same axial image, another oval ROI (as large as possible) was fitted into the ipsilateral erector spinae muscles excluding visible vessels and larger interseptations. All ROIs were placed by two observers in consensus. From both ROIs, the mean absolute SI was recorded for further calculation. Mural ratio (T2- and T1-ratio) was expressed as ratio with the SI values of the erector spinae muscles.

Enlarged regional lymph nodes with a size of more than 1 cm of the maximal transversal diameter on the axial images and accentuated contrast enhancement as assessed on a visual basis were read as positive indicator of active CD.

Extramural alterations due to CD including the comb sign, fistulae, and abscesses were documented.

2.5. Clinical and reference data

All available clinical reports were systematically reviewed by an experienced gastroenterologist. Age, sex, underlying medical conditions, CDAI and clinical outcome were recorded for each patient. Laboratory tests were performed at the day of submission including white blood cell (WBC) count and C-reactive protein (CRP) level. The CDAI was evaluated in all patients by an experienced gastroenterologist according to the criteria proposed by Best et al.16,17 Forty-five patients had ileocolonoscopy, in a subset of patients surgical exploration was performed (6 patients, also including the 3 patients with missing ileocolonoscopy). As a surrogate reference standard, we used an approximation by comparing the dominant segment of the MRE findings with the global assessment by CDAI with the aid of all available endoscopic and surgical information for statistical comparison. This surrogate reference standard (CD-activity, yes or no) was created by a research fellow and an abdominal radiologist.

2.6. Statistics

Statistical analyses were performed using the SPSS-software (release 11.0.4; SPSS Inc., Chicago, IL). Correlation was assessed with spearman rank correlation coefficient and unpaired Wilcoxon test with continuity correction. Concerning the prediction of inflammatory activity, a general linear model was used to analyze the association of one dependent and several independent variables. Receiver operator characteristic (ROC) curves were used to analyze the association of activity (based on the CDAI), local inflammation score (T2- and T1-activity), and SI-ratios (T2- and T1-ratio), respectively. The optimal cut-off values were defined by the point on the ROC curve with the minimal distance between the 0% false positive and the 100% true positive rate. All test were performed at a 95%-level of significance.

3. Results

3.1. Clinical data

All patients had proven CD with a duration of 9.9 (±9.8) years of whom 11 patients had prior operations (distal...
ileum and/or ileocecal resection, n = 7; right hemicolectomy, n = 2; left hemicolectomy, n = 1; sigmoid resection, n = 1).

Twenty-four patients had clinically active disease (CDAI, 312 (±105)); 24 patients were in remission (CDAI, 140 (±62)). In total, for 24 patients, CRP was assessed (active disease, 5.9 (±4); no active disease, 2.6 (±4); p = 0.026).

For WBC, no significant difference was found between the two groups (active disease, 8.6 (±4.1); inactive disease, 9.6 (±3.5); p = 0.290).

Almost all patients have had ileoendoscopy (45 out of 48 patients). In a subset of patients (including the 3 patients without endoscopy), surgical exploration with resection of the distal ileum/ileocaecal transition was performed (6 of 48 patients).

### 3.2. MRE Image quality

In total, 358 bowel segments were evaluated. The results regarding contrast filling and artifacts are shown in Table 1. In total, for the coronal Fiesta-2D sequence, image quality of 338 segments was graded as good and of 20 segments as moderate (transverse Fiesta-2D sequence: 314 segments good, 44 segments moderate). For the coronal T1-w Sequence post-contrast, image quality of 328 segments was graded as good and of 30 segments as moderate. In none of the segments image quality was graded as poor.

### Table 1  Bowel (358 eligible segments) filling and artifacts. Abbreviations: FIESTA, Fast Imaging Employing Steady State Acquisition.

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Filling</th>
<th>Artifacts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Very good</td>
<td>Good</td>
</tr>
<tr>
<td>Coronal Fiesta-2D</td>
<td>36 (10%)</td>
<td>197 segments (55%)</td>
</tr>
<tr>
<td>Transverse Fiesta-2D</td>
<td>36 (10%)</td>
<td>225 segments (63%)</td>
</tr>
<tr>
<td>T1-w-Sequence post-contrast</td>
<td>32 (9%)</td>
<td>251 segments (70%)</td>
</tr>
</tbody>
</table>

3.3. MRE findings

Regarding acute inflammatory activity, 24 of 48 eligible patients had 123 affected bowel segments by means of MRE (jejunum, n = 2; ileum, n = 15; distal ileum, n = 31; ileocaecal transition, n = 27; ascending colon, n = 12; transverse colon, n = 10; descending colon, n = 13; sigmoid and rectum, n = 13; Figs. 1 and 2). All patients who had affected segments of the proximal bowel which were not accessible by ileocolonoscopy or surgery (n = 17), also had affected distal segments which were confirmed by ileocolonoscopy or surgery.

Lengths of affected segments were: short, n = 37; intermediate, n = 49; long, n = 36; the wall thickness of these segments ranged from 4 to 17 mm (mean, 8 mm).

**Figure 1** 31 year-old female patient suffering from Crohn’s Disease (Crohn’s Disease Activity Index, 380) with endoscopically confirmed acute inflammatory activity in the ascending colon (white arrows) showing concordant findings on (A) contrast enhanced T1-weighted images (activity score, grade 4; T1-ratio, 2.83) and (B) T2-weighted images (grade 4; T2-ratio, 2.8).
Regarding contrast enhancement patterns, no significant difference was found between patients with inflammatory activity (homogeneous, n = 18; layered, n = 6) and inactive CD (homogeneous, n = 21; layered, n = 3; p > 0.05).

In 22 patients with inflammatory activity, enlarged lymph nodes were found (remission, n = 12 patients, p < 0.05). Regarding contrast-enhanced lymph nodes, in all 22 patients with acute inflammatory activity contrast enhancement of mesenteric lymph nodes was present (remission, 10 of 24 patients; p < 0.05). Ten patients with inflammatory activity presented the comb sign; 5 patients had fistulas, 1 patient had an abdominal abscess.

### 3.4. Indicators of disease activity and severity in MRE

ROC analysis revealed an AUC of 0.76 (p < 0.001) for the T2-ratio with an optimal cut-off value of 1.52 for the indication of inflammatory activity (sensitivity, 83%; specificity, 71%; accuracy, 77%; Fig. 3A) and an AUC of 0.93 (p < 0.001) for

![Figure 2](image_url)

**Figure 2** 47 year-old female patient suffering from Crohn’s Disease without symptoms of acute inflammatory activity (Crohn’s Disease Activity Index, 50) demonstrating (A) a contrast enhancing lesion on T1-weighted images (grade 4; T1-ratio, 4.7) in the distal ileum (white arrows). The lesion was negative on (B) T2-weighted images (activity score, grade 2; T2-ratio, 1.74) and confirmed to be free of acute inflammation endoscopically.

![Figure 3](image_url)

**Figure 3** Receiver operator characteristic (ROC) analysis (A, T2-ratio; B, T2-activity; C, T1-ratio; D, T1-activity).
the T2-activity with an optimal cut-off value of 4 for indication of inflammatory activity (sensitivity, 88%; specificity, 92%; accuracy, 90%; Fig. 3B). For the T1-ratio, ROC-analysis presented an AUC of 0.51 (p=0.93) with an optimal cut-off value of 1.6 for the detection of inflammatory activity (sensitivity, 46%; specificity, 58%; accuracy, 52%; Fig. 3C). For the T1-activity, the AUC was 0.63 (p=0.019) with an optimal cut-off value of 4 to indicate inflammatory activity (sensitivity, 96%; specificity, 29%; accuracy, 63%; Fig. 3D).

Concerning the correlation of CDAI and several independent variables, age, CRP, wall thickness, T2-ratio, T2-activity, T1-ratio, T1-activity, and contrast enhancement of lymph nodes showed a significant correlation to the CDAI, whereas white blood cells (WBC), sex, contrast enhancement patterns and the presence of enlarged lymph nodes did not (Tables 2 and 3).

By general linear regression model, T2-activity (p=0.001) and age (p=0.024) were significant indicators of acute bowel inflammation; all other tested parameters did not reach the level of significance (p>0.05).

4. Discussion

For decision making regarding medical or surgical treatment for symptomatic CD patients, it is crucial to know whether and where inflammatory activity is present. Today, the reference standard for diagnosing active CD and staging disease activity is still endoscopy. During the recent years, MRI has been shown to be accurate in diagnosing active CD and therefore promises to be a helpful adjunct in the evaluation of CD. The present study analyses retrospective data on MRE in 48 CD patients regarding disease activity.

Regarding inflammatory activity, most MR studies have been using symptom based scoring systems, endoscopic biopsies and biochemical markers as their standard of reference, which is often a major point of criticism. For example, a drawback of the CDAI is that this scoring system evaluates disease activity on a per patient basis, instead of per segment. Endoscopy cannot always be complete and assess the full transmural extent of the disease; tissue sampling for histopathological examination only provides mucosal specimens. Biochemical markers may be normal in patients with acute inflammation and therefore are of limited sensitivity. In the present study, WBC was not significantly higher in active CD. In contrast, similar to a study of Maccioni et al., CRP was found to be significant, however only in a small proportion of patients (24 eligible). Consequently, as in clinical routine, a combination of multiple parameters, also including endoscopy, surgery, and histopathology when available, was used to create a surrogate reference standard for CD activity in the present study. An approximation by comparing the dominant segment of the MRI data with the global assessment by CDAI with the aid of all available endoscopic and surgical information for statistical comparison was performed. Almost all patients have had ileoendoscopy (45 out of 48 patients). In a subset of patients (including the 3 patients without endoscopy), surgical exploration with resection of the distal ileum/ileo-caecal transition was performed (6 of 48 patients). According to these parameters, 24 out of 48 eligible patients with conclusive and largely reliable reference standard presented with active disease by means of overall MRE findings in 123 affected bowel segments. The most affected segments were the distal ileum (n=31) and the ileo-caecal transition (n=27). Regarding overall MRI findings, 17 segments of the proximal small bowel were affected (jejunum, n=2; ileum, n=15). These segments were not accessible by ileocolonoscopy or were confirmed by surgery. However, in all these patients also affected distal segments were present, which were confirmed by ileocolonoscopy or surgery. As a surrogate reference standard, we used an approximation by comparing the dominant segment of the MRE findings with the global assessment by CDAI with the aid of all available endoscopic and surgical information for statistical comparison.

The importance of selecting the adequate treatment strategy emphasizes the clinical relevance of an accurate differentiation between active and chronic disease. Lawrence et al. showed that MRI can be used as a diagnostic and prognostic tool in the management of patients with CD; patients can be categorized and that these categories

### Table 2 Correlation of Crohn's Disease Activity Index (CDAI) and several independent variables.

<table>
<thead>
<tr>
<th>CDAI (Spearman's rank correlation)</th>
<th>Age (n=48)</th>
<th>c-reactive Protein (n=24)</th>
<th>White blood cells (n=48)</th>
<th>Wall thickness (n=48)</th>
<th>T2-activity (n=48)</th>
<th>T2-ratio (n=48)</th>
<th>T1-activity (n=48)</th>
<th>T1-ratio (n=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correlation coefficient</td>
<td>-0.32</td>
<td>0.51</td>
<td>-0.19</td>
<td>0.41</td>
<td>0.75</td>
<td>0.34</td>
<td>0.37</td>
<td>0.05</td>
</tr>
<tr>
<td>Significance</td>
<td>p=0.027</td>
<td>P=0.014</td>
<td>p=0.197</td>
<td>P=0.003</td>
<td>P&lt;0.001</td>
<td>P=0.016</td>
<td>p=0.011</td>
<td>p=0.734</td>
</tr>
</tbody>
</table>

### Table 3 Correlation of Crohn's Disease Activity Index (CDAI) and several independent variables.

<table>
<thead>
<tr>
<th>CDAI (unpaired Wilcoxon test with continuity correction)</th>
<th>Sex (n=48)</th>
<th>Contrast enhancement of lymph nodes (n=48)</th>
<th>Enlarged lymph nodes (n=48)</th>
<th>Contrast enhancement patterns</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Median</td>
<td>203</td>
<td>151</td>
<td>235</td>
<td>110</td>
</tr>
<tr>
<td>Q25</td>
<td>138</td>
<td>106</td>
<td>151</td>
<td>102</td>
</tr>
<tr>
<td>Q75</td>
<td>305</td>
<td>317</td>
<td>343</td>
<td>125</td>
</tr>
<tr>
<td>Significance</td>
<td>P=0.274</td>
<td>p=0.001</td>
<td>p=0.082</td>
<td>p=0.57</td>
</tr>
</tbody>
</table>
correlate with patient response to ongoing medical therapy and the histological findings at surgery. 

Although bowel wall enhancement and bowel wall thickening are recognized as important MRI-parameters that indicate CD, no strict cutoff points have been defined yet to discriminate the different stages of disease. Contrast enhanced MRI is highly sensitive for diagnosing patients with active disease and enhancement is associated with clinical grade. However, factors influencing enhancement are complex and not just inflammation resulting in a tendency to "overstage" CD. The hypothesis behind this is that chronic disease activity causes an increased permeability of the affected microvascular surface area and therefore increased enhancement in patients with longstanding CD. This is also reflected by our results; regarding the post contrast T1-w images, more segments were falsely interpreted as active disease as compared to the T2-w-images. In case of bowel wall thickening and contrast enhancement with absence of increased signal on the T2-w FRFSE images, chronic disease with fibrotic tissue may be present, while increased T2-w signal indicates edema related to active inflammation. Accordingly, on a patient based evaluation, fs T2-w FRFSE images, achieved a higher sensitivity, specificity and accuracy in the detection of affected bowel segments compared to the post-contrast T1-w images in the present study. ROC analysis revealed an AUC of 0.76 for the T2-ratio (p<0.001; optimal cut-off value of 1.52) in contrast to the T1-ratio, with an AUC of 0.51 (p=0.93; optimal cut-off value of 1.6) for the detection of inflammatory activity. Furthermore, for the T2-activity, ROC analysis presented an AUC of 0.93 (p<0.001; optimal cut-off value of 4) in contrast to the T1-activity (AUC, 0.63; p=0.019; optimal cut-off value of 4) for indication of inflammatory activity. Also, in correlation to the CDAI, the T2-activity and the T2-ratio (correlation coefficient of 0.75 and 0.34; p<0.001 and p=0.016) were indicative of active disease in contrast to the T1-activity and T1-ratio (correlation coefficient of 0.37 and 0.05; p=0.011 and p=0.734). Our results are similar to other studies, however evaluation of the T2-w images were present. In contrast, according to Ziech et al., a high T2-w SI was not significantly associated with an increased acute inflammation. However, they used T2-w sequences without fs. This may reflects the need of fs images.

Regarding the technique of SI measurements, Sharman et al. showed, that relative bowel wall SI measurements lack of a satisfactory observer agreement, unrelated to reader experience; this, however, can be improved by using fixed ROIs. A potential drawback of fixed ROIs is, when using mean SI as the resultant parameter, that partial volume effects might bias the quantification. This is why consensus placement of oval ROIs, which could be fitted manually to the outlines of the interesting area were used in the present study.

As a further specification of contrast enhancement, a layered pattern of wall enhancement as marker for activity has been proposed. Herein, however, no significant difference between homogenous and layered pattern of enhancement was found. Gourtsoyianni et al. showed, that the enhancement ratio of mesenteric lymph nodes may vary across different subtypes of CD; in the present analysis, a visual scale of contrast enhancement with similar tendencies was applied. This turned out to be highly suggestive of active CD whereas the presence of enlarged lymph nodes regardless of their contrast behavior was not found to be significant. Wall thickening was indeed significant for active CD in the present series; the correlation with the CDAI, however, was poor. The comb sign was only found in patients with active disease. This is in agreement with previous studies reporting increased mesenteric vascularity and swelling of the mesenteric tissue as an indicator of disease activity. By general linear regression model, T2-activity (p=0.001) and age (p=0.024) were revealed as indicative factors of acute bowel inflammation, where as all other tested parameters were not significant (p>0.05). This reflects the need of fs T2-w images; an increased SI of the bowel wall is highly indicative of active CD, whereas again for the post contrast T1-w images a tendency to "overstage" CD may result.

MRI of the bowel requires luminal contrast to achieve adequate distension. Two major techniques are used to achieve this bowel distension, oral contrast administration and installation of the contrast through a nasojejunal tube. Neegard et al. showed that bowel distension was inferior when oral intake was used as compared to MRE. Furthermore, Masselli et al. observed a significant superiority of MRE in the detection rate of CD compared to oral intake. In the present study, a continuous filling after placement of a nasojejunal tube was employed. Thereby, most segments were graded as very good or good, only few segments were graded as non-diagnostic. The non-diagnostic visualization of segments was observed only in the Fiesta-2D images but not in the post contrast T1-w images, which is probably due to the ongoing infusion of oral contrast during the examination. Other factors potentially hampering the diagnostic quality and the study results such as movement artifacts were comparably low in the present series.

Regarding possible limitations of this study, the standard of reference, has to be mentioned; this has always been a problem in comparable CD studies as histopathological or at least macroscopic assessment cannot be obtained from all patients. However, as a surrogate reference standard we used an approximation by comparing the dominant segment in MRE findings with the global assessment by CDAI with the aid of all available endoscopic and surgical information's for statistical comparison; no segment based evaluation was performed. To our opinion, this approximation is the only possibility to approach and to reflect the ability of different MRE methods for assessing disease activity in the available cohort. Clinical underestimation of disease activity in MRE positive patients is a problem in the clinical routine – but also problematic for an appropriate study design to prove such a condition. However, in our patient cohort, no patient was present with high T2-activity without elevated CDAI. Thereby, false positive findings of contrast-enhanced T1-w images were resolved by using this additional parameter. Furthermore, the limited numbers of cases and the retrospective design as well as the mode of consensus reading are limitations of the present analysis. Despite this, the results obtained herein are promising enough to be adapted by protocols of upcoming larger studies to undergo further validation including determination of interobserver variability.

5. Conclusions

T2-w FRFSE-sequences can depict CD lesions and help to assess the inflammation activity, even with better accuracy as contrast-enhanced T1-w sequences. By general linear
regression, the parameter T2-activity and age were revealed as predictive factors of acute small-bowel inflammation; where as all other tested parameters were not predictive.

Conflicts of interest

The authors declare that they do not have any conflict of interest.

Acknowledgments

Statement of authorship: the author CG carried out the study and data analyses; TD, SW, TK, FP, JM, and RT recruited and followed up the enrolled patients. IS performed the statistical analysis of the data; RR participated in the study design and revised the manuscript, OG, DK, AS, BH revised and helped to draft the manuscript. All authors read and approved the final manuscript.

References