Systematic Review

Received: 2023-10-28
Accepted: 2023-12-12

BCCR
2023, No 4, Vol 15 :245-258
www.bccrjournal.com

MRI Features of Malignant Transformation of Pelvic Endometriosis: A Systematic Review

Behnaz Moradi[1,2], Masoumeh Gity[1], Sara Hassani[1,3], Mobin Azami[1,4], Maryam Rahmani[1], Fahimeh Azizi Nik[1,2], Arash Khameneh Bagheri[5], Shirin Yaghoobpoor[1,6*], Hamed Ghorani[1*]

1

1. Advanced Diagnostic and Interventional Radiology Research Center(ADIR), Tehran University of Medical Science, Tehran, Iran
2. Department of Radiology, Yas Complex Hospital, Tehran University of Medical Sciences, Tehran, Iran
3. Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania
4. Student Research , Kurdistan University of Medical Sciences, Sanandaj, Iran.
5. Shahid Beheshti University of Medical Sciences, Shohadaye Tajrish Hospital, Tehran, Iran.
6. Student Research Committee, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

*Corresponding authors:
Shirin Yaghoobpoor
Advanced Diagnostic and Interventional Radiology Research Center(ADIR), Tehran University of Medical Science, Tehran, Iran
Student Research Committee, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
sh.yaghoobpoor98@gmail.com

Hamed Ghorani
Advanced Diagnostic and Interventional Radiology Research Center(ADIR), Tehran University of Medical Science, Tehran, Iran
hamedqurani@gmail.com

ABSTRACT

Background: Endometriosis is a benign gynecologic condition that is estrogen-dependent. Malignant transformation is one of the complications of endometriosis; it can affect the woman`s ovarian and extra-ovarian regions. Diagnosing endometriosis-associated cancers has an essential role in treatment.

Purpose: Our study aimed to review magnetic resonance imaging (MRI) features of malignant transformation of pelvic endometriosis.

Material and Methods: We searched three online databases including Web of Science, Scopus, and PubMed, applying relevant keywords up to May 2022. We included English observational studies using MRI for endometriosis patients and comparing the MRI features of malignant pelvic endometriosis with non-malignant ones or studies reporting the MRI features of malignant pelvic endometriosis. Finally, a comprehensive systematic review of the included studies was conducted. The small number of qualifying studies was the most significant limitation. Also, the eligible studies were insufficient for conducting a meta-analysis.

Results: A total of eight papers were included as they matched our inclusion requirements. Eighty-seven individuals were included finally. Studies were published between 1992 and 2021. The larger size of the lesion, loss of T2-weighted images shading, mural nodules, mural nodules contrast enhancement, and mural nodules protruding from the cyst wall at acute angles were the main MRI features suggesting potential malignant transformation of pelvic endometriosis.

Conclusion: The endometriosis›s malignant changes can be observed on MRI. The predominant MRI findings are a large cyst, loss of shading on T2-weighted imaging, mural nodules enhancement, and acutely angled protrusion of mural nodules from the cyst wall.

Keywords: Endometriosis, magnetic resonance imaging (MRI), malignancy, mural nodules

INTRODUCTION:

Endometriosis is a chronic inflammatory gynecologic entity with endometrial glands and stroma outside the uterus; It is an estrogen-dependent condition affecting the reproductive years [1, 2]. Endometriosis affects 190 million women worldwide; 6%–10% of women of reproductive ages and 5% of postmenopausal women [3, 4]. Diagnosis of endometriosis is challenging and highly diverse. Symptoms are dysmenorrhea (60–80%), dyspareunia (40–50%), dysuria (1–2%), and chronic pelvic pain (40–50%); it also can cause infertility (30–50%) [5, 6].

Endometriosis is a benign condition, but it is possible to see some malignant characteristics such as neoangiogenesis, tissue invasion, and spread to organs [7]. Endometriosis-associated neoplasm occurs in almost 1% of women with endometriosis [8]. Ovarian and extra-ovarian cancers such as endometrial, breast, and colorectal cancer, non-Hodgkin lymphoma, and others can be associated with endometriosis [9, 10]. Endometriosis-associated ovarian cancer happens in 0.6%–0.8% and is 10–20 years younger than the typical population [11, 12].

Diagnosis is based on clinical findings, serum markers, pathological features, and imaging. In some cases, hemosiderin-laden macrophages with chocolate-colored hemorrhagic demonstrate endometrial cancers [13]. Imaging techniques like ultrasonography, CT scan, and magnetic resonance imaging (MRI) are essential in finding endometriosis-associated neoplasm and providing correct work-up and treatment [14, 15]. Previous studies [16-18] have reported MRI features of malignant endometriosis; however, no systematic review was conducted to investigate these features. Detecting MRI findings suggesting the malignant transformation of endometriosis can potentially result in an earlier diagnosis of malignancy and subsequently better management and outcomes for the patients.

Only a limited percentage of endometriotic lesions (2.5%), often those in the ovaries (75%), develop malignant transformation [19]. Since Sampson et al. [20] first identified some women with malignant transformation of endometriosis, gynecologic oncologists and pathologists have recognized a potential malignant entity in endometriotic lesions, which should be evaluated [16, 20]. In the current systematic review study, we systematically reviewed the reported magnetic resonance imaging (MRI) characteristics indicating the malignant transformation of pelvic endometriosis.

Methods:

Search strategy and screening

One author (M.A.) performed a comprehensive literature search in three online databases of PubMed, Scopus, and Web of Science up to May 2022. The applied keywords in the search strategy were as follows: ("Neoplasms" OR "Tumor" OR "Neoplasm" OR "Tumors" OR "Neoplasia" OR "Neoplasias" OR "Cancer" OR "Cancers" OR "Malignant Neoplasm" OR "Malignancies" OR "Malignancy" OR "Malignant Neoplasms" OR "Benign Neoplasm" OR "Benign Neoplasms") AND ("pelvic" OR "Pelvis" OR "Pelvic Region") AND ("Endometriosis" OR "Endometrioses" OR "Endometrioma" OR "Endometriomas") AND ("MRI" OR "NMR Imaging" OR "MR Tomography" OR "NMR Tomography" OR "steady state free precession mri" OR "steady state free precession mri" OR "Zeugmatography" OR "Chemical Shift Imagings" OR "Chemical Shift Imaging" OR "Magnetic Resonance Image" OR "Magnetic Resonance Images" OR "Magnetization Transfer Contrast Imaging" OR "MRI Scans" OR "MRI Scan" OR "Proton Spin Tomography" OR "fMRI" OR "Functional MRI" OR "Functional MRIs" OR "Functional Magnetic Resonance Imaging" OR "Spin Echo Imaging"). Also, we reviewed the reference list of the related articles to find further eligible studies.

Inclusion and exclusion criteria

We used the following inclusion parameters: 1) observational studies, such as cohort, cross-sectional, case series, and case reports; 2) studies on endometriosis patients; 3) research that used MRI on endometriosis patients; and 4) studies that compared MRI features of malignant pelvic endometriosis with non-malignant

ones or studies reporting the MRI features of malignant pelvic endometriosis. We excluded review, editorial, and commentary publications, non-English studies, animal studies, studies using imaging modalities other than MRI, and those which did not assess malignant endometriosis.

We removed the duplicate studies using the title of the published articles, their authors, and year of publication using Endnote software, version 9. Considering the inclusion criteria, the remaining papers were reviewed and assessed based on their title, abstract, and full text. Two authors (M.A. and Sh.Y.) performed title-abstract and full-text screening independently. A third author (S.H.) eventually resolved the disagreements between them.

Data extraction

Two authors (MA and Sh. Y.) extracted the following data in a structured form: study population, mean age, physical examination/ history, malignancy type, duration of disease, tumor marker, MRI method or contrast, clue findings of malignancy transformation, and clue findings of malignancy transformation on MRI.

Quality assessment

One author (Sh. Y.) assessed the quality of the included studies by conducting a critical appraisal of all included studies. We applied the Newcastle-Ottawa scale (NOS) checklists for cross-sectional studies. Also, we used the Joanna Briggs Institute (JBI) index to evaluate the case reports. (supplementary tables 1 and 2)

This study was approved by the Iranian National Committee for Ethics in Biomedical Sciences (Code of Ethics: IR.TUMS.IKHC.REC.1401.116).

Results:

Study selection

We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses for this systematic review (PRISMA).

Through using our search query, a total of 459 articles were identified for screening. After the removal of duplicates, 342 articles remained. After title-abstract screening and full-text screening, eight studies were included in our systematic review (Figure 1).

Study characteristics

Eight studies were included, from which five were case reports. All studies were published from 1992 to 2021 and conducted in China, France, the UK, the USA, and Japan. The included studies contained 87 individuals, 54 cases with malignant lesions (49 in cohort studies and five in case studies), and 26 controls (with benign lesions). The individuals' mean age was 41.9 years; those with benign lesions ranged from 25 to 57, and those with malignant lesions from 26 to 63. We assessed differences in cysts size, mural nodules size, multilocularity, the existence of shading, the signal intensities of mural nodules, shape and protruding angles of nodules, and the presence of contrast enhancement were evaluated between the malignant and benign lesions. (Tables 1 and 2).

Size of the lesions

In a study by Siegelman et al., the masses' short-axis dimensions ranged from 1 to 5 cm [17]. In a study by Tanaka et al. in 2000, the control group's mean endometrioma diameter was 5.0 cm. In comparison, that of the endometriomas with malignant transformation was 9.4 cm [16]. Also, in another study by Tanaka et al. in 2010, the mean cyst diameter was significantly higher in malignant lesions than in benign ones (11.2 cm versus 7.8 cm, respectively, $p<0.05$) [18].

T1 and T2 signal intensity of lesions

Eight of 10 masses in Tanaka et al.'s study in 2000 displayed T1 low signal intensity and T2 high signal intensity (approaching that of fluid) [16]. In the study by Siegelman et al., only two cases with malignant lesions had distinctive benign endometrioma characteristics (high in T1 and intermediate in T2), which were present in all control groups [17]. Finally, in the study by Tanaka et al. in 2010, only 11 of the 33 malignant cysts had shading visible on T2-weighted images, compared to 13 of the 16 benign cysts [18].

Mural nodules

In the study by Tanaka et al. in 2000, all endometrial

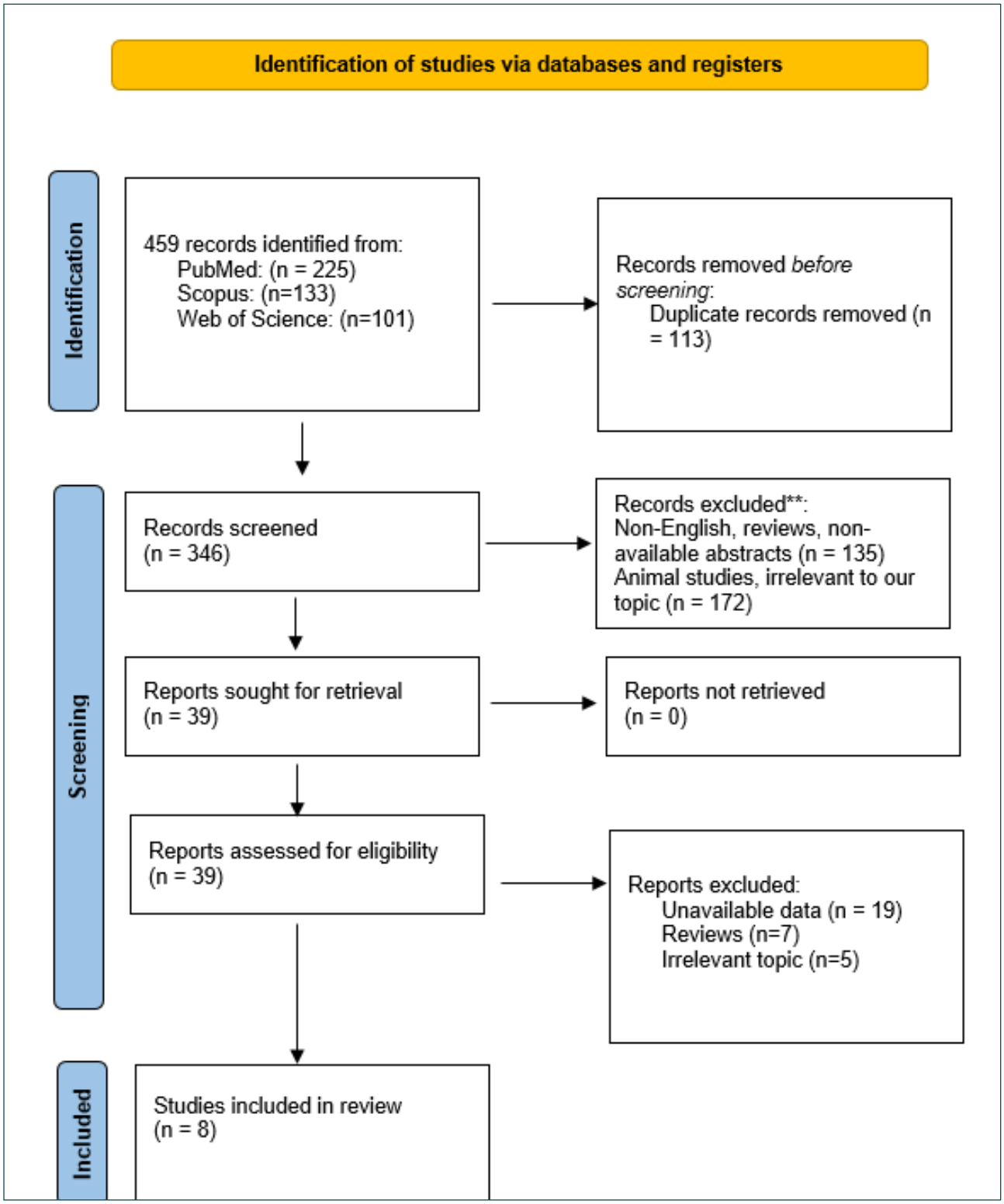

Figure 1. PRISMA flow diagram

cysts with malignant transformation had one or more visible mural nodules. None of the benign contralateral cysts in the malignant cases had mural nodules. Only three of the ten endometriomas in the control group had non-enhancing mural nodules. In contrast, the mural nodularity in the control cases varied from 0.6 to 1.5 cm. The mural nodules in the malignant lesions ranged from 2.0 to 6.5 cm [16]. In Tanaka et al.'s study (2010), the average mural nodule diameter ranged from 0.4 to 2.3 cm for benign lesions and from 1.0 to 8.7 cm for malignant lesions. Additionally, the malignant group's significance was statistically higher [18].

The malignant group mural nodules had a lower signal on T1-weighted images than the myometrium [16]. In Tanaka et al.'s study in 2010, using T1-weighted imaging, nine of 16 patients with benign mural nodules and 24 of 33 patients with malignant mural nodules displayed low signals. Mural nodules in nine of the 16 malignant lesions and 18 of 33 benign lesions showed high signals on T2 weighted imaging [18]. In the benign group of Tanaka et al.'s study 2000, two patients' nodules protruded from the cyst wall at an acute angle and one at an obtuse angle. In the malignant group, the nodules in nine patients protruded from the cyst wall at an acute angle, while in one patient, they did so at an obtuse angle [16]. Seven of the sixteen benign masses exhibited enhancing mural nodules, although all but one malignant lesion did not. Eight high T2 signal-intensity masses displayed substantial contrast enhancement compared to muscle. Mural nodule contrast enhancement was seen in 97% of malignant and 44% of benign tumours [17, 18].

Enhancing mural nodules were also seen in all five reviewed case reports of endometriosis-related malignancies [21-25].

The findings of the case studies are demonstrated in detail in Table 1.

Discussion:

In the current study, we systematically reviewed the reported MRI characteristics indicating the malignant transformation of pelvic endometriosis. According to our systematic review, the cyst's larger size, mural nodules, the loss of shading on T2 images, contrast enhancement of mural nodules, and mural nodules that protrude from the cyst wall at acute angles were the main MRI characteristics potentially indicating malignant transformation.

The most typical site of endometriosis is the adnexa. Endometriotic cysts, also known as endometriomas, are localized types of endometriosis in the ovary. Endometriomas can be single or numerous, unilateral or bilateral in approximately 50% of cases. The specificity of MRI in detecting endometriomas is more than 90%. They are cysts with thick walls and blood components associated with cyclic bleeding. Because of the subacute hemorrhage and high levels of protein content, endometriomas usually display T1 shortening. Also, due to the iron and protein accumulation resulting from repeated bleeding, they show a T2 shading [17, 26]. For identifying endometriomas, T2 shading has high sensitivity (93%) but low specificity (45%), and it occasionally appears in other hemorrhagic lesions of adnex. In such circumstances, looking for the T2 dark spot sign, appearing as small, typically several foci of extremely low signal strength on T2-weighted images inside the cyst but not inside its wall may be helpful. It may be possible to distinguish endometriomas from other functional hemorrhagic diseases using this T2 dark spot sign, which are strongly predictive of long-standing haemorrhage and may indicate persistent retracted clots [27]. Also, because of hemosiderin-laden macrophages inside the lesion's wall, a peripheral rim with low signal intensity T2 is another distinguishing characteristic of endometrioma in MRI [28]. Also, fluid levels may be visible on T2 due to recent bleeding, which shows a low signal intensity.

Several extra-ovarian locations have been linked to the malignant endometriosis progression, including round and broad ligament serosal surfaces, the uterus, the vagina, the cul-de-sac, intraperitoneal pelvic sidewall, intestinal wall, and postpartum surgical scars [29, 30]. According to Brooks et al.'s review of the literature related to malignancies associated with extragonadal endometriosis, the most common site of rectovaginal

involvement with (36%) and the least involved in about 4% is associated with the fallopian tube, cervix, navel, pelvic ligaments, and other cases, respectively, related to the vagina (7%) bladder (9%), colorectal sites (11%) [30]. This distribution resembles additional ovarian endometriosis implants in general. About 25% of endometriosis-related cancers develop outside the ovary [11, 29, 31].

Concurrent endometriosis must be found during surgery or histopathologic examination for a conclusive diagnosis. Histologic evidence of extrauterine endometrial glands and stroma, along with fibrosis and inflammation, in surgically removed lesions, are necessary for a definitive diagnosis of endometriosis [32]. Regarding imaging for endometriosis surveillance, neither precise data nor generally approved consensus recommendations are currently available. However, when surgical endometriosis treatment is considered, MR imaging is frequently used [33]. MR imaging in this scenario outlines a route that enables the surgeon to shorten procedure time and reduce the possibility of missing lesions, mainly when a laparoscopic technique is employed. Due to the rarity of endometriosis-associated ovarian malignancies and the tests' limited diagnostic sensitivity, it is not recommended to routinely screen endometriosis-affected women for ovarian cancer using serum marker assays (e.g., CA125, HE4) or imaging [15]. On T1- and T2-weighted images, malignancies in extra ovarian endometriosis often appear as solid lesions with moderate signal strength. When the gadolinium-based contrast material is administered, these pelvic lesions typically improve and exhibit constrained diffusion. When a lesion like this is discovered in a woman who has already been diagnosed with endometriosis or when an MR image reveals both an endometriosis-like lesion and a lesion with malignant characteristics, endometriosis-associated malignancy should be suspected [34, 35]. Endometriosis-associated ovarian Carcinoma (EAOC) patients typically occur earlier in life (Approximately 10–20 years younger than individuals with other subtypes of epithelial ovarian cancer), with a lower grade of illness, an earlier stage of disease, so as a result, with a significantly increased overall survival rate [36, 37].

The MR imaging findings of endometrioma contain numerous cysts, high signal intensity on T1 images, and shading on T2-weighted images [38]. Although the MR scans do not show this, solid vascularized masses of endometriosis are not rare [39]. A well-known pathologic characteristic of lesions is prominent fibrosis, especially in those that affect the bladder and bowel walls. Ectopic endometrial tissue can develop in organs outside the pelvis, a condition known as extra pelvic endometriosis. Nearly all other distant human organs, including the lungs, brain, urinary system, gastrointestinal tract, central nervous system, and abdominal wall, have been described as having it. The presence of an enhancing mural nodule on MR imaging is the most accurate sign of endometrioma malignancy [18, 36]. Other helpful but less accurate indicators of malignant degeneration include an interval increase in the cyst's size, a mural nodule diameter of more than 3 cm, and the absence of T2 shading in the endometriosis cyst [16, 18]. Predictable enhancing mural nodules were seen in all five case reports of endometriosis-related malignancies when imaging findings, particularly MRI, were evaluated [21-25]. In a study by Song et al. [25] using Diffusion-weighted imaging (DWI), DWI limitation was found to be the hallmark of malignancy in high-grade serous carcinoma from rectal endometriosis. The absence of the typical T2 shading, the increase in the serial size of the masses, and other findings indicating malignancy, such as tumor invasion of the adjacent bone and bone destruction, as well as a periosteal reaction, are additional imaging findings in this series that are in favor of malignancy [21]. In Wang et al. study, the thickened liver capsular enhancement may be noticed [22]. On T1-weighted images compatible with hemorrhage, all lesions detected in patients in the trials, as mentioned earlier, had punctate foci of high signal intensity. In every instance, adding contrast material to the lesions proved they were solid masses of vascularized tissue. Therefore, unlike many endometriomas, these lesions do not exhibit T2-weighted low signal intensity due to hemoglobin degradation. These lesions had abundant thick fibrosis intermingled with stroma, tiny

endometrial glands, and large amounts of fibrosis. There was little hemosiderin deposition. They contend that solid endometrial implants should produce imaging results comparable to the endometrium. This study demonstrates the importance of MR findings of pelvic endometriosis is more comprehensive than in previous studies. This study suggests that internal punctate foci of high signal on T1-weighted images consistent with bleeding and solid peritoneal pelvic masses with signal intensity compatible with fibrosis should not result in the diagnosis of ovarian carcinoma. Malignant pelvic tumors can also exhibit these features, despite the T2-weighted low signal intensity of the fibrotic masses being unusual for malignant ovarian tumors. In conclusion, the range of MR results in endometriosis includes solid enhancing masses. Such lesions, especially in the cul-de-sac or posterior bladder, are not always symptomatic of peritoneal metastases in patients with confirmed or suspected endometriosis [21-25].

According to our review, loss of T2 shading and contrast-enhanced mural nodules were among the MRI features indicating the malignant transformation of endometriomas. Consistently, Bourgioti et al. [19] reported that typical MRI features of endometriotic lesions with malignant transformation are the existence of solid components inside the endometriotic cyst, which typically appears as contrast-enhanced mural nodules, enlargement of the cyst on serial follow-up, thick internal septa (more than 3 mm), or loss of the T2 shading sign caused by tumor secretions. The most frequent subtypes of extra-adnexal endometriotic malignancy are endometrioid or clear cell carcinomas (CCCs), which develop in an existing endometrioid cyst. Compared to women who acquire ovarian cancer without any history of endometriosis, females with endometriosis-associated ovarian cancer are at least 10 to 20 years younger and possess a better prognosis. Secondary features like the presence of peritoneal nodules or ascites frequently demonstrate malignancy. Although CA-125 blood levels can also be increased in benign endometriosis, it is typically significantly higher in cases with malignant transformation. Tumor markers such as CA-125 may help differentiate malignant and non-malignant endometriomas [17, 26, 40].

We highlighted that contrast enhancement of mural nodules and mural nodules that protrude from the cyst wall at acute angles were MRI features pointing to malignant transformation of endometriotic lesions. Also, Saba et al., in a review study [41], demonstrated that endometriosis' malignant transformation is unusual, and the classic MRI feature is observing an enhancing mural nodule on the T1 gadolinium-enhanced sequence [16]. Endometrioma with malignant transformation might be exhibited by a loss of T2 shading due to hemorrhagic fluid dilution by tumor secretion [16]. Particular attention should be paid to the MR images following the administration of contrast since it can be a significant indicator of malignant transformation. When asymmetric signal intensity is observed on contrast-enhanced fat-saturated imaging, it should not be mistaken as a focus of endometriosis, and parametric involvement should be considered [42]. However, preoperative endometriosis expansion has been shown even without applying contrast material [42]. Thus, according to Saba et al. [41], solid components, septations, and a size bigger than expected for an endometrioma are indicators of malignancy. In addition, lesions greater than 15 cm, which have wall nodules, must be sampled to exclude cancer.

In pregnant women, decidualized endometriosis can mimic ovarian cancer. In pregnancy, elevated levels of progesterone stimulate the endometrial stromal cells' hypertrophy and the development of the vascular decidual lining of the uterine. Endometrial stromal cells in the endometriomas can also produce vascular mural nodules in response to the hormonal alterations of pregnancy. Decidualized endometriosis mimics ovarian cancer on ultrasonography (US) and MRI [43-47]. The T2 hyperintensity of mural nodules and isointense relative to the thickened decidualized endometrium may be characteristic of decidualized endometriosis on MRI. It is shown that after pregnancy termination or childbirth, decidualized endometriosis either cures or reverts to endometriomas without complications [48, 49].

In our study, there were various limitations. The small number of qualifying studies was the most significant limitation. Due to the lack of cohorts, case-control, or cross-sectional studies, we also included case studies. Also, the eligible studies were insufficient for conducting a meta-analysis.

In conclusion, Larger cyst size, loss of shading on T2 images, mural nodules, or enhancement of mural nodules in contrast phase, and mural nodules protruding from the cyst wall at acute angles were the main MRI features reported in endometriotic lesions with malignant transformations. Further comprehensive research assessing MRI in the follow-up of endometriosis patients is required to conduct statistical analysis and show sensitive and specific MRI features of malignant transformation of endometriotic lesions.

References:

1. Vercellini P, Viganò P, Somigliana E, et al. Endometriosis: pathogenesis and treatment. Nat Rev Endoe crinol 2014;10:261-275.
2. Burney RO, Giudice LC. Pathogenesis and pathophysiology of endometriosis. Fertil Steril 2012;98:511-519.
3. Kvaskoff M,1 Mahamat-Saleh Y, Farland LV, et al. Endometriosis and cancer: a systematic review and meta-analysis. HumReprodUpdate2021;27:393-420.
4. Eskenazi B, Warner ML. Epidemiology of endometriosis. Obstet Gynecol Clin N Am 1997;24:235-258.
5. Bulletti C, Coccia ME, Battistoni S, et al. Endometriosis and infertility. J Assist Reprod Genet 2010;27:441-447.
6. Parasar P, Ozcan P, Terry KL. Endometriosis: epidemiology, diagnosis and clinical management. Curr Obstet Gynecol 2017;6:34-41.
7. Neto JS, Kho RM, dos Santos Siufi DF, et al, histologic, and molecular changes associated with endometriosis and ovarian cancer. J Minim Invasive Gynecol 2014;21:55-63.
8. Koninckx PR, Muyldermans M, Moerman P, et al. CA 125 concentrations in ovarian 'chocolate'cyst fluid can differentiate an endometriotic cyst from a cystic corpus luteum. Hum Reprod 1992;7:1314-1317.
9. Munksgaard PS, Blaakaer J. The association between endometriosis and ovarian cancer: a review of histological, genetic and molecular alterations. Gynecol Oncol 2012;124:164-169.
10. Kok VC, Tsai H-J, Su C-F, et al. The risks for ovarian, endometrial, breast, colorectal, and other cancers in women with newly diagnosed endometriosis or adenomyosis: a population-based study. Int J Gynecol Cancer 2015;25:1.
11. Heaps JM, Nieberg RK, Berek JS. Malignant neoplasms arising in endometriosis. Obstet Gynecol 1990;75:1023-1028.
12. Scully RE, Richardson GS, Barlow JF. The development of malignancy in endometriosis. Clin Obstet Gynecol 1966;9:384-411.
13. Scully RE, Barlow JF. "Mesonephroma" of ovary. Tumor of müllerian nature related to the endometrioid carcinoma. Cancer 1967;20:1405-1417.
14. Leiserowitz GS, Gumbs JL, Oi R, et al. Endometriosis-related malignancies. Int J Gynecol Cancer 2003;13:1.
15. McDermott S, Oei TN, Iyer VR, et al. MR imaging of malignancies arising in endometriomas and extraovarian endometriosis. Radiographics 2012;32:845-863.
16. Tanaka YO, Yoshizako T, Nishida M, et al. Ovarian carcinoma in patients with endometriosis: MR imaging findings. AJR 2000;175:1423-1430.
17. Siegelman ES, Outwater E, Wang T, et al. Solid pelvic masses caused by endometriosis: MR imaging features. AJR 1994;163:357-361.
18. Tanaka YO, Okada S, Yagi T, et al. MRI of endometriotic cysts in association with ovarian carcinoma. AJR 2010;194:355-361.
19. Bourgioti C, Preza O, Panourgias E, et al. MR imaging of endometriosis: Spectrum of disease. Diagn Interv Imaging 2017;98:751-767.
20. Sampson JA. Endometrial carcinoma of the ovary, arising in endometrial tissue in that organ. Arch Surg 1925;10:1-72.
21. Stringfellow JM, Hawnaur JM. CT and MRI ap-

pearances of sarcomatous change in chronic pelvic endometriosis. Brit J Radiol 1998;71:90-93.
22. Wang D, Yang Q, Wang H, et al. Malignant transformation of hepatic endometriosis: a case report and literature review. BMC women's health. 2021;21:1-7.
23. Matsubara S, Kawahara N, Horie A, et al. Magnetic resonance relaxometry improves the accuracy of conventional MRI in the diagnosis of endometriosis-associated ovarian cancer: A case report. Mol Clin Oncol 2019;11:296-300.
24. N'Senda P, Wendum D, Balladur P, et al. Adenosarcoma arising in hepatic endometriosis. Eur Radiol 2000;10:1287-1289.
25. Song L, Xing A, Li Q, et al. High-Grade Serous Carcinoma Resulting From Rectal Endometriosis and Complicated With Ovarian Cancer. Front Oncol 2019;9:1252.
26. Grasso RF, Del Vescovo R, Cazzato RL, et al. Pelvic endometriosis: A mr pictorial review. endometriosis-basic concepts and current research trends InTech Open Access Publisher. 2012:447-458.
27. Corwin MT, Gerscovich EO, Lamba R, et al. Differentiation of ovarian endometriomas from hemorrhagic cysts at MR imaging: utility of the T2 dark spot sign. Radiology 2014;271:126-132.
28. Woodward PJ, Sohaey R, Mezzetti TP, et al: radiologic-pathologic correlation. Radiographics 2001;21:193-216; questionnaire 88-94.
29. Benoit L, Arnould L, Cheynel N, et al. Malignant extraovarian endometriosis: a review. EJSO 2006;32:6-11.
30. Brooks JJ, Wheeler JE. Malignancy arising in extragonadal endometriosis. A case report and summary of the world literature. Cancer 1977;40:3065-3073.
31. Modesitt SC, Tortolero-Luna G, Robinson JB, et al. Ovarian and extraovarian endometriosis-associated cancer. Obstet Gynecol 2002;100:788-795.
32. Clement PB. The pathology of endometriosis: a survey of the many faces of a common disease emphasizing diagnostic pitfalls and unusual and newly appreciated aspects. Adv Anat Pathol 2007;14:241-260.
33. Chamié LP, Blasbalg R, Gonçalves MO, et al. Accuracy of magnetic resonance imaging for diagnosis and preoperative assessment of deeply infiltrating endometriosis. Int J Gynaecol Obstet 2009;106:198-201.
34. Sala E, Rockall A, Rangarajan D, et al. The role of dynamic contrast-enhanced and diffusion weighted magnetic resonance imaging in the female pelvis. Eur J Radiol 2010;76:367-385.
35. Coutinho AC, Krishnaraj A, Pires CE, et al. Pelvic applications of diffusion magnetic resonance images. Magn Reson Imaging Clin 2011;19:133-157.
36. Takeuchi M, Matsuzaki K, Uehara H, et al. Malignant transformation of pelvic endometriosis: MR imaging findings and pathologic correlation. Radiographics 2006;26:407-417.
37. Eržen M, Rakar S, Klančar B, et al. Endometriosis-associated ovarian carcinoma (EAOC): an entity distinct from other ovarian carcinomas as suggested by a nested case-control study. Gynecol Oncol 2001;83:100-108.
38. Nyberg DA, Porter BA, Olds MO, et al. MR imaging of hemorrhagic adnexal masses. JCAT 1987;11:664-669.
39. Ja S. Perforating hemorrhagic (chocolate) cysts of the ovary; Their importance and specially their relation to pelvic adenomas of the endometrorial type. Arch Surg 1921;3:245-323.
40. Choudhary S, Fasih N, Papadatos D, et al. Unusual imaging appearances of endometriosis. AJR 2009;192:1632-1644.
41. Saba L, Sulcis R, Melis GB, et al. Endometriosis: the role of magnetic resonance imaging. Acta Radiol 2015;56:355-367.
42. Del Frate C, Girometti R, Pittino M, et al. Deep retroperitoneal pelvic endometriosis: MR imaging appearance with laparoscopic correlation. Radiographics 2006;26:1705-1718.
43. Iwamoto H, Suzuki M, Watanabe N, et al. Case study of a pregnant woman with decidualized ovarian endometriosis whose preoperative findings suggested malignant transformation. Eur J Gynaecol Oncol 2006;27:301-303.
44. Sammour RN, Leibovitz Z, Shapiro I, et al. De-

cidualization of ovarian endometriosis during pregnancy mimicking malignancy. J Ultrasound Med 2005;24:1289-1294.
45. Machida S, Matsubara S, Ohwada M, et al. Decidualization of ovarian endometriosis during pregnancy mimicking malignancy: report of three cases with a literature review. Gynecol Obstet Invest 2008;66:241-247.
46. Miyakoshi K, Tanaka M, Gabionza D, et al. Decidualized ovarian endometriosis mimicking malignancy. AJR 1998;171:1625-1626.
47. Yoshida S, Onogi A, Shigetomi H, et al. Two cases of pregnant women with ovarian endometrioma mimicking a malignant ovarian tumor. J Clin Ultrasound 2008;36:512-516.
48. Barbieri M, Somigliana E, Oneda S, et al. Decidualized ovarian endometriosis in pregnancy: a challenging diagnostic entity. Hum Reprod 2009;24:1818-1824.
49. Takeuchi M, Matsuzaki K, Nishitani H. Magnetic resonance manifestations of decidualized endometriomas during pregnancy. J Comput Assist Tomogr 2008;32:353-355.
50. Stringfellow JM, Hawnaur JM. CT and MRI appearances of sarcomatous change in chronic pelvic endometriosis. Brit J Radiol 1998;71:90-93.
51. Song L, Xing A, Li Q, Wang G. High-Grade Serous Carcinoma Resulting From Rectal Endometriosis and Complicated With Ovarian Cancer. Front Oncol 2019;9.
52. Matsubara S, Kawahara N, Horie A, et al. Magnetic resonance relaxometry improves the accuracy of conventional MRI in the diagnosis of endometriosis-associated ovarian cancer: A case report. Mol Clin Oncol 2019;11:296-300.

Author / Country (Year)	Age (years)	Physical examination	Malignancy type	Tumor markers	Transformation time malignancy	Pathology	MRI Findings	Other imaging findings	Clue findings of malignancy transformation	Clue findings of malignancy transformation in MRI
Stringfellow et al/ UK (1998)(50)	52	palpable mass in the right iliac fossa with tenderness and fullness in the right vaginal fornix due to right DVT dyspnea due to multi-infarct pulmonary emboli and	Pelvic Adenosarcoma arising from primary endometriosi	-	6years	glandular elements in a malignant stroma, consistent with adenosa-rcoma	Axial T1 weighted (SE) : multiloculated pelvic mass)With a mass involving obturator internus mixed signal intensity, predominantly isointense with muscle but containing several hyperintense areas with a crescent of very high signal posteriorly, representing hemorrhage Coronal T2 weighted SE: intermediate to high intensity with a complex internal structure STIR: suppression in the hyperintense focus consistent with hemorrhage Additional findings: • subcutaneous edema due to venous stasis • indistinction of right acetabulum and iliac wing cortex, indicating marrow infiltration or edema		• Right ilium bone destruction, periosteal reaction • Lack of response to hormonal manipulation	• Enlarging mass in the serial imaging • Solid component in the imagingfindings
Song et al/ China (2019)(51)	63	abdominal distension	high-grade serous carcinoma arising from rectal endometriosis+ complicated with bilateral high grade serous ovarian carcinoma +	CA125 258.32	1	high-grade rectal serous carcinoma positive for estrogen receptor(ER)	solid, cystic, irregular, and space-occupying lesions with unclear boundaries • T1 weighted (SE) : equal signals • T2 weighted :high signal intensity • DWI: high signal intensity in solid component • heterogeneous enhancement in solid component • irregularity between the lesion and adjacent structures • increased rectal wall thickness •	US: • the left posterior aspect of the uterus increased in size owing to the presence of a solid cystic mass 12 cm in diameter, of irregular shape, and with unclear boundaries • circulation signals in The solid part • fine dot echo in the cystic part • enlarged left ovary adenomyoma and adenomyosis, • mass in the left posterior aspect of the uterus • ascites	• bloody fluid in the pelvic cavity during surgery • thickened omentum • mass adhesion to the left peritoneum suspicion of peritoneal invasion • papillary protrusions in the inner layer of the cystic component	• DWI: high signal intensity in the solid component • heterogeneous enhancement in the solid component

Wang et al/ China (2021)(22)	50	recurrent right upper quadrant abdominal pain with progressive aggravation (right upper quadrant tenderness without any palpable masses)	endometrioid adenocarcinoma in the liver originating from preexisting hepatic endometriosis	CA 19-9 (112 U/mL)	4years	highly- to moderately-diferentiated endometrioid adenocarcinoma in the liver, pleomorphic nuclei and a high nucleus/cytoplasm ratio, arranged in a glandular or sieve pattern surrounded by proliferative fibrous tissue ,strongly positive for ER,PR,vimentin paired-box gene -	• T1- (Fig. 1E) and T2- weighted: increased signal • T2-spectral presaturation attenuated inversion recovery (SPAIR) sequence: No change indicating hemorrhagy within the mass. • thickened right liver lobe capsule with enhancement	Contrast-enhanced (CT) scan • an ill-defined, hypodense mass of 10.7×7.7 cm in the right liver lobe extending to the diaphragm with moderate enhancement in the periphery during the arterial phase	• thickened right liver lobe capsule with enhancement (MRI) • an ill-defined, hypodense mass with diaphragm invasion and moderate enhancement (CT) • large complicated mass in the left liver lobe with Multiple nodules on the diaphragm, densely adhered to the surface of the liver(Laparatomy)	• thickened right liver lobe capsule with enhancement • T2-spectral presaturation attenuated inversion recovery (SPAIR) sequence: No change indicating hemorrhagy within the mass.
Matsubara et al/ Japan (2019)(52)	42	mild cyclic pelvic pain	right endometriosis-associated ovarian cancer	CA 125 (50.4 U/ml) CA 19-9 (26.1 U/ml)	4years	(clear cell carcinoma) of right ovary hepatocyte nuclear factor-1β suggested clear cell carcinoma	• T1 and T2weighted :high signal intensity – suggestive of subacute intra-cystic hemorrhage • bilateral multilocular solid-cystic masses suggestive of mural nodules • heterogeneous enhancement in the solid component on the post-contrast • increased vascularity in the right adnexal mass • MR relaxometry identified an R2 value of 7.98 s-1 in the right cyst, which suggested a malignant transformation of OE	TVS: • a multilocular cystic mass with a size of ~64x52 mm in the right ovary • one cystic mass with a size of ~42x24 mm in the left ovary • solid mural nodules in the right adnexa with diameters of 12 mm	• solid mural nodules in the right adnexa with diameters of 12 mm in the TVS	• bilateral intracystic mural nodules • heterogeneous enhancement in the solid component on the post-contrast • increased vascularity in the right adnexal mass bilateral intracystic mural nodules
N'Senda et al/ France (2000)(24)	54	right-sided epigastric pain with hard palpable mass and tenderness in the right hypochondra	Liver Adenosarcoma arising from liver implant endometriosis	CA19-9 and CA15-3 3-4fold ULN	6years	fibrosis and small clusters of endometniotic glandular tissue, solid mass of glandular endometniosis and surrounding fibrosis	• T1 AND T2weighted : heterogeneous mass+ high signal intensity infavor of hemorrhagy • Cystic changes with fluid fluid levels • T1+CE:Marked heterogenicity in the mass+ high signal intensity	CT: • huge heterogenous hypodens mass with partially enhancement • Cystic changes with fluid fluid levels	• Partial enhancement in the solid component (CT) • Huge mass with diaphragm adhesion (Laparatomy)	• T1+CE:Marked heterogenicity in the mass+ high signal intensity

Table 1: Characteristics and main findings of endometriosis associated malignancy (Case report studies)

Author / Country (Year)	Study population		Age (mean)		Physical examination /history	Malignancy type	Duration (year)	Tumor Marker	Unilateral /Bilateral		Method/ Contrast	Pathology	MRI Finding	Clue findings of malignancy transformation	Clue findings of malignancy transformation on MRI
	Malignant	Benign	Malignant	Benign					Malignant	Benign					
Tanaka et al/ Japan (2000)(16)	10	10	43	38	asymptomatic (4) lower abdominal pain (2) cystitis (2) irregular menstruation (1) dysuria (1)	Ovarian carcinoma (Ia in two patients, Ic in three, IIa in one, Iic in two, and IIIc in two)	2.5	CA125(8of 9) CA19-9(5of9)	Uni=4 Bi=6	Uni=6 Bi=4	Malignant Axial Gyroscan 1.5-T superconducting magnet (5), Signa 1.5-T superconducting magnet (3), 1.0-T superconducting magnet (2) + Axial T1-weighted spin-echo (TR range/ TE range, 320–543/11–15) and axial T2-weighted spin-echo (1200–3000/80–90) or fast spin-echo (1836–4000/88–110) images were obtained in all + Contrast-enhanced T1-weighted axial images with 5 mmol of meglumine gadopentetate (Magnevist; were also obtained in all	clear cell adenocarcinoma:6 endometrioid adeno- carcinoma:2 mixed adenocarcinoma:2	1. the unilocular or multilocular endometrial cysts 2. Adnexal masses with characteristics of endometrial cysts, including a thick capsule or adhesion to adjacent structures 3. On T1-weighted images, 29 of 30 endometrioma in both groups of patients showed significantly higher signal intensity than myometrium; the remaining endometrioma with malignant transformation showed slightly higher signal intensity compared with that of the myometrium 4.Intracystic Mural Nodul	1.Cyst Size The sizes of unilateral endometrial cysts with associated cancers were larger than those of contralateral endometrial cysts in five patients and smaller in one patient of six with bilateral lesions 2. Cyst Size with moral nodul In the control group, the size of endometrial cysts with mural nodules on sonography was at least five times larger than that of contralateral endometrial cysts in two patients, the size was larger but less than five times the size in one patient, and the size was smaller in one of four patients with bilateral disease	1.significantly higher signal intensity than myometrium at T1 2. High signal intensity on T1- weighted images and low signal intensity on T2-weighted images relative to the myometrium 4.Mural Nodul None of the benign contralateral cysts had mural nodules. One or several mural nodules were observed in all the endometrial cysts complicated with cancer 5.Mural Nodule T1 Contrast enhancement 6. Mural Nodule protrusion with acute angle The nodules protruded from the cyst wall with an acute angle in nine patients and with an obtuse angle in one. Conversely, the
											Benign Axial one of two 1.5-T superconducting units (Signa [n = 1] or Gyroscan [n = 9]) with the same technique as that for the malignant + T1-weighted im- ages (n = 12); fat-saturated T1-weighted images (n = 4); dynamic contrast-enhanced images (n = 6); or dynamic subtraction contrast-enhanced images (n = 5)				

Tanaka et al/ Japan (2010)(18)	33	16	44	36	adnexal masses	Ovarian carcinoma (Ia in eight, Ib in two, Ic in six, IIc in three, IIIa in one, and IIIc in nine)	1		Uni=12 Bi=21	Uni=7 Bi=9	Axial 1.5-T superconducting units (Gyroscan, Philips Health-care) Axial T1-weighted images, T2- weighted images, and fat-saturated T1-weighted images/ 5 mmol of gadope-ntetate dimeglumine	Benign: Mucinous cystadenoma: 1 Endometriosis with inflammation: 1 Pure endometriosis: 14	Malignant: Serous: 2 Mucinous 1 Endometrioid :1 Serous: 5 Clear cell: 8 Endometrioid: 11 Mixed: 3 Undifferentiated Carcinoma: 1 Adenosarcoma:1	1. the unilocular or multilocular endometrial cysts 2. 4.Intracystic Mural Nodul On T1-weighted images, the malignant mural nodules showed high signal in two patients, intermediate signal in seven, and low signal in 24, whereas the benign mural nodules showed signal in three, four, and 9 4.All but one malignant lesion had enhancing mural nodules, but there were seven benign masses with enhancing mural nodule	1.older patients The mean age of the patients with a benign condition was 36 years (range, 25–57 years), whereas that of patients with a malignant condition was 44 years 2.larger cysts siza: The mean maximum cyst diameter was 7.8 cm (range, 3.2–14.2 cm) in the benign group and 11.2 cm (range, 4.0–19.2 cm) in the malignant group 3.Bilateral vs Unilateral Disease was unilateral in seven of the 16 benign cases and 12 of the 33 malignant	1.Atypical endometrioma featuring(Non T2 shading in malignant cases) Thirteen of the 16 benign cysts showed shading on T2-weighted images, whereas shading was seen in only 11 of the 33 malignant cysts 2.Larger Mural noduls The mean maximum diameter of the mural nodules was 1.2 cm (range, 0.4–2.3 cm) in benign and 4.3 cm in malignant lesion 3.Enhancing Mural Noduls All but one malignant lesion had enhancing mural nodules, but there were seven benign masses with enhancing mural nodule
Siegelman et al/USA (1994)(17)	6 (8 masses)	7	38-46	38-46	pelvic pain, painful defecation	solid masses (4 in the cul-de-sac at or above the vaginal fornix, 2 in bladder wall, and 2 In rectal wall and pararectal fat)	2		Uni=11 Bi=2	Uni=11 Bi=2	1 .5-T four-coil phased-array (multicoil) system of receiver coils T1- and T2-weighted SE imaging. Axial T1-weighted SE images T2- weighted images were obtained in axial, coronal, and sagittal planes by using fast spin-echo (FSE) sequence / gadopentetate dime-glumine	high-grade serous carcinoma Strong WT-1-positive staining of tumor cells +glandular endometniosis and surrounding fibrosis. (five masses showed fibrosis, variable amounts of endometriotic glandular tissue, little hemorrhage, and scant hemosiderin deposition)		1.Solid masses from endometriosis were found in six (46%) of 13 patients who had multicoil MR imaging 2.Seven solid masses had similar MR imaging findings: predominant signal intensity approximating that of muscle on both T1- and T2-weighted SE images and enhancement by both qualitative and quantitative criteria 3.All lesions showed small internal foci of high signal intensity on the T1 -weighted images. These foci showed low signal intensity similar to that of the rest of the lesion on the T2-weighted FSE images. 4.All but one (Fig. 2) of the lesions had spiculated outer margins with infiltration into the surrounding pelvic fat 5.An eighth mass (Fig. 3) had low signal intensity on Ti -weighted SE images and high signal intensity (approaching that of fluid) on T2-weighted FSE 6.This tissue with high signal intensity nonetheless showed intense contrast enhancement when compared with 7.In addition to the solid masses, three of the six patients had MR findings typical of endometriotic Cysts involving the ovaries: lesions with high signal intensity on Ti -weighted SE images and relatively low signal intensity on T2-weighted FSE images.		1. spiculated outer margins with infiltration All but one of the lesions had spiculated outer margins with infiltration into the surrounding pelvic fat 2.An eighth mass had low signal intensity on T1 -weighted SE images and high signal intensity (approaching that of fluid) on T2-weighted FSE 3.Contrast Enhancement This tissue with high signal intensity nonetheless showed intense contrast enhancement

Table 2: Characteristics of endometriosis associated malignancy (Other studies)