The value of MRI in assessing parametrial involvement in endometriosis

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Abstract

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Submitted on February 21, 2012; resubmitted on April 23, 2012; accepted on May 11, 2012

STUDY QUESTION: What is the accuracy of magnetic resonance imaging (MRI) in the diagnosis of parametrial endometriosis in comparison with surgicopathological findings?

SUMMARY ANSWER: MRI displayed an accuracy of 96.4% in the preoperative diagnosis of parametrial involvement by deep infiltrating endometriosis (DIE).

WHAT IS KNOWN AND WHAT THIS PAPER ADDS: MRI is the best technique for preoperative mapping of DIE. This preliminary paper shows that T2-weighted MRI is a valuable tool for the preoperative evaluation of parametrial involvement by endometriosis.

DESIGN: A retrospective study of an MRI database was used to identify examinations performed in women, who had a clinical suspicion of pelvic endometriosis (n = 666), between 2005 and 2009 in a university medical centre in France.

PARTICIPANTS AND SETTING: Exclusion criteria were previous surgery for DIE, incomplete surgical evaluation, repeat MRI examinations and incomplete MR protocol. Only symptomatic patients who underwent surgery with a pathological correlation were included (n = 83). An experienced radiologist, blind to the surgical and histological findings, evaluated sagittal, axial and thin-section oblique axial MR images obtained from the 83 patients.

DATA ANALYSIS METHOD: Descriptive statistics and Fisher exact test were used.

MAIN FINDINGS: The prevalence of DIE and parametrial endometriosis was 76/83 (91.6%) and 12/83 (14.5%), respectively. The sensitivity, specificity, positive and negative predictive values, accuracy and positive and negative likelihood ratios for the diagnosis of parametrial endometriosis of low signal intensity on T2-weighted MRI, pelvic wall involvement and ureteral dilatation, were 83.3%, 98.6%, 90.9%, 97.2%, 96.4%, 59.2 and 0.17, 58.3%, 98.6%, 87.5%, 93.3%, 92.8%, 41.4 and 0.42 and 16.7%, 100%, 100%, 87.7%, 88%, infinity and 0.83, respectively, with the patient as the unit of analysis.

BIAS AND LIMITATIONS: The study design was retrospective, and thus prone to bias. Only one experienced reader performed the analysis, so no data are available on intra- or interobserver variability.

GENERALISABILITY: At present, no consensus exists on the optimal MR protocol to be used for the evaluation of DIE, thus limiting the wider implications of this study.

STUDY FUNDING AND COMPETING INTERESTS: No funding was obtained for this study. The authors have no conflict of interest.

Key words: endometriosis / parametrium / magnetic resonance imaging / deep infiltrating endometriosis / pelvic pain
Introduction

Deep infiltrating endometriosis (DIE) is defined as the presence of endometrial implants, fibrosis and muscular hyperplasia penetrating >5 mm into the peritoneum (Koninckx et al., 1991). Various structures can be affected by DIE, including the uterosacral ligaments (USL), rectosigmoid colon, vagina, rectovaginal septum and bladder. Recent studies have suggested that parametrial involvement can also occur, representing a severe form of endometriosis (Ballester et al., 2011a; Ruffo et al., 2011). The preoperative assessment of the parametrium is therefore crucial.

Several studies have demonstrated that physical examination has poor accuracy in detecting the different locations affected by DIE (Koninckx et al., 1996; Chapron et al., 2002; Abrao et al., 2007; Bazot et al., 2009). Little information is therefore available for the evaluation of parametrial involvement in patients with a clinical suspicion of endometriosis (Ballester et al., 2011a,b). In contrast, parametrial involvement in uterine cervical cancer has been extensively evaluated, and the best non-invasive modality for this evaluation appears to be T2-weighted magnetic resonance imaging (MRI) (Hricak et al., 2005, 2007; Mitchell et al., 2006). We recently demonstrated that a combination of thin-section oblique axial T2-weighted MR images and conventional sequences (sagittal and axial) improved the assessment of USL involvement by endometriotic implants. However, our earlier study did not focus on the contribution of this MRI protocol to the detection of parametrial involvement in endometriosis. The aim of the present preliminary study was therefore to define MRI criteria for the diagnosis of parametrial endometriosis and to evaluate their accuracy in comparison with surgicopathological findings.

Materials and Methods

The study was approved by the institutional review board, which waived the requirement for informed patient consent. The MRI database between September 2005 and May 2009 was retrospectively reviewed to identify examinations performed on women who had a clinical suspicion of pelvic endometriosis (n = 666). In this study, only symptomatic patients (i.e. those with chronic pelvic pain, dysmenorrhea, dyspareunia or dyschezia) who underwent surgery with a pathological correlation were included. We excluded women who had undergone previous surgery for DIE (i.e. resection of the USL, rectosigmoid colon or vagina; n = 220); an incomplete evaluation of all deep endometriotic lesions (e.g. frozen pelvis with complete obliteration of the pouch of Douglas, without complete dissection) (n = 17); repeat MRI examinations (n = 60); or the absence of a thin-section oblique T2-weighted Turbo Spin Echo MRI (n = 286).

The final cohort included 83 patients with a mean (SD) age of 34.1 years (7.4 years).

MRI technique

MR images were acquired on a 1.5-Tesla system (GE Healthcare, Milwaukee, USA) with pelvic phased array. All patients received an i.v. injection of an antispasmodic drug (Tiemonium methyl sulphate, 10 mg; Organon, Livron, France) at the onset of the examination to decrease bowel peristalsis.

The protocol always included sagittal, axial and thin-section oblique axial (3 mm-thick and perpendicular to the long axis of the cervix) T2-weighted images.

In addition to T2-weighted MR images, axial and sagittal gradient-echo T1-weighted images with and without fat suppression were acquired. All sequences were performed with anterior and posterior saturation bands placed in such a way that high signal from subcutaneous fat was eliminated.

MRI analysis

A highly experienced radiologistblind as to clinical and ultrasonographic findings retrospectively analysed the MR images. First, the radiologist was asked to determine the presence or absence of pelvic endometriosis (i.e. endometrial cysts, deep pelvic endometriotic locations including USLs, rectosigmoid colon, vagina, rectovaginal septum or bladder). Second, the radiologist was asked to determine the presence or absence of parametrial endometriosis, and its laterality (bilateral, right or left).

In accordance with evaluation methods for the parametrial extension of cervical cancer, MR images were simultaneously reviewed using a review workstation (Advantage Workstation, GE Healthcare, Buc, France). In the setting of pelvic endometriosis, we postulated that parametral endometriosis was present if at least one of the following MRI features was present.

Direct signs of parametrial involvement:

(a) A low-signal-intensity area on T2-weighted MRI, with or without the inclusion of tiny high-signal-intensity spots in the paracervical or paravaginal region (Fig. 1).

(b) Pelvic wall involvement by endometriosis (e.g. a low-signal area on T2-weighted MRI with or without the inclusion of tiny high-signal-intensity spots extending up to the pelvic muscles (piriformis, coccygeus or obturator muscles) (Fig. 2).

Indirect signs of parametrical involvement:

- Unilateral (or bilateral) ureteral dilatation (Fig. 3).

The unilateral/bilateral nature of the involvement was noted. The presence of associated posterior deep endometriotic lesions, including those involving the rectosigmoid colon, vagina or rectovaginal septum, was also noted in accordance with previously described criteria (Kinkel et al., 1999; Bazot et al., 2004; Kataoka et al., 2005).
Surgicopathological findings (the reference standard)

Laparoscopy and laparotomy were performed in 65 (78.3%) and 18 (21.7%) of cases, respectively. All locations of endometriosis were recorded in surgical reports. The surgeons were not blinded to the MRI results. Whatever the results of preoperative MRI, the surgeons performed a complete surgical exploration independent of the results of the MRI.

At surgery, parametrial endometriosis was confirmed when a parametrectomy was performed. During this operative step, the uncrossing manoeuvre was performed after ureterolysis.

During histological analysis, DIE was diagnosed when endometrial tissue (endometrial glands and stroma) was present in resected specimens (Clement, 2002).

Statistical analysis

The goal of this study was to estimate the value of MRI in the diagnosis of parametrial involvement by DIE. Our primary objective was to determine the value of MRI when regarding each patient as a unit of analysis. Our secondary objective was to estimate the value of MRI when regarding each hemipelvis as the unit.

Categorical variables were compared using the Fisher exact test. A $P$-value $<0.05$ was considered statistically significant. The sensitivity, specificity, positive and negative predictive values (PPV and NPV), accuracy and positive and negative likelihood ratios (PLR and NLR) were determined for each MRI criteria in the diagnosis of parametrial endometriosis.

Results

Surgicopathological findings

The mean ($\pm$ SD) interval time between MRI and surgery was 56 days ($\pm$ 54 days).

The prevalence of pelvic and ovarian endometriosis and DIE was 81/83 (97.6%), 46/83 (54.4%) and 76/83 (91.6%), respectively. Only 5/83 patients (6%) had ovarian endometrial cysts without associated deep endometriotic lesions.

USL, vaginal, rectovaginal septum and rectosigmoid colon endometriosis were noted in 69 (83.1%; bilateral: 56, right: 5, left: 8), 23 (27.7%), 8 (9.6%) and 33 patients (39.8%), respectively.

Ureterolysis was performed in 35/83 patients (42.2%; bilateral: 25, right: 3, left: 7).

At surgery, parametrial involvement by endometriotic lesions was noted in 12/83 patients (14.5%), requiring parametrectomy and the uncrossing manoeuvre. The prevalence of bilateral, right and left parametrial endometriosis was 5/83 (6%), 5/83 (6%) and 2/83 (2.4%), respectively.

All patients with parametrial endometriosis had associated DIE in posterior locations (Table 1). There was a significant association between parametrial involvement and rectosigmoid colon endometriosis ($P<0.005$) and vaginal endometriosis ($P = 0.01$).

MRI criteria for the diagnosis of parametrial involvement by DIE

The diagnostic performance of each direct or indirect MRI criterion (paracervical or paravaginal low signal intensity in T2-weighted images, ureteral dilatation, pelvic wall involvement) was evaluated with respect to its correlation with surgical findings. Each patient was considered as a unit of analysis.

For direct criteria of parametral involvement

A low-signal-intensity area in T2-weighted MRI sequences, with or without the inclusion of tiny high-signal-intensity spots in the...
Table 1 Correlation between surgicopathological findings of parametrial endometriosis and other endometriotic locations in patients.

<table>
<thead>
<tr>
<th>Surgical locations</th>
<th>Parametrium + (n = 12)</th>
<th>Parametrium − (n = 71)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometriomas</td>
<td>5 (42%)</td>
<td>41 (58%)</td>
<td>0.35</td>
</tr>
<tr>
<td>DIE</td>
<td>12 (100%)</td>
<td>65 (92%)</td>
<td>0.58</td>
</tr>
<tr>
<td>USL</td>
<td>12 (100%)</td>
<td>58 (82%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Right USL</td>
<td>11 (92%)</td>
<td>52 (73%)</td>
<td>0.27</td>
</tr>
<tr>
<td>Left USL</td>
<td>12 (100%)</td>
<td>53 (75%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Rectosigmoid colon</td>
<td>9 (75%)</td>
<td>24 (34%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Vagina</td>
<td>7 (58%)</td>
<td>17 (24%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Rectovaginal septum</td>
<td>3 (25%)</td>
<td>5 (7%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Ureterolysis (b, r, l)</td>
<td>11 (92%) (5, 5, 1) (42%, 42%, 8%)</td>
<td>23 (32%) (15, 2, 6) (65%, 9%, 26%)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Parametrium+, patients with parametrial involvement detected at surgery; Parametrium −, patients without parametrial involvement detected at surgery; DIE, deep infiltrating endometriosis; USL, uterosacral ligament; b, bilateral; l, left; r, right.

Overall evaluation of MRI for the diagnosis of endometriosis

The association between MRI results and surgicopathological findings in the evaluation of different locations of endometriosis is described in Tables 2 and 3.

Evaluation of parametrial endometriosis with the hemipelvis as the unit of analysis

By MRI, parametrial endometriosis was noted bilaterally, on the right only or on the left only in 5/83 (6%), 4/83 (4.8%) and 2/83 patients (2.4%), respectively.

MRI yielded a diagnosis of right parametral involvement by DIE in 9 of the 83 patients (10.8%). There was one false positive result and two false negative results.

MRI yielded a diagnosis of left parametral involvement by DIE in 7 of the 83 patients (8.4%). There was one false positive result and one false negative result.

Evaluation of endometrial locations and parametrial endometriosis with the patient as the unit of analysis

MRI revealed ovarian endometriosis and DIE in 53/83 (63.9%) and 73/83 patients (87.9%), respectively. Out of 83 patients, 6 (7.2%) had isolated ovarian endometrial cysts.

Parametral involvement by DIE was diagnosed if at least one of the following MRI criteria were present: paracervical or paravaginal low signal intensity in T2-weighted MRI sequences, ureteral dilatation and pelvic wall involvement. MRI revealed parametral involvement by DIE in 11/83 patients (13.3%). There was one false positive result and two false negative results.

Other posterior locations of DIE revealed by MRI were noted (Table 3). In patients with parametral involvement, there was also a significant correlation with rectosigmoid colon (<0.005), vaginal (<0.001) and rectovaginal septum endometriosis (<0.0001).

Discussion

Our preliminary results suggest that MRI can be a valuable tool in the preoperative diagnosis of parametrial involvement by DIE, with an accuracy of 96.4%.

Anatomically, the parametrium consists of connective tissue forming a sheet containing blood vessels, the ureter and the inferior hypogastric plexus, and extending from the lateral surface of the cervix and vagina to the lateral pelvic wall in the frontal plane (Ercoli et al., 2005; Touboul et al., 2008). This structure has been extensively studied with regard to radical hysterectomy performed for early-stage cervical cancer (Yabuki et al., 2005; Hockel, 2007). Recently, a few studies have emphasized the importance of a finding of parametrial involvement by endometriosis in surgical planning for DIE (Ballester et al., 2011a,b). When the subperitoneal space is infiltrated, with parametrial involvement, a parametrectomy with the uncrossing manoeuvre is required for the complete removal of DIE. Hence, the risk of post-operative complications is high. This is firstly linked to ureteral injury causing the possibility of ureteral fistulae and secondly urinary or anorectal dysfunction due to nerve injury being directly correlated with...
the radicality of the operation. Preoperative MRI is thus required to obtain an exact mapping of DIE lesions, allowing the planning of preoperative ureteral stenting in case of ureteral dilatation, and allowing patients to be informed of the possibility of ureteral resection with end-to-end suture or ureteral reimplantation involving the neurogenic bladder, despite plans for nerve-sparing surgery.

T2-weighted MRI sequences are the best sequences for the preoperative staging and evaluation of uterine cervical cancer, especially with respect to its extension to the parametrium (Choi et al., 2004). There is consensus among members of the European Society of Urogenital Radiology (ESUR) that the protocol must include a combination of at least two T2-weighted sequences obtained in the sagittal and oblique planes respectively (Balleyguier et al., 2011), with the oblique images being acquired perpendicular to the long axis of the cervical canal. Even though there is significant variability in the literature regarding MRI protocols used for the evaluation of pelvic endometriosis, T2-weighted MRI sequences are considered the gold-standard technique here as well (Kinkel et al., 1999; Bazot et al., 2004, 2007, 2009; Kataoka et al., 2005; Del Frate et al., 2006; Abrao et al., 2007; Chassang et al., 2010; Saba et al., 2010).

However, until now, most authors have used two orthogonal planes, the sagittal and the axial (Kinkel et al., 1999; Bazot et al., 2004, 2007, 2009; Kataoka et al., 2005; Del Frate et al., 2006; Abrao et al., 2007; Chassang et al., 2010; Saba et al., 2010). We recently demonstrated that thin-section oblique axial T2-weighted imaging improves the efficacy of conventional (sagittal and axial) MRI in assessing USL endometriosis (Bazot et al., 2011). In the current study, we therefore evaluated the value of this MRI protocol in detecting parametrial involvement by DIE.

In the absence of predetermined MRI criteria for the diagnosis of parametrial endometriosis, we postulated that certain features could be used. In uterine cervical cancer, the disruption of the cervical stroma associated with the presence of an intermediate intensity signal within the paracervical or paravaginal region on T2-weighted MRI is highly suggestive of parametrial involvement (Hricak et al., 1988). In addition, pelvic wall involvement or ureteral dilatation by the cervical tumour is also related to distal parametrial involvement. Accordingly, we considered that the presence of a low-signal-intensity area in the paracervical or paravaginal region on T2-weighted MRI or pelvic wall involvement could be a direct criterion suggestive of

<table>
<thead>
<tr>
<th>Table 2</th>
<th>MRI versus surgery for the evaluation of parametrial involvement, analysed by patient and by hemipelvis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI</td>
<td>By patient</td>
</tr>
<tr>
<td></td>
<td>Both parametria</td>
</tr>
<tr>
<td></td>
<td>Sensitivity (CI 0.95) 83.3% (58.2–91.2)</td>
</tr>
<tr>
<td></td>
<td>Specificity (CI 0.95) 98.6% (94.3–99.9)</td>
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<tr>
<td></td>
<td>PPV (CI 0.95) 90.9% (63.5–99.5)</td>
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<tr>
<td></td>
<td>NPV (CI 0.95) 97.2% (93–98.5)</td>
</tr>
<tr>
<td></td>
<td>Accuracy (CI 0.95) 96.4% (89.1–98.7)</td>
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<tr>
<td></td>
<td>PLR (CI 0.95) 59.2 (10.3–1185.9)</td>
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<tr>
<td></td>
<td>NLR (CI 0.95) 0.17 (0.08–0.44)</td>
</tr>
</tbody>
</table>

CI 0.95, 95% confidence interval; MRI, magnetic resonance imaging; PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; NLR, negative likelihood ratio.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Association between MRI findings and surgery in the evaluation of different endometriotic locations.</th>
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<tbody>
<tr>
<td>MRI locations</td>
<td>Surgery</td>
</tr>
<tr>
<td>Endometriomas</td>
<td>5 (42%)</td>
</tr>
<tr>
<td>DIE</td>
<td>11 (92%)</td>
</tr>
<tr>
<td>USL</td>
<td>11 (92%)</td>
</tr>
<tr>
<td>Right USL</td>
<td>11 (92%)</td>
</tr>
<tr>
<td>Left USL</td>
<td>12 (100%)</td>
</tr>
<tr>
<td>Rectosigmoid colon</td>
<td>9 (75%)</td>
</tr>
<tr>
<td>Vagina</td>
<td>6 (50%)</td>
</tr>
<tr>
<td>Rectovaginal septum</td>
<td>5 (42%)</td>
</tr>
</tbody>
</table>

Parametrium+, patients with parametrial involvement detected by MRI. Parametrium−, patients without parametrial involvement detected by MRI. DIE, deep infiltrating endometriosis; USL, uterosacral ligament.
parametrial involvement by DIE. Moreover, ureteral dilatation has been considered as an indirect criterion of parametrial involvement by DIE. In our series, the most sensitive finding (83.3%) was the presence of a low intensity signal in the paracervical or paravaginal area. However, despite low sensitivities, the presence of pelvic wall involvement or ureteral dilatation was highly specific (98.6% and 100%) for the diagnosis of parametrial involvement by DIE. These preliminary results may suggest a possible difference between proximal parametrial involvement characterized by a low-signal-intensity area in the paracervical and paravaginal regions on T2-weighted MR imaging and distal parametrial involvement exhibiting pelvic wall involvement or ureteral dilatation. Further studies are required to demonstrate the clinical relevance for distinguishing these two entities. Using these different criteria, we demonstrated that MRI was sensitive (83.3%) and specific (98.6%) for the overall diagnosis of parametrial involvement by DIE. Interestingly, no difference was observed when considering either the patient or the hemipelvis as the unit of analysis.

In our study, the prevalence of parametrial involvement by DIE was 14.5%. No statistical difference was observed between parametrial locations (i.e. right versus left). Whatever the parametrium affected by DIE, a significant correlation was found at surgery with rectosigmoid colon (<0.005) or vaginal (0.01) endometriosis or extensive ureterolysis with uncrossing manoeuvre during surgery (0.0001). Consistent with the above, a significant association was seen in patients between an MRI finding of parametrial involvement and the rectosigmoid colon (<0.005), vaginal (<0.001) and rectovaginal septum endometriosis (<0.0001). All these results reinforce the value of a preoperative MRI in achieving optimal presurgical mapping.

Some limitations of the study must be underlined. First, the study was based on the retrospective analysis of a limited number of patients with a suspicion of endometriosis. Larger prospective studies are required to validate these preliminary results. Secondly, only one experienced radiologist evaluated the MRI sequences. Under the circumstances, no data are available regarding potential intra- or interobserver variability. Finally, no consensus exists on the optimal MR protocol to be used for the evaluation of DIE. In this study, a thin-section oblique axial T2-weighted MRI was performed in addition to sagittal and axial T2-weighted MRI. An independent evaluation of each specific T2-weighted MRI sequence is required to define the best MR protocol for the evaluation of parametrial endometriosis.

In conclusion, T2-weighted MRI seems to be a valuable tool for the preoperative evaluation of parametrical involvement by DIE. Further studies are needed to evaluate intra- and interobserver variability in the diagnosis of parametrical involvement by DIE using this protocol.

Authors’ roles

All authors took part in the design and implementation of the study, and read and approved the final report. The first and corresponding author (M.B.) has had access to all data in the study and had final responsibility for the decision to submit for publication. The first author also collected and analysed all the data, wrote the paper and performed the statistical analysis. L.J., M.B., C.T. and I.T.N. collected the data from patients and approved the final version of the article. E.D. collected the data from the patients, wrote the paper, and reviewed the final version of the article.

Funding

No specific funding was obtained for this study.

Conflict of interest

None declared.

References


