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Diagnostic accuracy of laparoscopy, magnetic resonance imaging, and histopathologic examination for the detection of endometriosis

Pamela Stratton, M.D.,[a] *Craig Winkel, M.D.,*[b] *Ahalya Premkumar, M.D.,*[c] *Catherine Chow, M.D.,*[c] *Jan Wilson, L.P.N.,*[d] *Rhonda Hearns-Stokes, M.D.,*[a] *Sunyeong Heo, Ph.D.,*[e] *Maria Merino, M.D.,*[f] *and Lynnette K. Nieman, M.D.*[a]

Warren G. Magnusen Clinical Center, National Institutes of Health, Bethesda, Maryland, and Georgetown University Medical Center, Washington, DC

Objective: To evaluate the utility of fat-suppressed magnetic resonance imaging (MRI) in the diagnosis of endometriosis.

Design: A prospective clinical trial.

Setting: A government research hospital.

Patient(s): Forty-eight women with pelvic pain.

Intervention(s): Magnetic resonance imaging followed by surgical excision and pathologic diagnosis of endometriosis.

Main Outcome Measure(s): Presence and extent of endometriosis suggested by preoperative MRIs compared with surgical inspection and biopsy.

Result(s): A preoperative MRI in 46 women detected fewer endometriosis lesions than histopathology or laparoscopy (78 vs. 101 vs. 150). Few MRI lesions correlated with those identified by laparoscopy (50 of 150) or pathology (38 of 101). Of 42 women with surgically diagnosed endometriosis, 28 had at least one corresponding abnormality on MRI, 5 had abnormalities that didn't correlate with surgical findings, and 9 had normal MRIs. The sensitivity of MRI in detecting biopsy-proven endometriosis for any woman was 69% (25 of 36), and the specificity was 75%.

Conclusion(s): Although MRI identifies fewer areas of endometriosis than seen at surgery, it suggested endometriosis in 75% of those with at least mild disease. Only 67% of lesions identified at surgery contained histologic evidence of endometriosis. (Fertil Steril® 2003;79:1078–85. ©2003 by American Society for Reproductive Medicine.)

Key Words: Endometriosis, laparoscopy, MRI, histopathology

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Reprint requests: Pamela Stratton, M.D., PREB/NICHD, Building 10, Room 9D42, Bethesda, Maryland 20892-1583 (FAX: 302-480-6703; E-mail: ps79c@nih.gov).

[a] Pediatric and Reproductive Endocrinology Branch, National Institute of Child Health and Human Development, National Institutes of Health.

[b] Georgetown University.

[c] Department of Radiology, Clinical Center, National Institutes of Health.

[d] Department of Nursing, Clinical Center, National Institutes of Health.

[e] University of Seoul, Seoul, Korea.

[f] Department of Surgical Pathology, National Cancer Institute, National Institutes of Health.

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Pelvic pain associated with endometriosis is difficult to distinguish from that caused by pelvic infection or nongynecologic conditions such as urologic, gastrointestinal, or musculoskeletal diseases. Because each of these conditions require different treatments, accurate diagnosis is important. To date, operative methods are the gold standard to diagnose endometriosis but may be no more reliable than diagnoses based on clinical findings (1). Ultrasound appears to be useful in confirming ovarian endometriomas but is not helpful in detecting small peritoneal lesions (2–4).

Recent studies suggest that the technique of fat suppression used in magnetic resonance imaging (MRI) improves the detection of both endometriomas and peritoneal lesions and may aid in defining the extent and location of disease (5–7). In one study of women with severe disease, MRI was very sensitive, detecting all 27 endometriosis implants of >4 mm in diameter (8). However, in another study of women with all stages of disease, it failed to detect endometriosis in 7 of 27 women, including in two with severe disease (9).

Currently, the diagnosis of endometriosis often is made by surgical inspection without biopsy. However, surgical diagnosis may either overestimate or underestimate the extent of endometriosis because lesions vary in size, color,

depth, and location. For example, black, powder-burn lesions may easily be identified, but subtle red or white lesions may also be endometriosis (10–13). Additionally, lesion depth is difficult to gauge at laparoscopy, even by palpation with a probe, and deep lesions such as those seen with cul-de-sac obliteration may not be recognized. Thus, surgical detection varies and depends on surgical skill (10).

In this study, we hypothesized that preoperative MRI can identify endometriosis but underestimates its extent, whereas lesions identified laparoscopically would overestimate the extent of biopsy-proven disease. To test this hypothesis, we compared the diagnostic accuracy of preoperative MRI to the visual findings at laparoscopy and the histologic evaluation of lesions excised at laparoscopy.

MATERIALS AND METHODS

Preoperative Evaluation

Between January 1999 and November 2000, women were recruited for a randomized, double-blind, placebo-controlled study of surgical excision followed by an innovative medical treatment for endometriosis. The study was approved by the investigational review boards of the National Institute of Child Health and Human Development and Georgetown University and was conducted at the Warren G. Magnusen Clinical Center in Bethesda, Maryland, with surgical procedures performed at the Clinical Center and Georgetown University.

Women aged 18 to 45 years with pelvic pain, who were otherwise in good health, were evaluated to exclude other causes of pain. None had been treated for endometriosis in the last 6 months nor had taken hormonal medication in the last 3 months. The presence of menstrual, coital, and nonmenstrual pelvic pain was confirmed by a standardized questionnaire using a visual analog scale. In addition, women reported pelvic pain at study visits and on daily calendars.

Magnetic Resonance Imaging

Magnetic resonance imaging was performed on a 1.5T magnet (Signa; GE Medical Systems, Milwaukee, WI), using a phased array body or pelvic coil resulting in T1- (fat suppressed) and T2-weighted sequences. Axial and sagittal T2-weighted fast-spin echo images with fat saturation (4300/80-TR/TE; ETL 8) and axial and sagittal T1-weighted spin echo images (500-700/15-18 TR/TE) were obtained with 5-mm-thick contiguous sections. For the last 25 patients, the T1-weighted images were substituted with FMPSPGR sequences (150/4.2/60-TR/TE/flip angle) to shorten the scan time. Axial and sagittal FMPSPGR sequences with fat saturation (TR/TE-150/4.2 flip 60) were repeated after administration of intravenous contrast material (Gadolinium-DTPA, 0.1 mM/kg). All images were obtained with a 35- to 38-cm field of view using a 256 $\times$ 192 matrix.

Two experienced, board-certified radiologists (A.P. and C.C.) analyzed the preoperative magnetic resonance images and recorded a consensus reading of the extent and location of possible endometriosis. The radiologists were aware of the clinical possibility of deep endometriosis in all subjects but did not know the results of surgery, pelvic ultrasound, history, physical exam findings, or histopathology.

Lesions were characterized by signal intensity (high, low, or isodense to adjacent muscle) on unenhanced T1-weighted and T2-weighted sequences and whether they showed enhancement with Gadolinium contrast. An attempt was made to diagnose all implants, including superficial ones. No attempt was made to diagnose adhesions.

Surgery

Laparoscopy was performed by insufflating the abdomen with carbon dioxide through a Verres needle inserted at the umbilicus and then passing a 10-mm trocar into the distended abdominal cavity. When intraabdominal adhesions were expected, an open laparoscopy using a Hassan canula was performed. In most cases, two other incisions were made, one each in the left and right lower abdomen through which 5-mm trocars were passed under direct vision. Next, with the patient in Trendelenberg position, the peritoneal surfaces, reproductive organs, bowel, and appendix were systematically examined for endometriosis and adhesions. The liver, gallbladder, and bowel surface were also inspected for abnormalities.

The surgical team included at least one of two surgeons (P.S., C.W.). An Nd-YAG contact laser with a coated sapphire scalpel (Surgical Laser Technologies, The Oaks, PA) was used at a power setting of 15 watts to excise all lesions. This contact laser system has a penetration depth of $\leq$0.5 mm. All typical (black or white lesions or endometriomas) and subtle (red or clear lesions, or peritoneal defects) endometriotic lesions were excised, and all adhesions were lysed. Hemostasis was secured with bipolar cautery.

During excision of endometriotic lesions, the abnormal area was grasped, and the peritoneum was tented. Normal peritoneum adjacent to the lesion was incised, and the lesion was excised en bloc. Care was taken to identify normal and distorted anatomy to avoid blood vessels, ureters, bowel, and other vital structures. Similarly, peritoneal defects (Allen-Masters window) were inspected for endometriosis and excised en bloc.

Endometriomas were incised, drained, and inspected to exclude tumors. The peritoneal cavity was then suction lavaged to remove all endometrioma debris. Then the pseudocyst wall was teased from the normal ovary, and the base of the pseudocyst was fulgurated with the laser tip or bipolar cautery. If the endometrioma was $>$4 cm, Interceed (Gynecare, Somerville, NJ) was placed around the ovary to prevent adhesions, or a simple stitch was placed to approximate the edges of the ovary and close the ovarian defect.

Adhesions involving the reproductive organs were lysed, except when the bowel was densely adherent to other struc-

tures, as is seen with cul-de-sac obliteration from endometriosis. When endometriosis involved the appendix, a laparoscopic appendectomy was accomplished using an endoscopic gastrointestinal anastomosis (GIA) staple device. Serosal bowel lesions were excised, but intramural endometriotic lesions and dense adhesions of bowel to other pelvic organs were not. Adhesions of the omentum or bowel to the anterior abdominal wall were lysed when located in the same area as the woman's pain.

Characterization of Lesions

We recorded the location, size, depth, and color of each peritoneal lesion; the presence of endometriomas, peritoneal defects, and pelvic adhesions; and whether all lesions were excised. The extent of endometriosis was staged using the American Society for Reproductive Medicine (ASRM) infertility classification system (14). The pelvic locations included the cul-de-sac, uterus, and colon, the right and left side of the bladder and pelvic side walls, and the right and left uterosacral ligaments, ovaries, and their respective ovarian fossa. The superficial extent of lesions was measured at surgery in two dimensions and averaged, and the depth was measured as the deepest portion of the lesion.

The peritoneal lesions were categorized by color, depth, and width. Lesion color was categorized as follows: [1] blue, black, or brown; [2] red or clear; [3] white or yellow; or [4] a mixture of the other categories. For analytic purposes, endometrioma and peritoneal lesion depth was categorized as <0.5 cm, as 0.5 to 1 cm, or as >1 cm. Similarly, lesion width was categorized as <0.5 cm, as 0.5 to 1 cm, as >1 to 2 cm, or as >2 cm. Lesions were categorized as endometriomas, peritoneal defects, deep lesions, superficial lesions, and small lesions. Endometriosis measuring >1 cm below the surface was considered to be deep. Lesions measuring >1 cm but <1 cm deep were considered to be superficial and large. Those of <1 cm in both dimensions were considered to be small.

All excised tissue was examined histologically for confirmation of endometriosis with glands or stroma. Hemosiderin-laden macrophages were not considered sufficient for the diagnosis of endometriosis. For lesions that initially were not diagnosed as endometriosis, three slides from different depths in the block were examined. When multiple biopsies were obtained in any area, if any was positive, the pelvic region was considered positive for endometriosis.

Comparison of Surgical, MRI, and Histologic Findings

Findings at surgery were correlated with histology and MRI using the anatomic regions defined above. Surgeons (C.W. and P.S.) and radiologists (A.P. and K.C.) were unaware of each other's findings. Because of this, only the lesions seen at surgery were biopsied.

The detection of endometriosis by histology was compared with magnetic resonance and laparoscopic findings. For an individual patient, the diagnosis of endometriosis by MRI was considered to be positive when it correlated with at least one biopsy-proven lesion. The histology detection rate for lesions was calculated as the number of lesions with positive histology divided by the number resected at surgery. The histology detection rate for women was calculated as a percentage of the number of women with biopsy-proven endometriosis, divided by the number of women with surgically diagnosed endometriosis.

Similarly, the MRI detection rate for lesions was calculated as the number of lesions detected by MRI, divided by the number of lesions detected at laparoscopy or by histology. The MRI detection rate for women was calculated as the number with findings on MRI divided by the number diagnosed with endometriosis at surgery or by pathology. The sensitivity and specificity of MRI for detection of endometriosis lesions and of individuals with endometriosis was compared with those of pathology using a χ^2 test.

The detection rate of endometriomas and Allen-Masters windows were calculated for MRI and histology. Fisher's exact test or χ^2 test was used to determine whether a certain lesion size, color, or lesion type was related to histologic or MRI detection.

RESULTS

We evaluated 58 women with pelvic pain, aged 20 to 44 years. Three dropped out, and 7 were excluded because they had other causes of pelvic pain ($n = 4$, one with pelvic inflammatory disease, two with fibroids, one with musculoskeletal pain) or did not meet entry criteria ($n = 3$, one with morbid obesity, one with bipolar disorder and history of a major depression on GnRH agonist, and one with untreated depression).

Surgical findings

Forty-eight women had surgery for diagnosis and excision of endometriosis. At surgery, visual inspection led to a diagnosis of endometriosis in 44 women. Six of these did not have endometriosis on histologic examination of excised lesions. By inspection, these women had minimal endometriosis ($n = 5$) or a frozen pelvis with unresectable endometriosis ($n = 1$). Those four women without visually diagnosed endometriosis had adhesions unrelated to endometriosis ($n = 1$), an inguinal hernia ($n = 1$), Crohn's disease ($n = 1$), and a pelvic infection ($n = 1$).

At surgery, most women had minimal or mild disease ($n = 29$) using the ASRM endometriosis classification (Table 1). Overall, 0 to 12 lesions were resected from each woman (4.2 ± 3.1: mean $\pm$ SD). Each woman with minimal endometriosis that was not biopsy proven had lesions removed from two or three pelvic areas (2.4 ± 0.5 lesions). Those with biopsy-proven endometriosis had lesions resected from one to seven pelvic areas (4.0 ± 1.7 lesions). Sixteen endometriomas ranged in size from 1 to 9 cm in diameter, with

TABLE 1

Surgical findings of endometriosis by ASRM stage[a].

Surgical ASRM Stage no.	History	Adhesions	Deep lesions[c]	>5 lesions excised
I (n = 15)[b]	9	1	0	0
II (n = 14)	12	4	6	5
III (n = 8)	8	1	3	3
IV (n = 7)	7	6	7	2

[a] ASRM infertility classification system (14).
[b] n represents the number of patients.
[c] Deep lesions extended >1 cm below the surface.

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six ≤3.0 cm in diameter. None were malignant. Eleven peritoneal defects were excised. Ten women had at least five areas of endometriosis, and 12 women had pelvic adhesions. Of three appendectomies, two appendices had endometriosis, and one had a fecalith.

Of 38 women with a prior surgical diagnosis of endometriosis, 34 had biopsy-proven endometriosis, and 2 had surgical findings of endometriosis but negative biopsies. Of the 10 with pelvic pain without a previous diagnosis of endometriosis, 4 had biopsy-proven endometriosis, and 4 were believed to have endometriosis at surgery but had negative biopsies.

Six women had endometriosis lesions that were not completely resected, including five with dense adhesions of bowel to other pelvic organs and one with an intramural bowel lesion. Three of these five had a prior laparotomy for severe endometriosis. The only surgical complications were cystotomy during excision of endometriosis overlying the bladder (n = 1) and abdominal wall vessel laceration requiring suturing (n = 2), but not a transfusion.

Utility of MRI

Forty-two of 44 women with presumed endometriosis at surgery had a preoperative MRI. The surgical diagnosis of endometriosis was confirmed by biopsy in 36 (86%) of these patients. Magnetic resonance imaging corresponded to at least one lesion found at laparoscopy or biopsy in 28 (67%) of 42 or 25 (69%) of 36 women, respectively (Table 2). Magnetic resonance imaging suggested endometriosis in one woman who did not have endometriosis and in five others whose MRI abnormalities did not correlate with surgical or biopsy findings. Magnetic resonance imaging failed to identify endometriosis in nine women who had endometriosis. The sensitivity of MRI for detecting biopsy-proven endometriosis for an individual woman was 69%, and the specificity was 75%.

Magnetic resonance imaging suggested endometriosis in all patients with severe disease; of these, three had lesions seen on MRI that could not be resected at surgery because these were below the peritoneal surface. Surprisingly, moderate endometriosis (n = 8) was difficult to visualize by MRI, which identified lesions for only three women (38%), whereas most of those with mild endometriosis were detected (12 of 14 women; 86%). The MRI detection rate for women with minimal disease (n =13) was low, compared with that for surgical inspection (46%) or biopsy (50%). Overall, the more extensive endometriosis was at surgery or by histology, the more accurately that MRI suggested endometriosis ($P = .03$ for surgery and $P = .08$ for histology; χ^2 for trend).

One hundred one (67%) of excised lesions were biopsy positive. Endometriomas, deep lesions, and large superficial ones were usually histologically confirmed to be endometriosis. Small lesions and peritoneal defects were less likely to be biopsy positive (Table 3).

Overall, MRI detected fewer lesions than did surgery (78 vs. 150), and only 50 (64%) of these were endometriosis at

TABLE 2

Comparison of surgery, pathology, and MRI diagnosis of endometriosis by ASRM stage.

				MRI findings not correlating with surgical diagnosis (n = 18 of 46)	
Surgical ASRM stage (n = 46)	Biopsy proven (n = 36)	MRI confirms surgery diagnosis (n = 28 of 42)	MRI confirms biopsy diagnosis (n = 25 of 36)	MRI different from surgery or biopsy (n = 6)	No MRI lesion seen (n = 12)
No endometriosis (n = 4)	0	0	0	1	3
Stage I[a] (n = 13)	8	6	4	1	6
Stage II (n = 14)	14	12	12	2	0
Stage III (n = 8)	8	3	3	2	3
Stage IV (n = 7)	6	7	6	0	0

[a] Two women with stage I disease were excluded because they did not have an MRI study.

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TABLE 3

Comparison of surgery, pathology, and MRI diagnosis of endometriosis by lesion type.

	Modality used to establish diagnosis			
Lesion type seen at surgery	Inspection (n = 150)	MRI corresponding to surgery (n = 50)	Histology (n = 101)	MRI corresponding to biopsy (n = 38)
Small[a]	62	14	33	11
Superficial[b]	36	4	29	4
Deep[c]	24	10	20	8
Endometrioma[d]	17	14	13	10
Peritoneal defects[e]	11	8	6	5

[a] Small lesions were <1 cm in diameter and <1 cm deep.
[b] Superficial large lesions measured >1 cm in width but <1 cm in depth.
[c] Deep lesions extended >1 cm below the surface.
[d] Endometriomas were cystic structures, usually of the ovary, filled with chocolate-colored material.
[e] Peritoneal defects had endometriosis lesions seen in the base.

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surgery. Twenty-eight lesions detected by MRI were not biopsied because they were not seen. Compared with the number of surgically observed lesions, MRI identified the same number in only 12 women, fewer in 21, and none in 9. Thus, compared with surgery, MRI depicted less extensive endometriosis.

Magnetic resonance imaging detected most endometriomas (82%, Fig. 1) and peritoneal defects (72%, Fig. 2; Table 3) that were visualized and excised at surgery. Histology detected slightly fewer, but in similar proportions, with 76% of endometriomas and 54% of peritoneal defects detected. Thus, compared with the case of inspection, MRI and histology had similar sensitivity for detecting these lesions ($P = .29$ and $P = .62$, by χ^2, respectively).

Although it is not surprising that small lesions were not seen on MRI, large superficial lesions and those >1 cm deep (Fig. 3) also were identified less commonly by MRI (Table 3). When endometriomas were excluded, no particular color, size, or location correlated with MRI detection, presumably because of the small number of lesions detected. Overall, compared with biopsy results for each lesion, MRI had a diagnostic sensitivity of 38% and a specificity of 74%.

FIGURE 1

Magnetic resonance imaging of an endometrioma (*arrow*) on a T-2–weighted image (**A**) and a Gadolinium-enhanced T-1–weighted image (**B**). (**C**), An endometrioma seen at surgery.

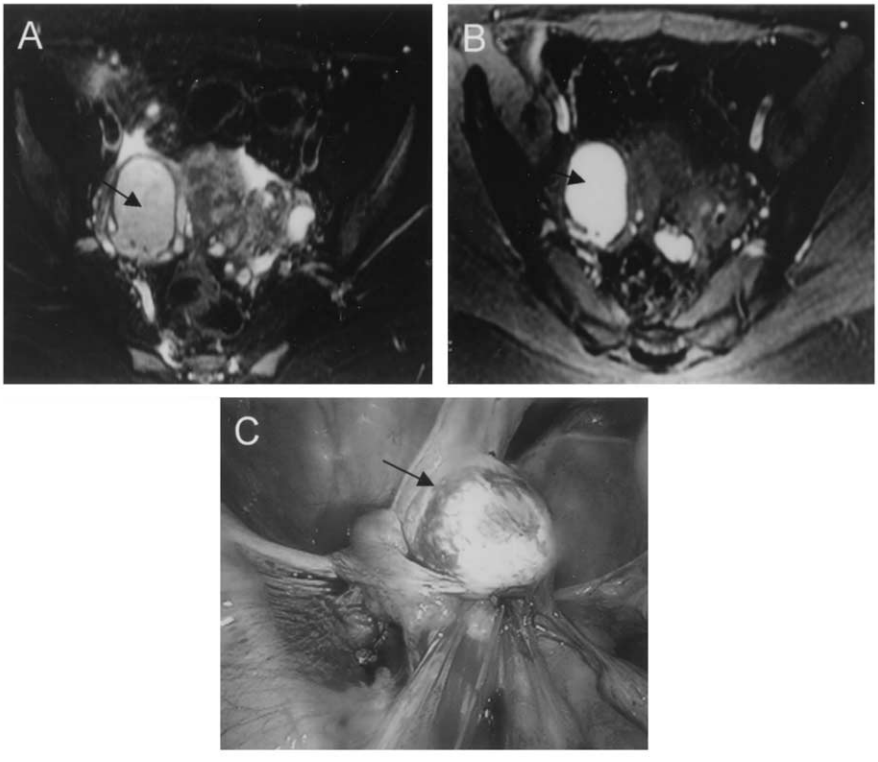

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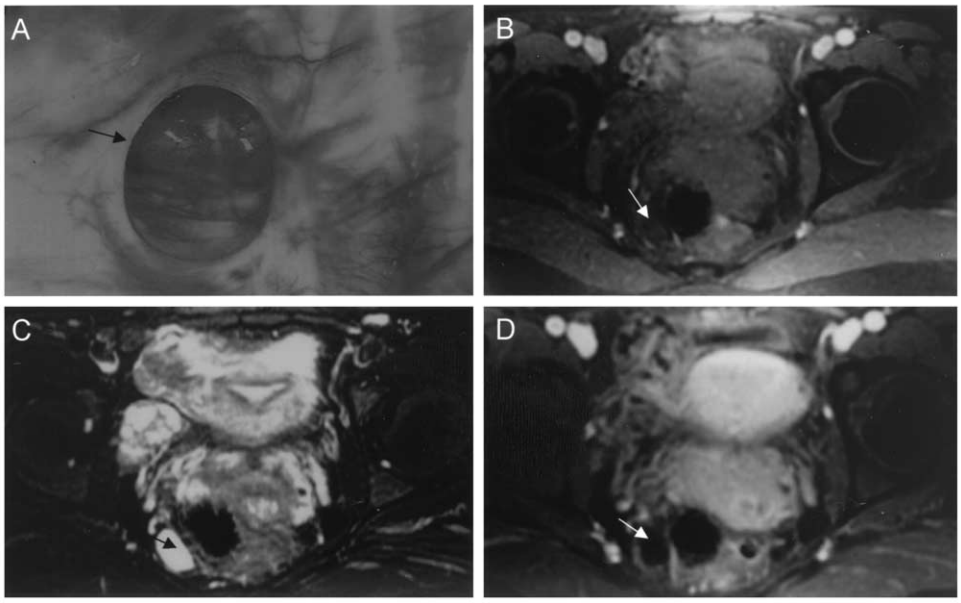
FIGURE 2

A peritoneal defect (*arrow*) seen at surgery (**A**) and T-2–weighted magnetic resonance image (**B**). The peritoneal defect is seen as an area of increased signal because of fluid. Precontrast and postcontrast T-1–weighted magnetic resonance image (**C, D**). No enhancement of the peritoneal defect is seen.



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The most frequent MRI pattern for endometriosis was high signal intensity on T1, low on T2, and nonenhancing after Gadolinium (n = 29) followed by a high signal intensity on T1 and T2 and nonenhancing after Gadolinium (n = 11). Both patterns were common among lesions noted at laparoscopy (20 of 29 and 9 of 11, respectively). Gadolinium enhancement identified nine lesions, of which only four were biopsy-proven endometriosis. Two of these four were seen without enhancement. Endometriomas had mixed patterns (n = 3), were low on T1 and high on T2 (n = 2), or were high on T1 and isodense on T2 (n = 4). The remainder of the lesions had mixed patterns.

DISCUSSION

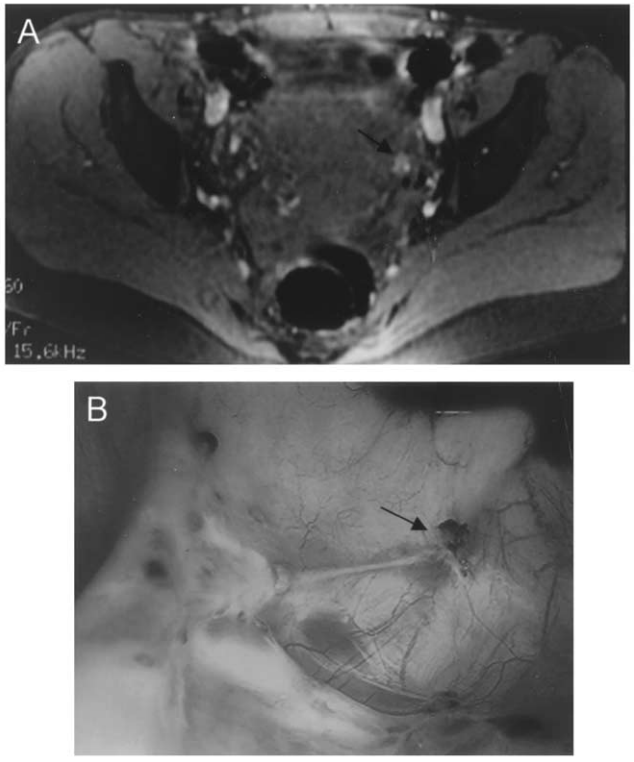
In this study, MRI accurately identified endometriosis in 76% of women with at least stage II endometriosis and correlated with at least one biopsy-proven lesion in 75%. Magnetic resonance imaging was most useful in detecting lesions that were large in three dimensions, such as peritoneal defects or endometriomas, confirming the conclusions of another, smaller study (6). As others have reported, we found evidence of endometriosis in half of the peritoneal defects (15, 16).

Magnetic resonance imaging was relatively insensitive in defining the extent of disease or in identifying peritoneal lesions, even deep or large superficial ones. Mild (stage II) and moderate (stage II) disease often differ only in the number and size of peritoneal lesions. The higher detection rate of mild disease in this study reflects the insensitivity of MRI in detecting peritoneal disease, especially large superficial lesions. On the basis of these preliminary data, MRI appears most useful for the detection of endometriomas, with a diagnostic sensitivity similar to that of ultrasound (2, 3), and was somewhat useful in detecting peritoneal defects. By contrast, MRI appears to have some, albeit limited, utility for detection of other peritoneal lesions that cannot be seen by ultrasound.

In addition to having a reduced ability to predict endometriosis in a given woman, MRI also detected fewer individual endometriosis lesions than did inspection at surgery or biopsy (150 vs. 101 vs. 78), and only half of those were endometriosis at biopsy. Given that there were only 36 women with endometriosis who had a total of 38 lesions identified by MRI, in most cases, only one area identified by MRI per patient was histologically confirmed. Our findings are similar to those of Tanaka et al. (9), in which MRI correctly identified 74% of women with endometriosis, and of Ha et al. (17), who reported a sensitivity of 61% by fat-suppressed MRI. However, these results contrast with those of Takahashi et al. (8), who identified all lesions seen at surgery.

FIGURE 3

A deep peritoneal lesion (*arrow*) was noted on MRI (**A**) and at surgery (**B**).



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One limitation of our surgical approach is that we did not specifically target inspection or surgical excision based on MRI abnormalities. Because we systematically inspected all areas and attempted to excise all visualized lesions, we assumed that we would identify and remove those seen on MRI. We recognized that this approach might decrease the apparent sensitivity of magnetic resonance. We doubt that many visible lesions were missed, given our systematic approach and reports from others that random peritoneal biopsies rarely have endometriosis confirmed by light microscopy (18).

There are a variety of ways that MRI might overestimate or underestimate endometriosis lesions. At times, pelvic fluid obscured tissue borders and reduced visualization, possibly decreasing the ability to detect lesions by magnetic resonance. Also, MRI is not specific for endometriosis, and in some instances, we speculate that uterine vessels or bowel were miscategorized as endometriosis. The use of Gadolinium did not improve detection because it did not enhance most endometriosis lesions. Perhaps the limited sensitivity and specificity of MRI also could be attributed to inherent differences between MRI and laparoscopy. Magnetic resonance imaging provides a series of cross-sectional images at 5-mm intervals, whereas laparoscopy offers a panoramic view of the peritoneal surfaces that are not in the same plane and are seen after distending the abdomen with carbon dioxide.

This study also demonstrates the gap between surgical and histologic identification of endometriosis. In fact, three women had disease that could not easily be excised and thus could not be histologically confirmed; one patient had extensive endometriosis that could not be resected at all, and two others had cul-de-sac disease that could not be biopsied.

In all women, because we wanted to optimize pain relief, when possible, we excised all lesions, including suspicious ones. Many lesions were very small, and several women with minimal endometriosis lesions did not have biopsy-proven disease. Thus, laparoscopically detected endometriosis lesions not confirmed by biopsy may occur in those with minimal disease. However, the fact that those with minimal disease did not have biopsy-proven endometriosis raises the possibility that surgeons who only ablate lesions without biopsying them may overdiagnose and overtreat endometriosis.

What then, is the role for MRI in the detection of endometriosis in a woman with pelvic pain? In women for whom endometriosis is likely after other causes of pelvic pain are excluded, MRI appears to be useful in confirming endometriomas, but not in defining peritoneal lesions or the extent of disease. As it costs less than MRI, ultrasound may be the preferred noninvasive method of confirming endometriomas, although like MRI, it has a low sensitivity for other peritoneal lesions. Because we made a serious attempt to exclude women with other causes of pelvic pain, we do not know the utility of MRI in finding other pathology. A negative MRI study was most likely to occur in someone with minimal endometriosis, yet a negative study did not exclude endometriosis. Thus, given the cost of MRI, when surgical diagnosis and treatment is indicated, magnetic resonance is not a cost-effective diagnostic tool.

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