Magnetic resonance imaging in Crohn’s disease

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SUMMARY

Aim — To evaluate the value of gadolinium enhanced MRI with oral opacification using a 5% mannitol solution (CE-Mannitol-MRI) to reveal bowel inflammation in pediatric patients with known or suspected Crohn’s disease (CD).

Materials and Methods — Sixty-two consecutive children (median age 13.9 years) with known or suspected CD underwent ileocolonoscopy with biopsy, ultrasonography and CE-Mannitol-MRI. CD activity was measured with the Pediatric Crohn’s Disease Activity Index (PCDAI). Image quality, wall thickness, bowel wall enhancement and complications identified on CE-Mannitol-MRI were evaluated by two blinded radiologists.

Results — The sensitivity and specificity of CE-Mannitol-MRI for the diagnosis of CD were 83% and 100%, respectively. Bowel wall enhancement was higher in the group of patients with abnormal small bowel loops versus control group (P = 0.001). In patients with known CD, there was a positive correlation between wall thickness and PCDAI (P = 0.003). However, no significant correlation was demonstrated between partial contrast enhancement and PCDAI (P = 0.497). CE-Mannitol-MRI enabled identification of complications in 18 patients (9 fistulae, 8 strictures and 1 intussusception).

Conclusion — In pediatric patients with CD, CE-Mannitol-MRI contributes significantly to the identification of disease extension, severity and intestinal complications with adequate diagnostic accuracy. This technique could also be useful as the first line diagnostic exploration in young patients with suspected CD.

RÉSUMÉ

Imagerie par résonance magnétique dans la maladie de Crohn

Frank PILLEUL, Claire GODEFROY, Delphine YZEBE-BEZIAT, Frédérique DUGOUGEAT-PILLEUL, Alain LACHAUX, Pierre-Jean VALETTE (Gastroenterol Clin Biol 2005;29:803-808)

Objectif — Évaluer la valeur de l’imagerie par résonance magnétique (IRM) avec injection de Gadolinium et opacification per os de mannitol à 5 % sans entérolyse (entéro-IRM) pour la détection de segments digestifs inflammatoires dans une population présentant une maladie de Crohn (MC) connue ou suspectée.

Méthodes — Ont été inclus 62 jeunes malades consécutifs (âge moyen 13,9 ans) suspects ou suivis pour une MC qui ont eu une iléocoloscopie avec biopsies, une échographie abdominale et une entéro-IRM. L’activité inflammatoire de la maladie de Crohn a été mesurée selon l’index PCDAI. La qualité des images, l’épaisseur pariétale, le rehaussement digestif après injection de gadolinium et les complications identifiées en entéro-IRM ont été évaluées indépendamment par deux radiologues. Les résultats ont été comparés aux données PCDAI, endoscopiques et histologiques.

Résultats — La sensibilité de l’entéro-IRM pour le diagnostic de MC a été de 83 % et sa spécificité de 100 %. Il existait une différence significative entre le rehaussement de l’idion terminal sain et pathologique (P = 0,001). Chez les malades suivis pour MC, il existait une corrélation significative entre l’épaisseur pariétale des segments digestifs atteints et le PCDAI (P = 0,003). En revanche, il n’existait pas de corrélation significative entre le PCDAI et le rehaussement pariétal (P = 0,497). Des complications ont été diagnostiquées en entéro-IRM dans 18 cas (9 fistules, 8 sténoses, 1 invagination iléo-iléale).

Conclusion — L’entéro-IRM identifie l’extension, la sévérité et les complications digestives avec une bonne exactitude diagnostique en cas de MC et semble utile dans l’approche diagnostique de première intention chez les jeunes malades suspects de MC.

Introduction

Crohn’s disease is typically observed in young adults [1], with preferential involvement of the distal small bowel and colon [2]. CD is a discontinuous inflammatory process spreading to the different layers of the intestinal wall and sometimes leading to the development of fistulae, strictures or abscesses. The characteristic histological feature is the presence of giant-cell epithelioid granulomas without caseous necrosis [3]. The combination of clinical, biological, endoscopic, histological and radiological findings [4-9] allows for the diagnosis of CD with certainty. In young patients, the diagnostic approach should enable a positive diagnosis and proper assessment of extension as well as an evaluation of disease activity using minimally invasive investigative methods with limited radiation exposure. Endoscopy with targeted biopsies is indispensable to evaluate changes in the intestinal mucosa but cannot provide transmural analysis nor identify extraluminal complications [10, 11]. Imaging provides complementary data and can be helpful in characterizing lesions in intestinal segments inaccessible to endoscopy and to evaluate possible complications. At the present time, the standard radiographic exploration, based on a barium study with enteroclysis, provides general information on disease localization and extension, but at the cost of radiation and poor patient tolerance. Abdominal ultrasonography with gradual compression is a readily available diagnostic method [12] but unfortunately remains operator-dependent with a poor sensitivity for the diagnosis of complications [13-16]. Currently, most institutions propose computed tomography as the principal imaging method because of its...
accessibility and good spatial resolution which enables the detection and characterization of abnormal intestinal loops [17]. Recent progress in the techniques of magnetic resonance imaging (MRI) now enables exploration of the digestive tract [9, 18-21]. Thanks to these technical improvements, the peristaltic movements are no longer an obstacle to MRI. The excellent contrast resolution of soft tissues, the absence of radiation exposure, the possibility of multiple plane images, and the safety of the contrast agent make MRI an exploration method of choice for bowel investigations. Several reports have demonstrated the feasibility of MRI for digestive tract explorations [18, 22-25]. Like with conventional radiology, correct analysis of the small bowel using MRI requires opacification of the intestinal lumen to distend the digestive structures and improve image analysis. Several oral contrast agents are available [9, 19]. Water is a "negative" agent for T1 weighted images and a "positive" agent for T2-weighted images. Unfortunately rapid absorption before reaching the distal portion of the small bowel is a major drawback [26, 27]. In the present study, we present our experience with MRI imaging of the small bowel using an oral water-soluble hyperosmotic distension agent without enterocolysis for the assessment of Crohn's disease in a young population.

Patients and methods

The main objective of this study was to assess the value of contrast-enhanced mannitol-MRI (CE-Mannitol-MRI) in young patients with known or suspected CD in comparison with clinical, biological, endoscopic, and histological data. We also evaluated inter-observer agreement for CE-Mannitol-MRI readings for the diagnosis and surveillance of CD.

This prospective cross-sectional study of 62 patients was conducted in the digestive radiology unit of the Edouard Herriot Hospital in Lyon France between August 2001 and June 2003. All patients were referred by the hepatogastroenterology unit of the Edouard Herriot Hospital and before undergoing the CE-Mannitol-MRI provided their informed written consent to participate in the study.

The study population was divided into two groups. The first group included patients with suspected CD who underwent radiographic exploration for diagnostic purposes followed by ileo-colonoscopy with selected biopsies. The second group included patients with known CD who underwent radiographic examination to monitor disease status, explore a pseudo-polyp, or evaluate therapeutic efficacy.

CE-mannitol MRI

CE-mannitol MRI was performed with a 1.5 Tesla machine (Siemens, Symphony, Erlange, Germany). After ruling out any contraindication, a one-liter solution of mannitol was administered orally one hour before the examination to distend the intestinal structures. An anti-spasmodic agent (Viscéralgine™) was administered intravenously (after ruling out contraindications) before gadolinium injection to reduce artifacts resulting from intestinal peristalsis. Transverse or coronal images were acquired during a period of apnea 60 seconds after the gadolinium injection (0.3 mL/kg body weight, 2 mL/s). The standardized protocol is summarized in table I.

Endoscopy

Ileo-colonoscopy with systematic biopsies at selected levels was performed shortly before or after CE-mannitol MRI in patients with suspected CD. The patients were given a strict residue-free diet ten days before the endoscopic procedure. The day before endoscopy, the colon was prepared with oral ingestion of polyethylene glycol (Fortrans™ or Colopeg™) (80-100 mL/kg body weight, maximum dose 4 liters) and a water-soluble enema (Dulcolax®). Ileo-colonoscopy was performed under general anesthesia. Biopsies were obtained during ileo-colonoscopy to confirm the diagnosis of CD.

Histology

For patients with suspected CD, the initial endoscopic biopsy material was examined to establish the histological diagnosis. Biopsies were identified by localization in order to assess disease extension and localization. All biopsies obtained during the endoscopic procedure were examined by the pathology unit of the Edouard Herriot Hospital. The same pathologist established the histological diagnosis for all biopsies.

Interobserver agreement between the two radiologists who read the CE-mannitol MRI was assessed with the Kappa coefficient in comparison with the 95% interval of confidence. Agreement was considered satisfactory if the Kappa coefficient was greater than 0.60 and poor if it was less than 0.30.0. Statistical analysis was performed with SPSS software version 10.0 for Windows (SPSS Inc Illinois, USA).

Table 1 – MRI parameters.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>« True FISP »</th>
<th>Flash 2D</th>
<th>Flash 3D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slice thickness (mm)</td>
<td>5</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Number of slices</td>
<td>26-30</td>
<td>26</td>
<td>56</td>
</tr>
<tr>
<td>Inter-slice distance [mm]</td>
<td>0.5</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Matrix (mm)</td>
<td>256*160</td>
<td>256*160</td>
<td>512*512</td>
</tr>
<tr>
<td>TR [ms]</td>
<td>4.9</td>
<td>183</td>
<td>3.7</td>
</tr>
<tr>
<td>TE [ms]</td>
<td>2.3</td>
<td>2.3</td>
<td>1.4</td>
</tr>
<tr>
<td>Tilt angle [°]</td>
<td>80</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Fat saturation</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>

Interobserver agreement between the two radiologists who read the CE-mannitol MRI was assessed with the Kappa coefficient in comparison with the 95% interval of confidence. Agreement was considered satisfactory if the Kappa coefficient was greater than 0.60 and poor if it was less than 0.30.

Statistical analysis

The study population was divided into two groups. The endoscopic and histological results were considered as the gold standard for diagnosis. The descriptive analysis was performed on data from included patients. Quantitative variables were expressed as means, medians and standard deviations. Qualitative variables were expressed as percentages. The diagnostic yield of CE-mannitol MRI was determined for positive diagnosis of CD by estimating its sensitivity and specificity in comparison with the gold standard. Sensitivity and specificity are expressed with the 95% interval of confidence. The Pearson coefficient of correlation for paired variables was used to search for correlations between the PCDAI and wall thickness, the PCDAI and enhancement, and between wall thickness and enhancement. Mean enhancement was compared between healthy and pathological portions of the ileum in patients with CD using Student’s t test for paired variables.

Results

CE-mannitol MRI was performed in fifteen patients in the first group, eight girls and seven boys, with suspected CD based on the radiological and clinical signs.
clinical and biological criteria. Mean age was 12.6 years (range: 8-18) at the time of the CE-mannitol MRI. Mean time between ileo-colonoscopy with biopsy and CE-mannitol MRI was 24.9 days. Characteristic lesions observed at ileo-colonoscopy and confirmed at the histological analysis of the biopsy specimens were in favor of CD in six patients. A giant-cell epithelioid granulomas characteristic of Crohn’s disease was identified in ten biopsies.

The CE-mannitol MRI was considered pathological in five patients, with isolated involvement of the distal ileum in two, ileocolonic involvement in two, and isolated colonic involvement in one. The sensitivity of the CE-mannitol MRI for positive diagnosis of CD was 83% (95CI: 0.63-1.00). The specificity was 100%. Complications - ileocecal fistula, anal fistula, and obstructive inflammatory stricture - were identified in three patients.

In the second group of 47 patients, 24 girls and 23 boys, mean age 14.9 years (range: 8-18), the mean PCDAI was 15.41 at the time of the CE-mannitol MRI (range: 0-47.5, median 12.5). All patients in this group were taking treatment for their CD at the time of the CE-mannitol MRI. Localization of the inflammatory lesions, wall thickness and length of the diseased segments are presented in table II.

Ileo-colonoscopic findings (normal, abnormal) were used to assess the CE-mannitol MRI results (table III). The ileo-colonoscopy was considered normal in 24 patients. For these 24 patients, the CE-mannitol MRI was considered abnormal in 13. Bowel segments considered abnormal at CE-mannitol MRI and explored by ileo-colonoscopy were: the right colon (N = 2), the transverse colon (N = 1), the left colon (N = 4), the sigmoid (N = 3), and the rectum (N = 4). Bowel segments considered abnormal at the CE-mannitol MRI and not explored by ileo-colonoscopy were all located in the ileum (N = 8). The ileo-colonoscopy was considered abnormal in five other patients whose CE-mannitol MRI was considered normal: pancolitis (N = 2), rectosigmoid involvement (N = 2), sigmoid involvement (N = 1).

There was a statistically significant correlation (Spearman coefficient of correlation between PCDAI and wall thickness measured by CE-mannitol MRI True FISP sequence, R = 0.465, P = 0.003 and post-gadolinium T1 sequence, R = 0.411, P = 0.009). No statistically significant correlation was identified between PCDAI and wall enhancement (R = 0.149, P = 0.197).

The correlation (Spearman coefficient of correlation) was not statistically significant between mean wall thickness and wall enhancement (True FISP sequence, R = 0.007, P = 0.965) and post-gadolinium T1 sequence (R = 0.084, P = 0.615).

We also compared post-gadolinium enhancement observed in healthy and pathological portions of the ileum. The mean enhancement of the healthy portion of the terminal ileum was 98 ° 132% compared with 171 ° 132% in the inflammatory ileum (P = 0.001).

Interobserver agreement (Kappa value) for reading the CE-mannitol MRI was 0.85 (95CI: 0.74-0.96) demonstrating excellent agreement between the two radiologists concerning the identification of the pathological bowel segment. CE-mannitol MRI identified 18 complications: 9 fistulae, 4 inflammatory strictures, 4 fibrous strictures, and one ileoileal intussusception. These complications were all confirmed at ultrasonography and/or surgery.

**Discussion**

Our findings demonstrate the performance of CE-mannitol MRI for the diagnosis of CD. We found that the sensitivity and specificity of CE-mannitol MRI for positive diagnosis of CD were 83% and 100% respectively, with excellent interobserver agreement (K = 0.85). This was achieved because of adequate distension of the bowel loops [28]; a collapsed loop can be wrongly considered to be thickened [29, 30]. Proper loop distension can be achieved by enteroclysis [28, 31] with administration of methylcellulose in 1.5-3 liters water (150 mL/min) enabling excellent MRI results [24]. The quality of the images obtained with this method led to much enthusiasm which was tempered by the drawbacks of this technique, i.e., the radiation exposure during fluoroscopy-guided insertion of the nasojejunal tube, the invasive nature of the examination, and considerable patient discomfort. Use of an enteroclysis tube is poorly adapted to a pediatric population and has led to a search for an alternative oral method for opacification [32]. Although several important contrast agents have been developed over the last few years, no one agent has been found to be superior over the others [22, 26, 28, 33, 34]. Water has been found to be an interesting alternative to other contrast agents. After gadolinium injection, the intestinal wall is enhanced and contrasts with the hydrous contents of the intestinal lumen. Unfortunately, use of pure water has its limits and distension of the distal small bowel loops is insufficient in 20-25% of patients [27]. Absorption of water can be reduced by adding osmotic substances (mannitol) or non-resorbable agents (methylcellulose). This latter solution leads to artifacts related to increased peristalsism and can provoke severe diarrhea [21, 33, 35]. A 5% mannitol osmotic solution was tested in volunteer adults and produced significantly superior distension

**Table II – Contrast-enhanced mannitol-MRI findings in a group of 47 patients with Crohn’s disease.**

<table>
<thead>
<tr>
<th>Intestinal segment</th>
<th>number</th>
<th>%</th>
<th>Mean thickness [mm]</th>
<th>Mean length [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>TF</td>
<td>T1post</td>
</tr>
<tr>
<td>Terminal ileum</td>
<td>28</td>
<td>59.6</td>
<td>6.3 ± 1.9</td>
<td>6.1 ± 1.8</td>
</tr>
<tr>
<td>Right colon</td>
<td>6</td>
<td>12.8</td>
<td>6.2 ± 2.2</td>
<td>6.7 ± 1.9</td>
</tr>
<tr>
<td>Transverse colon</td>
<td>2</td>
<td>4.3</td>
<td>4.0 ± 0.9</td>
<td>4.0 ± 0.9</td>
</tr>
<tr>
<td>Left colon</td>
<td>5</td>
<td>10.6</td>
<td>5.7 ± 1.6</td>
<td>5.5 ± 1.2</td>
</tr>
<tr>
<td>Sigmoid</td>
<td>6</td>
<td>12.8</td>
<td>4.7 ± 1.5</td>
<td>5.3 ± 1.5</td>
</tr>
<tr>
<td>Rectum</td>
<td>4</td>
<td>8.5</td>
<td>6.1 ± 2.4</td>
<td>7.4 ± 2.8</td>
</tr>
</tbody>
</table>

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Table III. – Comparison of MRI and ileo-colonoscopy for the evaluation of abnormal bowel loops in 47 patients with Crohn’s disease.

<table>
<thead>
<tr>
<th></th>
<th>CE-mannitol MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pathological</td>
</tr>
<tr>
<td>Pathological</td>
<td>18</td>
</tr>
<tr>
<td>Normal</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>31</td>
</tr>
</tbody>
</table>

compared with water alone [36]. Based on these observations, we established an imaging protocol using an oral solution of 5% mannitol. Our opacification technique enabled us to obtain distention considered excellent in 89% of healthy subjects and which could be sustained for the time of the examination (figure 1). Furthermore, the last ileal loop was collapsed in 72% of patients with CD. Among these patients, 32 had an inflammatory lesion in the last loop with wall thickening which did not allow expansion of the lumen. Overall, only 11% of our patients with CD had a collapsed last loop due to technical deficiency without producing false positives.

In our experience, CE-mannitol MRI is very well tolerated, the patients not report digestive symptoms during the examination.

The combination of fat-saturation sequences with an intraluminal contrast agent and gadolinium injection is crucial for analysis of the intestinal walls [19, 20, 37]. A significant correlation between disease severity and the degree of wall enhancement after gadolinium injection has been demonstrated [20, 38, 39]. There is nevertheless some controversy concerning this correlation between disease severity and enhancement [40, 41]. In our study, PCDAI and wall enhancement were not significantly correlated. This could be due to insufficient statistical power or to intrinsic features of our study population which had a mean PCDAI of 15.4, i.e., clinical remission. None of our patients presented an episode of severely active disease (PCDAI > 50). Another possible explanation could be the fact that 91% of the patients with CD were on treatment which modified the inflammatory response of the diseased segments. Thus treatment could reduce gadolinium delivery to the intestinal walls and thus lessen enhancement [42]. Conversely, there was a significant difference in the percent enhancement between healthy and pathological portions of the ileum (P < 0.001). This is in agreement with data in the literature [43, 44]. We also demonstrated a statistically significant correlation between PCDAI and wall thickness on the different sequences used. It was demonstrated in a population of 30 CD patients (22 with active disease and 8 with inactive disease) that wall thickening of the inflammatory loops was significantly greater than in normal loops but without significant correlation between the clinico-biological index of disease activity and wall thickness data [44]. Other teams have demonstrated significantly decreased wall thickness before and after treatment [43]. The thickness of the intestinal wall observed in CD is a key sign enabling identification of the disease on acquired images; however, in patients in remission, in many cases it simply represents sequelae to prior active disease. Thus it was not surprising to observe a significant correlation between wall thickness and PCDAI. The choice of the MRI sequences is crucial to obtain a good anatomical map of the abdomen necessary to identify pathological loops and extraluminal complications [19, 34, 44-47]. Use of adapted sequences produces a complete map of the intestinal loops (figures 2a and 2b). The contrast between the enhanced wall and the low-intensity signal from the lumen combined with thin slices provides an excellent visualization of extraluminal paths of fistulae materialized by a linear contrast uptake in the mesenteric fat linking two digestive loops.

Our prospective population of 62 pediatric patients including 15 with suspected CD is equivalent in size to other published reports [33, 39]. We did not however have a homogeneous population and none of our patients had severe inflammation (mean PCDAI = 15.4). Furthermore we did not validate the MRI data on wall thickening, parietal hypervascularization, or extramural involvement with a reference technique. We did not consider it acceptable to expose our patients to the radiation dose necessary for an invasive barium study (6.8 Gy/m²) [48] to correlate with our MRI findings since this examination has low sensitivity and specificity for the diagnosis of extraluminal complications [26, 46, 47]. Moreover, it has been demonstrated that CE-mannitol MRI has better sensitivity and specificity than barium study for the diagnosis of loop involvement (95.2% versus 85.4% and 92.6% versus 76.9% respectively) [9].

Half of our patients with a normal ileo-colonoscopy presented pathological CE-mannitol MRI results. A preliminary study on the recently developed video capsule endoscopy has shown its potential as a minimally invasive diagnostic tool in patients with suspected CD not detected with conventional imaging [49].

A measurement bias was found because of the lack of colonic distension. Unlike analysis of the last small bowel loop, the presence of a collapsed colon led to several false negatives. Thus the agreement between CE-mannitol MRI and endoscopy was poor for identifying colonic involvement. It would be interesting to use rectal administration to obtain good colonic distension.

In conclusion, our findings corroborate data in the literature and suggest that CE-mannitol MRI will shortly become an attractive alternative useful for screening, diagnostic and monitoring purposes. At the present time, CE-mannitol MRI is generally considered as an appropriate method for the diagnosis of CD, but several points will have to be clarified before it can be recommended for routine use. The significance of parietal enhancement after intravenous gadolinium injection appears to be...
variable depending on the inflammatory episode and its severity, suggesting that gadolinium enhancement is correlated with disease stage.

REFERENCES


