Development and clinical applications of the time intensity curve shape analysis in dynamic contrast enhanced MRI: a pixel-by-pixel approach
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CHAPTER 4

Evaluation of dynamic contrast enhanced MRI as indicator of disease activity in perianal fistulizing Crohn’s disease

Horsthuis K, Lavini C, Bipat S, Stokkers PCF, Stoker J.


CHAPTER 4  DCE-MRI in Crohn’s Disease

ABSTRACT

Purpose: To prospectively determine clinical value of dynamic contrast enhanced magnetic resonance (MR) imaging in the evaluation of disease activity in perianal Crohn disease (CD).

Materials and Methods: Patients provided written informed consent. Study approval was waived by an institutional review board. Thirty-three patients with perianal CD underwent pelvic MR imaging; 17 were male (mean age, 37.4 years ± 10.8 [standard deviation]; age range, 18–54 years) and 16 were female (mean age, 32.0 years ± 8.3; age range, 16–43 years). Dynamic contrast enhanced MR imaging was performed; time-intensity curves (TICs) were obtained. Each pixel was classified as one of six predefined TIC shape types. For each MR imaging examination, a region of interest (ROI) was drawn around the fistula on the single section corresponding to the most extensive and most hyperintense lesion; maximum enhancement ($ME$), slope of enhancement, and TIC shapes were calculated. Absolute and relative numbers of pixels for each curve type were calculated in a two-dimensional ROI. These results were compared with Perianal Disease Activity Index (PDAI), C-reactive protein (CRP) level, an MR imaging–based severity score, and clinical outcome. A Spearman rank correlation test was used to calculate correlation coefficients between dynamic contrast enhanced MR imaging parameters and reference parameters. A Mann-Whitney $U$ test was used to calculate differences in dynamic contrast enhanced MR imaging parameters between predefined groups of patients.

Results: Significant correlations were found between the absolute amounts of the TIC shape types and PDAI and between ROI volume and PDAI. The ratio of quickly enhancing versus slowly enhancing pixels correlated with higher MR imaging scores as did the ROI volume. The absolute amounts of pixels displaying TIC types 2, 3, 4, and 5 correlated significantly with MR imaging score. CRP level showed a significant correlation with mean $ME$. Larger numbers of quickly enhancing pixels were observed in patients who needed medication changes or developed new abscesses during follow-up.

Conclusion: Dynamic contrast enhanced MR imaging can help determine disease activity in perianal CD and might be helpful in selecting a subpopulation of patients who should be monitored more closely for development of more extensive disease.
INTRODUCTION
Crohn disease (CD) is a chronic inflammatory bowel disease that frequently results in perianal complications such as abscesses and perianal and/or ano- or rectovaginal fistulas (1). Adequate assessment of perianal CD, including information on anatomic extent and degree of inflammation, is important to determine the optimal treatment strategy and response to treatment.

Magnetic resonance (MR) imaging has become the reference standard for anatomic evaluation of perianal and ano- or rectovaginal fistulas (2,3). Increased enhancement on T1-weighted MR images after intravenous administration of gadolinium-based contrast material is generally considered indicative of active inflammation (4,5). The observed T1 hyperenhancement is due to increased tissue perfusion and vascular permeability (6–8). However, conventional postcontrast imaging provides a limited amount of information about tissue behavior because it is performed after most of the contrast material distribution has been accomplished and some of the contrast material has already washed out.

![Classification of TICs](image)

**Figure 1**: Classification of TICs. Type 1: no enhancement. Type 2: slow enhancement, maximum of the curve is reached after half of the imaging. Type 3: quick enhancement, followed by a signal plateau. Type 4: fast enhancement and quick washout. Type 5: quick enhancement followed by a slow constant enhancement. Type 6: arterial enhancement characterized by a quick uptake and a quick decay, followed by a slowly decaying plateau. Type 7 (dashed line): unclassified enhancement including all the curves that could not be classified as any of the above. SI=signal intensity.

In contrast, with dynamic contrast material enhanced MR imaging, images are acquired during the delivery of the contrast material in the tissue of interest, thus highlighting the dynamic response of the tissue to the inflow of blood and the
subsequent distribution in the extracellular fluid space. Analysis of the time-dependent changes of signal intensity on dynamic contrast enhanced MR images might provide valuable information about disease activity. The purpose of our study was to prospectively determine the clinical value of dynamic contrast enhanced MR imaging in the evaluation of disease activity in patients with perianal CD.

### Table 1

**Severity Indexes of the Study Population**

<table>
<thead>
<tr>
<th>Index</th>
<th>Mean ± Standard Deviation</th>
<th>Median*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDAI (n = 27)</td>
<td>6.0 ± 3.8</td>
<td>6.0 (0–14)</td>
</tr>
<tr>
<td>MR imaging–based score of disease severity (n = 33)</td>
<td>11.1 ± 4.0</td>
<td>10.0 (4–20)</td>
</tr>
<tr>
<td>CRP level (n = 31)</td>
<td>15.8 ± 37.9</td>
<td>4.8 (1.0–203.4)</td>
</tr>
</tbody>
</table>

Note.—PDAI was not scored in six of 33 patients because of absence of perianal lesions (n = 3) or failure to examine patient on the day of MR imaging (n = 3). CRP values were not available in two patients.

* Data in parentheses are ranges.

**MATERIALS AND METHODS**

A research grant was received from the Nuts Ohra Foundation (Amsterdam, the Netherlands). The Nuts Ohra Foundation was not involved in designing and conducting the study and did not have access to the data. The Nuts Ohra Foundation was not involved in data analysis or preparation of the manuscript.

**Study Population.**

From September 2005 through March 2007, 45 consecutive patients known to have CD who underwent pelvic MR imaging at the radiology department of a tertiary referral center (Academic Medical Center, Amsterdam, the Netherlands) were included in this prospective study. The indication for MR imaging was evaluation of known or suspected perianal, anovaginal, and/or rectovaginal fistulas. The general exclusion criteria to MR imaging (eg, claustrophobia, pregnancy) were applicable. No other explicit inclusion or exclusion criteria were used. All patients provided written informed consent for use of their data for study purposes. Study approval was waived by the institutional review board. Data from 12 patients had to be excluded because of absence of perianal, anovaginal, or rectovaginal fistulas (n = 8) or for technical reasons (n = 4; insertion of a 20-gauge needle was impossible, necessitating insertion of a catheter with a needle of smaller diameter in three patients, whereas in one patient six sections were imaged dynamically instead of five). Thus, 33 patients were finally included, of whom 17 were male (mean age, 60
37.4 years ± 10.8 [standard deviation]; age range, 18–54 years) and 16 were female (mean age, 32.0 years ± 8.3; age range, 16–43 years).

**MR Imaging Technique**

MR imaging was performed with a 1.5-T imager (Signa Horizon Echospeed, LX 9.0; GE Medical Systems, Milwaukee, Wis) with a torso phased-array surface coil. Sagittal, coronal, and transverse T2-weighted fast spin-echo sequences were performed (repetition time msec/echo time (msec), 2500/70 [effective]; field of view, 30 × 30 cm; matrix, 512 × 256; section thickness, 4 mm; intersection gap, 0.4 mm; echo train length, 16; total bandwidth, ± 20.83 kHz; number of signals acquired, two; sections, 32) with the coronal sequence angled parallel and the transverse sequence angled perpendicular to the anal canal. In addition, a fat-suppressed T2-weighted fast spin-echo sequence (4000/85 [effective]; field of view, 30 × 30 cm; matrix, 256 × 256, section thickness, 4 mm; intersection gap, 0.4 mm; total bandwidth, ±20.83 kHz; number of signals acquired, two; sections, 28–32) was performed in the transverse plane before administration of contrast material. After completion of these series, a dynamic transverse two-dimensional T1-weighted fast spoiled gradient-echo sequence was performed (7.4/2.4; flip angle, 30°; field of view, 28 × 28 cm; section thickness, 4 mm; intersection gap, 1.0 mm; matrix, 256 × 160; total bandwidth, ±31.25 kHz; number of signals acquired, three; imaging duration, 5 minutes 59 seconds). The dynamic sequence consisted of a five-section volume that was imaged 20 consecutive times with a temporal resolution of 5 seconds (thus resulting in 20 time points per section). The high time resolution was chosen after our earlier observation that most fistulas tend to show early enhancement, probably as a result of their high vascularization. This situation limited the number of sections acquired to five. The location of the volume on the dynamic image was chosen at the presumed site of maximum inflammatory activity as determined by means of the fat suppressed T2-weighted series. Great care was taken to ensure that the dynamic studies were obtained in the same way (eg, we carefully checked the dose of contrast agent and the speed of injection, and we used the same intravenous catheter diameter and MR imaging protocol parameters in all patients). One minute after the start of imaging, 0.2 mL of contrast agent (gadodiamide, 0.5 mmol/mL gadolinium, Omniscan; GE Healthcare, Chalfont St Giles, United Kingdom) per kilogram of body weight was injected through a 20-gauge intravenous catheter in the antecubital vein by means of bolus injection (5 mL/sec) by using an automated injection pump (Spectris; Medrad, Warrendale,
Injection of contrast medium was immediately followed by a flush of 10 mL of saline (5 mL/sec). After completion of the dynamic sequence, a transverse T1-weighted fast spin-echo sequence with fat saturation was performed (600/10 [effective]; field of view, 45 × 45 cm; matrix, 256 × 256; echo train length, three; bandwidth, ±20.83 kHz; section thickness, 4.0 mm; intersection gap, 0.4 mm; number of signals acquired, two; concatenations, four; sections, 32). The orientation of all transverse series was identical.

### Table 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PDAI</th>
<th>CRP Level MR</th>
<th>Imaging–based Score of Disease Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative pixel count 5</td>
<td>NS*</td>
<td>NS*</td>
<td></td>
</tr>
<tr>
<td>Absolute pixel count TIC type 2</td>
<td>$r = 0.434$ ($P = .024$)</td>
<td>$r = 0.153$ ($P = .411$)</td>
<td>$r = 0.522$ ($P = .002$)</td>
</tr>
<tr>
<td>Absolute pixel count TIC type 3</td>
<td>$r = 0.435$ ($P = .023$)</td>
<td>$r = 0.050$ ($P = .788$)</td>
<td>$r = 0.564$ ($P = .001$)</td>
</tr>
<tr>
<td>Absolute pixel count TIC type 4</td>
<td>$r = 0.313$ ($P = .112$)</td>
<td>$r = 0.014$ ($P = .942$)</td>
<td>$r = 0.531$ ($P = .001$)</td>
</tr>
<tr>
<td>Absolute pixel count TIC type 5</td>
<td>$r = 0.410$ ($P = .034$)</td>
<td>$r = 0.051$ ($P = .784$)</td>
<td>$r = 0.643$ ($P &lt; .001$)</td>
</tr>
<tr>
<td>Ratio TIC2</td>
<td>$R = -0.075$ ($P = .712$)</td>
<td>$r = 0.036$ ($P = .846$)</td>
<td>$r = 0.380$ ($P = .029$)</td>
</tr>
<tr>
<td>ROI volume</td>
<td>$r = 0.507$ ($P = .007$)</td>
<td>$R = 0.039$ ($P = .836$)</td>
<td>$r = 0.570$ ($P = .001$)</td>
</tr>
</tbody>
</table>

* NS _ not significant for any of the individual TIC types.

† Indicates statistically significant difference.

‡ Ratio between TIC types 3, 4, and 5 versus type 2.

### Analysis of Conventional MR Imaging Data

All MR images were evaluated by an experienced abdominal radiologist (J.S.) with extensive prior experience in evaluation of pelvic MR images (approximately 1000 examinations for perianal fistulas). To preserve homogeneity of the analyzed group, we excluded patients from further analysis if no fistulas were observed. The MR imaging–based score of disease severity, as developed by Van Assche et al (9), was used to determine disease activity. This score consists of both anatomic parameters and parameters indicative of active inflammation. Scores range from 0 to 22, with higher scores indicating more severe disease.

### Analysis of Dynamic Contrast enhanced MR Images

Of the five sections that were acquired during the dynamic sequence, the single section corresponding to the most extensive and most hyperintense lesion on the
fat-saturated T2-weighted images was used for analysis. In this section, a research fellow (K.H.) manually drew a single free-form region of interest (ROI) around the fistula on the fourth dynamic T1-weighted image after the beginning of enhancement, corresponding to 20 seconds after injection, to exclude all non-pathologically enhancing areas such as the gluteal muscles. In each ROI, we calculated maximum enhancement (ME), defined as
\[ ME = \frac{S_{\text{max}} - S_b}{S_b}, \]
where \( S_{\text{max}} \) is maximum signal intensity and \( S_b \) is baseline, and the slope of enhancement (SOE), defined as
\[ SOE = \max \left\{ S(t_{i+1}) - S(t_i) \right\}, \]
where \( t \) is time. We calculated time intensity curve (TIC) shapes on a pixel-by-pixel basis. Six curve shapes, classified according to the scheme described by Lavini et al (10), were each assigned a colour (Fig 1): type 1 indicated no enhancement; type 2, slow enhancement, maximum of the curve is reached after half of the imaging; type 3, quick enhancement, followed by a signal plateau; type 4, fast enhancement and quick washout; type 5, quick enhancement followed by a slow constant enhancement; type 6, arterial enhancement characterized by a quick uptake and a quick decay, followed by a slowly decaying plateau. A large initial slope (as in slopes 3, 4, and 5) reflects high vascularisation. As described in some pharmacokinetic models, a large initial slope followed by quick washout reflects large capillary permeability. The extracellular extravascular space is reflected in the curve amplitude (11–13).

A seventh curve shape was used to group all unclassified pixels. The pixel-by-pixel TIC classification was then rendered in a color-coded map, providing a high spatial-resolution description of the curve shapes in the whole area of interest. Dynamic contrast enhanced MR imaging data were analyzed off-line by using software we developed.

**Clinical Evaluation**

The Perianal Disease Activity Index (PDAI) was scored prospectively by one of two research fellows (K.H.) by interviewing the patient and visual inspection of the perianal region at the time of the visit to the radiology department. Both research fellows were experienced in scoring the PDAI because they had participated in an earlier study by our group on perianal CD (n = 30 patients).

For patients with an ano- or rectovaginal fistula and no perianal manifestations, the PDAI was not calculated. The PDAI incorporates five elements: the presence or absence of discharge, pain or restriction of activities of daily living, restriction of
sexual activity, type of perianal disease, and degree of induration. Scores ranged from 0 to 20, with higher scores indicating more severe disease (14). Peripheral venipuncture was used to determine C-reactive protein (CRP) (in milligrams per litre) level as a biological marker of disease activity. In most patients, peripheral venipuncture was performed at the outpatient laboratory before or after MR imaging (mean, 3.6 days ± 6.3 from MR imaging; range, 0–26 days). In some patients, blood was drawn from the intravenous catheter inserted for contrast material administration before MR imaging.

<table>
<thead>
<tr>
<th>ME and Slope versus Reference Parameters</th>
<th>PDAI</th>
<th>CRP Level</th>
<th>MR Imaging–based Score of Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ME</td>
<td>( R_{9} = -0.093 ) ((P = .646))</td>
<td>( r = 0.506^* ) ((P = .004))</td>
<td>( r = 0.020 ) ((P = .914))</td>
</tr>
<tr>
<td>Mean SOE</td>
<td>( R_{9} = -0.169 ) ((P = .401))</td>
<td>( r = 0.192 ) ((P = .301))</td>
<td>( R_{9} = 0.134 ) ((P = .458))</td>
</tr>
<tr>
<td>SOE of the individual TICs averaged for TIC type 2</td>
<td>( NS_{T} )</td>
<td>( NS_{T} )</td>
<td>( R_{9} = -0.388^* ) ((P = .026))</td>
</tr>
<tr>
<td>ME of the individual TICs averaged</td>
<td>( NS_{T} )</td>
<td>( NS_{T} )</td>
<td>( NS_{T} )</td>
</tr>
</tbody>
</table>

* Indicates statistically significant difference.
† NS = not significant for any of the individual TIC types.

Table 3

Clinically Active versus Inactive Disease
We placed the patients into one of two groups on the basis of CRP and PDAI values. We defined clinically inactive disease as a CRP value of 5.0 mg/L or less because a cutoff value of 5 mg/L is used at our institution’s laboratory to distinguish between normal and elevated CRP values. For the PDAI, no cut-off value between active perianal disease and remission has been established yet. Thus, we chose a cut-off value of 5 on the basis of findings by Present et al (15) in a large cohort of patients with perianal fistulising CD; in their study, median PDAI values before infliximab treatment were 8 or higher, whereas after infliximab treatment, remission induction therapy median values were 5 or lower.

Follow-up
Follow-up data were collected by a research fellow (K.H.) by means of medical record review for all patients for a minimum of 6 months. Three separate events were recorded: if surgery had been performed for treatment of the fistula, if new abscess formation had taken place, and if a change in medication was necessary.
because of inadequate response to treatment (addition of antibiotics, immunosuppressive medication, and/or biologicals).

**Statistical Analysis**
For each ROI, we calculated the mean $ME$ and the mean $SOE$, as well as the volume of all enhancing pixels within the ROI. Calculation was also performed of the $ME$ and $SOE$ averaged over all pixels of the same TIC shape type within the ROI.

We calculated the absolute and relative amount of each TIC shape type within the ROI and the ratio of quickly enhancing versus slowly enhancing types of TIC (ratio between TIC types 3, 4, and 5 vs 2). A Spearman rank correlation test was used to calculate correlation coefficients between dynamic contrast enhanced MR imaging parameters and reference parameters (PDAI, CRP level, and MR imaging–based score).

Correlation coefficient values were interpreted as follows: 0.0 indicated not correlated; 0.2, weakly correlated; 0.5, moderately correlated; 0.8, strongly correlated; and 1.0, perfectly correlated (16). A Mann-Whitney U test was used to calculate differences in dynamic contrast enhanced MR imaging parameters between the predefined groups of patients. P values less than .05 were considered to indicate statistical significant differences.

**RESULTS**
Disease severity indexes of the 33 included patients at the time of MR imaging are displayed in Table 1. Image quality was adequate in all examinations (Figs 2, 3, 4).

**Relationship of Dynamic Contrast enhanced MR Imaging Parameters with Clinical Findings**

**PDAI.** Fourteen patients had clinically active disease, as defined according to a PDAI value of more than 5. No significant differences were observed in dynamic contrast enhanced MR imaging parameters between patients with clinically active disease versus patients with clinically inactive disease. Weak to moderate correlations were found between PDAI and absolute pixel counts of TIC types 2, 3, and 5. The ROI volume also showed a weak to moderate correlation with PDAI (Table 2). $ME$ and $SOE$ calculated for the individual TIC types did not show significant correlations with the PDAI (Table 3).
Figure 2: Dynamic contrast enhanced MR imaging findings in 44-year-old man with transsphincteric fistula. A, Axial oblique fat-saturated T2-weighted fast spinecho image shows perianal fistulising disease. B, TIC shape type map with ROI drawn around the disease as identified on A. In the ROI, many pixels with TIC type 2 are present, but pixels with TIC types 3 and 4 are also observed. C, ME map of the same section. ME of the perianal fistula is higher than that of the surrounding tissue.

Figure 3: Dynamic contrast enhanced MR imaging findings in 48-year-old man with transsphincteric fistula with seton drainage. A, Axial oblique fat-saturated T2-weighted fast spin-echo image shows the perianal fistula track with seton drainage. B, TIC shape type map of the same section. In the perianal fistula, a relatively large number of quickly enhancing pixels (types 3, 4, and 5) are present. C, ME map of the same section. ME of the perianal fistula is higher than that of the surrounding tissue.

Figure 4: Dynamic contrast enhanced MR imaging findings in 53-year-old man with complex infralevatoric transsphincteric fistula. A, Axial oblique fat-saturated T2-weighted fast spinecho image shows the complex perianal fistula with infiltration of the surrounding fat. B, TIC shape type map of the same section. In the perianal fistula, a relatively large number of quickly enhancing pixels of TIC types 4 and 5 are present, but not many pixels of TIC type 3 are. C, ME map of the same section. ME of the perianal fistula tracks is higher than that of the surrounding tissue.
CRP level. Thirteen patients had active disease, as indicated by elevated CRP values. In patients with active disease, the mean \( ME \) was significantly higher than that in patients with inactive disease (\( P = .001 \)). CRP values did not show significant correlations with any of the TIC type counts (Table 2) or with the averaged \( ME \) or \( SOE \) for any of the TIC types. A weak to moderate correlation was seen with the mean \( ME \) (Table 3).

**Correlation with Conventional MR Imaging Findings**

Absolute pixel counts of TIC types 2, 3, 4, and 5 showed weak to moderate correlations with the MR imaging score. The ratio of quickly enhancing pixels versus slowly enhancing pixels was significantly higher in patients with higher MR imaging scores, as was the case with the ROI volume (Table 2). \( ME \) and \( SOE \) calculated for the individual TIC types did not show significant correlations with the MR imaging–based score (Table 3), with the exception of the \( SOE \) of TIC type 2, which showed a negative correlation with the MR imaging–based score of severity.

**Follow-up**

Clinical follow-up data were available for 29 of 33 patients. For four of 33 patients, no follow-up data were available. Mean follow-up was 58 weeks ± 23 (range, 27–97 weeks).

There were no significant differences for any of the dynamic contrast enhanced MR imaging findings between patients who underwent surgery for fistulas (\( n = 8 \)) and patients who did not (\( n = 21 \)). Dynamic contrast enhanced MR imaging findings differed significantly between patients who subsequently had a change in medication during follow-up (\( n = 17 \)) and patients who did not (\( n = 12 \)). The ROI volume was significantly higher in patients with medication changes (\( P = .034 \)). The total pixel counts of TIC types 3 (\( P = .001 \)), 4 (\( P = .043 \)), and 5 (\( P = .001 \)) were higher in patients for whom medication regimens had to be altered, as was the ratio of quickly enhancing versus slowly enhancing pixels (\( P = .021 \)). In six patients, new abscesses developed during follow-up. Significantly higher counts of TIC types 2 (\( P = .026 \)), 3 (\( P = .014 \)), 4 (\( P = .001 \)), and 5 (\( P = .014 \)) were seen in these six patients, and ROI volumes were significantly higher (\( P = .019 \)).

When the dynamic contrast enhanced MR imaging data are approached in a dichotomous manner (i.e., by defining whether an event had occurred), significant differences were seen between the group of patients in which no event was observed (\( n = 8 \)) and the group in which one or more events were observed (\( n = 21 \)); in the latter group, the total pixel count of TIC types 2, 3, and 5 were
significantly higher (P = .041, .011, and .047, respectively). The relative pixel count of TIC type 3 was significantly higher (P = .010).

DISCUSSION
With this study, we found that in patients with elevated CRP values, ME values were higher than in patients with normal CRP values. In more severe disease, as indicated by the PDAI, more quickly enhancing pixels were seen. Quick uptake of gadolinium suggests highly vascularised tissue. The fact that a larger number of pixels with quick enhancement was observed in more severe disease indicates greater vascularity of the inflamed perianal tissue. Because increased vascularity is present only in tissues with active inflammation (17), pixel counts of TIC shape types demonstrating rapid enhancement might be used to identify more severe disease.

This hypothesis is supported by the fact that the absolute counts of pixels with quick enhancement were increased in patients in whom a new abscess developed or in whom medication changes were necessary.

In our study, we analyzed dynamic contrast enhanced MR imaging data in a quantitative manner (ME and SOE) and by looking at the TIC shape type counts on a pixel-by-pixel basis. An advantage of this approach is that the inhomogeneity of the tissue response to contrast medium inflow within the imaged area can be appreciated, since the individual TICs are separately classified. This approach is novel with respect to the standard way of looking at TIC shapes, in which the TICs are first averaged and then classified.

In rheumatoid arthritis, a chronic inflammatory disease of the joints, dynamic contrast enhanced MR imaging findings correlated with histologic and clinical parameters of inflammation (18,19). In the study by Østergaard et al (19), the rate of early enhancement (ie, SOE) correlated with disease activity, whereas in our study the SOE did not significantly correlate with the PDAI, CRP level, or MR imaging–based score of disease severity. In a study by Florie et al (20) in which dynamic MR imaging in luminal CD was investigated, the SOE did not show significant correlations with clinical indexes, which is consistent with our results.

One of the limitations of our study was the fact that we could image only five sections dynamically owing to the high demands on the time resolution. Ideally, dynamic imaging should encompass the entire lesion because perianal CD disease can be extensive. The fact that we could image only a limited number of
sections means that we were not able to analyze the entire diseased area in all patients. Although an observer bias was introduced by this limitation, we tried to compensate for it by using only one section from the original five section data set for our dynamic analysis. To do this, we tried to identify the section with the most extensive and most active inflammation as judged by means of the fat-saturated T2-weighted images. Improvements in MR imaging hardware and software now make it possible to perform dynamic imaging even faster, making dynamic imaging of larger volumes possible. Implementation of a dynamic contrast enhanced MR imaging protocol on a state-of-the-art machine would prevent observer bias by including the entire lesion. Using state-of-the-art hardware and software would also make it possible to include an internal iliac vessel in the dynamically imaged volume to serve as an internal control. This internal control would be beneficial because enhancement curves may be altered by patient dependent variables, such as atherosclerotic disease in the iliac vessels or cardiac output. Use of the arterial input function would obviate any confusion caused by confounding variables, probably making dynamic contrast enhanced MR imaging more accurate. The pixel-by-pixel classification of TIC shapes depends on some arbitrary choices such as noise thresholds and other parameters used for classification (10). The quality of the images in terms of signal-to-noise ratio determines the noise threshold, which determines the amount of analyzed pixels and at the same time the amount of pixels that cannot be appropriately classified (type 7 in our classification). The final results are thus sensitive to the original quality of the MR imaging acquisition.

Although we tried to keep our study population homogeneous by excluding patients without fistulas (eg, with infiltrate), we included patients with only recto- or anovaginal fistulas. Although these fistulas can often be seen in perianal CD, they are usually smaller and less easy to demarcate than are perianal fistulas. In the area around recto- or anovaginal fistulas, strong enhancement of anovaginal septum tissue can be seen because of the high vascularisation of this area. The combination of more difficult demarcation of disease and the strong enhancement of pixels around the disease might have caused some distortion of the data. However, in most patients (n = 29), perianal fistulas and not ano- or rectovaginal fistulas were present, making the effect of the signal enhancement coming from the recto- or anovaginal fistulas less substantial. The fact that there is no ideal reference standard available to determine disease activity in perianal CD was
another limitation of our study. Although the PDAI has been mentioned as the perianal equivalent of the Crohn’s Disease Activity Index (21), it is an index that partly depends on clinical rather than anatomic or inflammatory parameters and thus is partly subject to patients’ perception of disease rather than the anatomic and inflammatory substrate. CRP level is a good indicator of inflammation, but is not specific; high CRP values could indicate active luminal CD and not necessarily perianal activity. By using conventional MR imaging in combination with a dynamic sequence, both anatomic and inflammatory information is provided, making MR imaging a possible single technique for comprehensive evaluation of perianal CD.

In conclusion, dynamic contrast enhanced MR imaging can be used to help determine disease activity in perianal CD. Dynamic contrast enhanced MR imaging findings might be helpful in selecting a subpopulation of patients with perianal CD who should be monitored more closely for development of more extensive disease. Further studies with more patients are needed to clarify the clinical usefulness of dynamic contrast enhanced MR imaging as guidance for the treatment strategy and as a marker of therapeutic response.

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