Evaluation of the predictive value of dynamic MRI in determining treatment response in perianal fistulizing Crohn's disease

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Purpose

1. Perianal fistula is a condition that is reported to occur in up to 38% of patients with Crohn's disease [1]. The detection and evaluation of these fistulas is of utmost importance in planning and evaluating proper therapy. Magnetic Resonance Imaging (MRI) is an effective imaging modality in the evaluation of patients with perianal Crohn’s disease as it can accurately demonstrate localization and extent of disease including clinically undetected fistula or abscess [2,3].

2. A contrast-enhanced fat saturated T1-weighted sequence is recommended for imaging in Crohn's disease as this sequence can be helpful in differentiating between fluid and inflammatory changes; fluid does not enhance after administration of intravenous contrast medium whereas inflammatory tissue does enhance. This marked increase in signal intensity of inflammatory tissue can be seen due to increased tissue perfusion and vascular permeability. Analysis of the time-dependent changes of signal intensity after administration of contrast medium by dynamic contrast-enhanced MRI (DCE-MRI) can add valuable information about disease activity in Crohn's disease as the kinetic of the signal variation reflects the status of tissue microcirculation. An earlier study showed that DCE-MRI can be used to determine disease activity in perianal fistulizing CD [4].

3. Anti-TNF (anti-bodies against tumor necrosis factor, Infliximab) reduces the number of Crohn related fistulas in patients [5]. A few studies using MRI in patients treated with Infliximab showed that patients in clinical remission in fact may have almost unchanged or even more extensive disease. Interpretation of these MRI examinations is subjective and changes may not reflect early changes.

4. The purpose of this study was to determine whether dynamic contrast-enhanced MRI (DCE-MRI) can predict treatment response in patients with perianal Crohn's disease.
Methods and Materials

Study population

Patients with perianal fistulizing Crohn’s disease, who were scheduled to start with anti-TNF therapy (either Infliximab or Adalimumab), were included in this prospective study. All patients gave written informed consent.

All patients had DCE-MRI before starting therapy (baseline), 6 weeks after and 12 weeks after. C-reactive protein and perianal disease activity index (PDAI) were also determined at these time points.

PDAI

This index consists of five items (discharge, pain/restriction of activities, restriction of sexual activity, type of perianal disease and degree of induration) that each are graded on a 5-point Likert scale ranging from no symptoms to severe symptoms. Maximum is 20 points.

PDAI was determined for each patient on the same day as the baseline MRI scan and at 6 weeks and 12 weeks.

MR imaging technique

MR imaging was performed at 3.0 Tesla. Transversal DCE-MRI was performed at 3T during intravenous contrast injection (TE 2.3 ms, TR 5.1 ms, Flip Angle 30°, 15 slices, total duration of dynamic scan 5.05 min, 70 scans per slice, temporal resolution 4.2 sec per volume).

A region of interest (ROI) around the fistula was manually drawn on each slice.

In each ROI, we calculated Average Maximum Enhancement and the slope of the enhancement curve (figure 1).

Statistical analysis

Associations were tested with the chi-square test. Differences between groups were tested with the Mann-Whitney test. Patients were defined as responders if they had a drop in PDAI of 5 points.
Fig. 1: Contrast enhancement curve. Maximum enhancement = (A/B)\text{Initial Slope of increase alpha. TTP = time to peak.}
Results

Six patients (3 males) were included, aged 22-63 years (mean 39 years).

Two patients were responders. There were no significant differences between responders and non-responders in PDAI and CRP at all measured time points.

<table>
<thead>
<tr>
<th></th>
<th>Responders</th>
<th>Non-responders</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>PDAI baseline mean</td>
<td>12 (11-15)</td>
<td>10 (4-15)</td>
<td>0.623</td>
</tr>
<tr>
<td>PDAI 6 weeks mean</td>
<td>10 (10)</td>
<td>10 (4-15)</td>
<td>1.000</td>
</tr>
<tr>
<td>PDAI 12 weeks mean</td>
<td>8 (6-10)</td>
<td>9 (2-14)</td>
<td>0.800</td>
</tr>
<tr>
<td>CRP baseline mean</td>
<td>66 (16-116)</td>
<td>11 (&lt;1-37)</td>
<td>0.267</td>
</tr>
<tr>
<td>CRP 6 weeks mean</td>
<td>2 (2)</td>
<td>6 (&lt;1-20)</td>
<td>0.533</td>
</tr>
<tr>
<td>CRP 12 weeks mean</td>
<td>2 (2)</td>
<td>21 (&lt;1-80)</td>
<td>0.800</td>
</tr>
</tbody>
</table>

**Table 1: PDAI and CRP values of responders and non-responders.**

P-value calculated with Mann-Whitney test

The mean difference (mean drop) in PDAI was 5.0 for responders versus 1.5 for non-responders (p=0.060). No significant differences in DCE-MRI parameters were found between responders and non-responders, although there was a trend that in responders average maximum enhancement was lower at 12 weeks (p=0.052). (see figure 1 for example of DCE-MRI maps)

<table>
<thead>
<tr>
<th></th>
<th>Responders</th>
<th>Non-responders</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope baseline</td>
<td>21 (29-33)</td>
<td>17 (9-32)</td>
<td>0.151</td>
</tr>
<tr>
<td>Slope week 6 mean</td>
<td>21 (20-21)</td>
<td>21 (14-28)</td>
<td>0.991</td>
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<tr>
<td></td>
<td>Week 12 Mean (Range)</td>
<td>Week 6 Mean (Range)</td>
<td>Week 12 Mean (Range)</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>----------------------</td>
<td>---------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Slope</td>
<td>14 (12-17)</td>
<td>25 (14.32)</td>
<td></td>
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<tr>
<td>Maximum enhancement baseline</td>
<td>1.76 (1.73-1.79)</td>
<td>1.91 (1.45-2.33)</td>
<td></td>
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<tr>
<td>Maximum enhancement week 6</td>
<td>1.50 (1.38-1.61)</td>
<td>1.89 (1.25-2.25)</td>
<td></td>
</tr>
<tr>
<td>Maximum enhancement week 12</td>
<td>0.94 (0.73-1.14)</td>
<td>1.52 (1.36-1.71)</td>
<td></td>
</tr>
</tbody>
</table>

*Table 2: Associations of different DCE-MRI parameters. P-value calculated with Chi-square test.*
Fig. 1: Dynamic contrast-enhanced MR imaging findings in a 63-year-old man with Crohn’s disease related complex perianal fistula six weeks after starting Adalimumab. A. Axial oblique fat-saturated T2-weighted fast spin-echo image shows the transsphincteric perianal fistula. B. Maximum enhancement type map of the same section. Maximum enhancement of the perianal fistula is higher than that of the surrounding tissue. C. Slope map of the same section. The fistula shows a steeper slope of enhancement than the surrounding tissue.
Conclusion

Conclusion

Average maximum enhancement at DCE-MRI at 12 weeks might be a good parameter for predicting therapy response of perianal fistulas.

References


Personal Information

Manon Ziech MD, department of radiology, Academic Medical Center, University of Amsterdam, The Netherlands.

contact: m.l.ziech@amc.uva.nl