

# Cloverleaf Sign in Pelvic Magnetic Resonance Imaging for Deep Infiltrating Endometriosis

## Association With Longer Operation Times, Greater Blood Loss, and Higher Rates of Bowel Resection

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**Objectives:** The aim of this study was to evaluate the significance of a new imaging sign, the “cloverleaf sign,” in diagnosing deep infiltrating endometriosis (DIE) with magnetic resonance imaging (MRI) in concordance to intraoperative findings.

**Materials and Methods:** This retrospective study included 103 patients operated during the January 2016 to June 2018 period with preoperative 1.5 T and 3 T MRI, with or without vaginal and rectal gel filling. Magnetic resonance imaging scans were read blinded to intraoperative findings by a specialized gynecologic radiologist and a junior radiologist, and then compared with intraoperative findings by looking at the operation report, postoperative diagnosis, and intraoperative images and videos by an experienced gynecologist surgeon specialized in endometriosis surgery. All endometriosis lesions were confirmed by pathology. The “cloverleaf sign” was defined as a cloverleaf-like figure in imaging morphology; the “leaves” formed by at least 3 different organs come together in the center of the figure formed by constrictive adhesions including T2-weighted (T2W) hypointense DIE. Operation times, intraoperative blood loss, and the frequency of DIE and bowel resections were analyzed in cloverleaf and noncloverleaf groups. The 2-sample Wilcoxon rank-sum (Mann-Whitney *U*) test and multivariate analysis of variance were used to calculate the significance of an overall impact of cloverleaf sign on operation time, blood loss, and the amount of the bowel resection rate.  $P < 0.05$  was considered statistically significant.

**Results:** The prevalence of DIE in the study population was 79.6%. A total of 11.5% of the patients had no endometriosis, 32.6% had rASRM I and II, and 55.9% had rASRM III and IV. Forty-six patients (45%) had received rectal and vaginal gel opacification before scanning, 57 (55%) did not. A cloverleaf sign on MRI was detected in 34 patients (15 in gel filling and 19 in nonfilling group). The interreader agreement was almost perfect 0.91 ( $\kappa$ ). The median operation time in the cloverleaf group was 248 minutes (interquartile range [IQR], 165–330) compared with 145 minutes in the noncloverleaf group (IQR, 90–210), that is, significantly higher ( $P < 0.001$ ). Intraoperative blood loss was also significantly higher in the conglomerate group (125 vs 50 mL; IQR, 100–300 vs 50–100;  $P < 0.001$ ). Of the bowel resections in our study population, 41% (14/34) were performed on patients with a cloverleaf sign in the MRI, compared with 13% (9/69) in patients without the cloverleaf sign.

**Conclusions:** The “cloverleaf” MRI sign was associated with significantly longer operation time, increased intraoperative blood loss, and higher rates of bowel resection in DIE patients.

**Key Words:** deep infiltrating endometriosis, magnetic resonance imaging, endometriosis MRI, protocols, bowel endometriosis

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The diagnosis of endometriosis is a complex undertaking. In planning a surgical intervention in cases of endometriosis, the risks and benefits need to be carefully assessed. The prevalence of deep infiltrating endometriosis (DIE), defined as an endometriosis lesion infiltrating more than 5 mm beneath the peritoneum,<sup>1</sup> is known to be underestimated due to the fact that symptoms vary considerably and often do not correlate with the severity of DIE. For example, Chapron et al<sup>2</sup> concluded that only the presence of rectal or vaginal infiltration or extensive adnexal adhesions confirmed the relationship between the severity of dysmenorrhea and endometriosis. Endometriosis is classified either by rASRM (revised American Society of Reproduction Medicine) or, especially for DIE, by the ENZIAN score (from the German Endometriosis Research Foundation [SEF]).<sup>3</sup> The rASRM classification is applied with a standardized point system and focused on lesions affecting fertility. The ENZIAN score is newer and developed to classify DIE according to its degree of infiltration in compartments and its size, analog to the TNM system used for malignant tumors.

Magnetic resonance imaging (MRI) serves as an accurate imaging method in the staging of DIE, providing superior soft tissue contrast and a large field of view (FOV), especially if the findings in clinical gynecologic examination and transvaginal ultrasound (TV-US) are unequivocal.<sup>4</sup> Further, in obese or virgin patients, as well as in patients experiencing pain, vaginal examination and TV-US might be limited. Guidelines for minimal and optimal endometriosis MRI acquisition protocols are provided from the European Society of Urogenital Radiology.<sup>5</sup> A significant variability in endometriosis protocols used is found in the literature.<sup>6–8</sup> A frequent indication for imaging is the staging of the disease and the assessment of the risks and benefits of surgery. In endometriosis surgery, the preoperative evaluation of the need for a bowel resection is crucial. However, it is estimated that, in 80% of cases, the decision to do bowel resection is made during the surgery; this makes the planning of the surgery more difficult for multidisciplinary surgeon team and also the more complex intervention, which requires obtaining more comprehensive informed consent from the patient, just in case.<sup>9</sup> There is currently no method to predict whether conservative surgery is feasible or whether bowel resection is required. Therefore, precise diagnosis is essential in order to allow the surgeon to obtain the appropriate preoperative informed consent and to organize the multidisciplinary surgical team that is required.

Missing the diagnosis of DIE with bowel infiltration preoperatively can compromise the intraoperative decision regarding the optimal surgical approach. A more precise diagnosis allows the surgeon to obtain the appropriate preoperative informed consent and to organize the multidisciplinary surgical team that is required. Above all, it is

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**TABLE 1.** Patient Characteristics (n = 103)

Age, (mean ± SD), y	35 ± 10.5
BMI (mean ± SD), kg/m <sup>2</sup>	23 ± 4.0
Estrogen and progestin medications and/or GnRH-agonist	40/103 (39%)
Nullipara	58/103 (56%)
Hysterectomy or oophorectomy or both due to endometriosis before MRI	8/103 (8%)
rASRM III + IV	55.9%

BMI indicates body mass index; MRI, magnetic resonance imaging.

important to determine the method of bowel resection in DIE surgery; compared with a segmental bowel resection or disc resection, it is suggested that carefully identifying the shaving method could reduce the rate of severe complications,<sup>10</sup> for example, anastomotic leakage and rectovaginal fistula.<sup>11,12</sup>

In this study, the role of a new MRI sign, the “cloverleaf sign,” is evaluated as a tool to improve the diagnosis of DIE using endometriosis MRI along with intraoperative findings.

## MATERIALS AND METHODS

This retrospective study included 113 patients with suspicious DIE; 10 patients had to be excluded from the study because of the poor quality of MRI (2 patients), inadequate MRI protocol (2 patients), missing pelvic MRI due to diaphragmatic endometriosis MRI protocol (2 patients), too old MRI examination (2 patients), and surgery before the MRI (2 patients). One patient underwent 2 operations during the study period, and only the first one was included in the study. All patients were referred to our university SEF-certified endometriosis center and had undergone previously gynecologic clinical and TV-US examination. A laparoscopic operation was performed in the period from January 2016 to June 2018, and all included patients underwent a preoperative MRI of the pelvis. All endometriosis lesions were confirmed by pathology. Operation reports were reviewed, and the intraoperative photo and video documentation was examined. The MRI examinations were performed in-house (47%) and in external facilities (53%). Patient characteristics were gathered from the hospital internal database and analyzed. Intraoperative findings from operation reports as well as intraoperative images and videos were blinded to the MRI results. The decision to perform bowel resection was made on a case-by-case basis,

taking into consideration the size of the lesion, depth of invasion, and symptoms of the patient. The main data on patient characteristics are presented in Table 1.

## Endometriosis MRI Protocol and Image Analysis

Magnetic resonance imaging scans were performed using a 1.5 T scanner (58 examinations/56%) or a 3.0 T scanner (45 examinations/44%). All in-house patients received an antispasmodic drug to reduce bowel peristalsis. The information of the use of antispasmodic drug was not available for external MRIs. The standard endometriosis imaging protocol of our institution is shown in the Table 2. The imaging FOV covered the pelvis, except in T1 Dixon Vibe sequences, where the scan area reached from the diaphragm to symphysis. This extended scan area enables to exclude extragenital, extrapelvic endometriosis, and hydronephrosis. The standard protocol does not include an intravenous contrast medium, which can be administered in initially unclear cases, for example, if exclusion of a tumor or an abscess is required. The in-house MRI protocol includes vaginal and rectal filling (“MRI jelly method” described later). Also included in the in-house protocol are diffusion-weighted sequences, not analyzed in the context of this study.

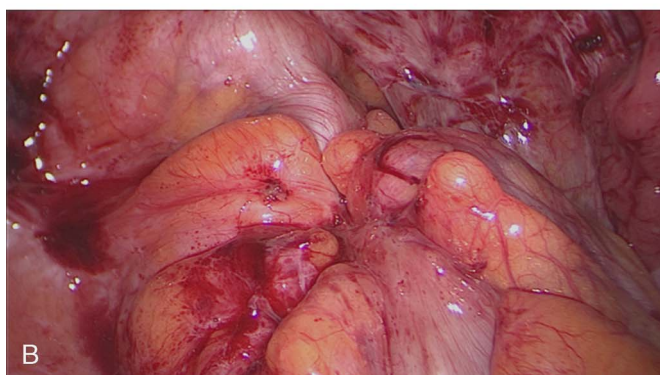
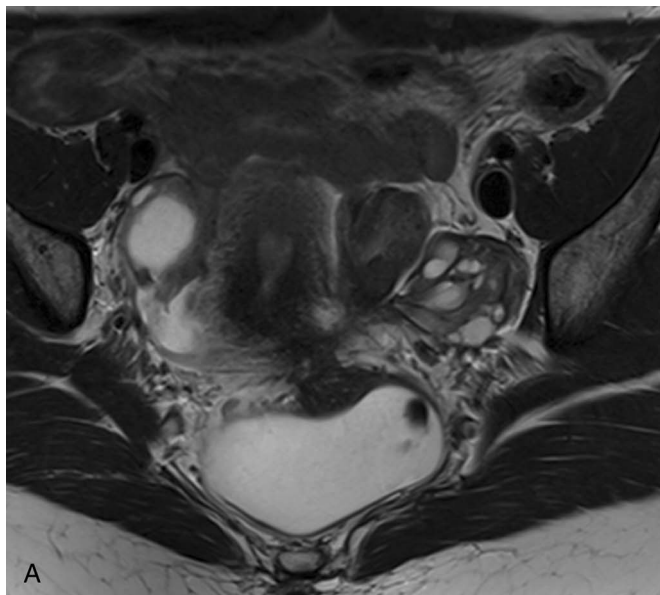
Magnetic resonance imaging data were evaluated by 2 radiologists (1 senior reviewer with 8 years of experience in pelvic MRI and 1 junior reviewer with more than 3 years of experience), blinded to the clinical data and intraoperative diagnosis of the patients. Numerous anatomic regions were evaluated: rectum, sigmoid colon, rectovaginal septum, posterior vaginal fornix, uterosacral ligaments, urinary tract, and extra genital sites. The image reading was always done in the same way: beginning with T2W sequences in 3 planes followed by T1 and T1

**TABLE 2.** Endometriosis MRI Protocol

MRI Sequence*	T2 TSE	T1 TSE	T1 Fat-Sat	EPI DWI	T1 VIBE DIXON
Plane	Sag, cor, ax	Ax	Ax	Ax	Ax
Slice thickness, mm	3	5	5	5	3.5
Gap	20%	20%	20%	20%	20%
In-plane resolution, mm <sup>2</sup>	0.8 × 0.8	0.8 × 0.8	0.8 × 0.8	1.6 × 1.6	1.0 × 1.0
Repetition time, ms					
1.5 T	3970–4080	750	698	8300	6.84
3.0 T	4000–5000	650	761	7800	5.23
Echo time, ms	90–100	10	10	54	
1.5 T					In/opposite-phase
3.0 T	83–91	20	20	48	
b-values, s/mm <sup>2</sup>	—	—	—	50, 300, 800	—
Acquisition time, min	3:11–3:17	3:11	3:44	4:14	0:19

\*The MRI sequences of external facilities varied and are discussed in the text.

MRI indicates magnetic resonance imaging; TSE, turbo spin echo; DWI, diffusion-weighted imaging; EPI DWI, echo-planar diffusion-weighted imaging; sag, sagittal; cor, coronal; ax, axial.



**FIGURE 1.** The figure is demonstrating a cloverleaf sign on MRI (A; T2W transaxial plane), the “leaves” being the uterus, sigmoid colon, and left ovary with the presence of hypointense deep infiltrating endometriosis where the leaves of the formation come together. The correlation was seen in intraoperative situs (B).

fat-sat sequences. All deviations, respectively missing sequences in the images of external facilities, were noted: all patients had at least 2 planes of T2W sequences. In 61% of patients, one plane was missing but replaced with another sequence in the missing plane. T1W and T1W fat-sat sequences existed in 71% and 75% of the outside images, respectively. Sixty-six percent of the external MRIs were done using contrast media. The presence of the “cloverleaf sign” was first verified on a consensus basis by the senior and junior radiologists, who made sure that the exact criteria for the identification of the new sign were met. After more than 6 months, each radiologist repeated the reading on cloverleaf sign radiologists individually to confirm or reject mutual agreement.

### Definition of “Cloverleaf Sign” on MRI in DIE

In cloverleaf-like figure in imaging morphology, the “leaves” are formed by at least 3 different organs coming together in the center of the figure formed by constrictive adhesions including T2-weighted (T2W) hypointense DIE. A visual example is presented in Figure 1.

### MRI Jelly Method

For the past 3 years, prescan vaginal and rectal gel filling is routinely included in the endometriosis MRI protocol of our institute.

Ultrasound gel diluted with water (3:1 relation) is filled slowly using a Foley catheter and a 50-mL syringe: a 50-mL vaginal filling in supine position followed by 100- to 150-mL rectal filling in side position. Patients undergoing the MRI because of dyschezia or other bowel symptoms receive the maximum 150-mL gel filling to fill also the distal sigmoid colon. After the filling, patients remain lying until scanned, so that the gel does not flow out.

### Statistical Analysis

For the statistical analysis, STATA/IC 12.1 and Excel (all calculated correlation coefficients and confusion matrix for the prevalence) were used. The 2-sample Wilcoxon rank-sum (Mann-Whitney *U*) test was used to compare operation times and intraoperative blood loss in cloverleaf and noncloverleaf groups. Multivariate analysis of variance was used to calculate the significance of an overall impact of cloverleaf sign on operation time, blood loss, and the amount of the bowel resection rate.  $P < 0.05$  was considered statistically significant.

Ethical approval for the study was obtained from the Ethics Committee of Bern (BASEC No. KEK BE 2017-00952).

### RESULTS

The current study included 103 endometriosis patients. Mean age of the patients was 35 ( $\pm 10.5$ ) years. The prevalence of DIE in the study population was 79.6%. Of the patients, 55.9% had severe endometriosis (rASRM III + IV), classified as intraoperative. A cloverleaf sign on the MRI was observed in 34/103 (33%) of the patients. The mean BMI did not differ significantly in cloverleaf and noncloverleaf groups: 23 ( $\pm 4.0$ ) kg/m<sup>2</sup> ( $P = 0.63$ , Wilcoxon rank-sum Mann Whitney *U* test). There were 8 reoperations (12%) in the noncloverleaf group, and zero in the cloverleaf group. In the entire study population, 46 patients (45%) had received rectal and vaginal gel filling before scanning, whereas 57 (55%) had not. Of the patients in the cloverleaf group, 44% had received gel filling, as opposed to 46% in noncloverleaf group.

Multivariate analysis showed that the presence of the cloverleaf sign has a significant influence on operation time, blood loss, and bowel resection rate (Wilk's  $\lambda$ , Lawley-Hotelling trace, Pillai's trace, Roy's largest root,  $P < 0.001$ ). The median operation time and median intraoperative blood loss were significantly higher in the cloverleaf group than in noncloverleaf group (Table 2). Within the cloverleaf group, significantly longer operation times were observed when additional bowel resection was done intraoperatively ( $P = 0.001$ ). The intraoperative blood loss was not influenced by additional bowel resection ( $P = 0.222$ ).

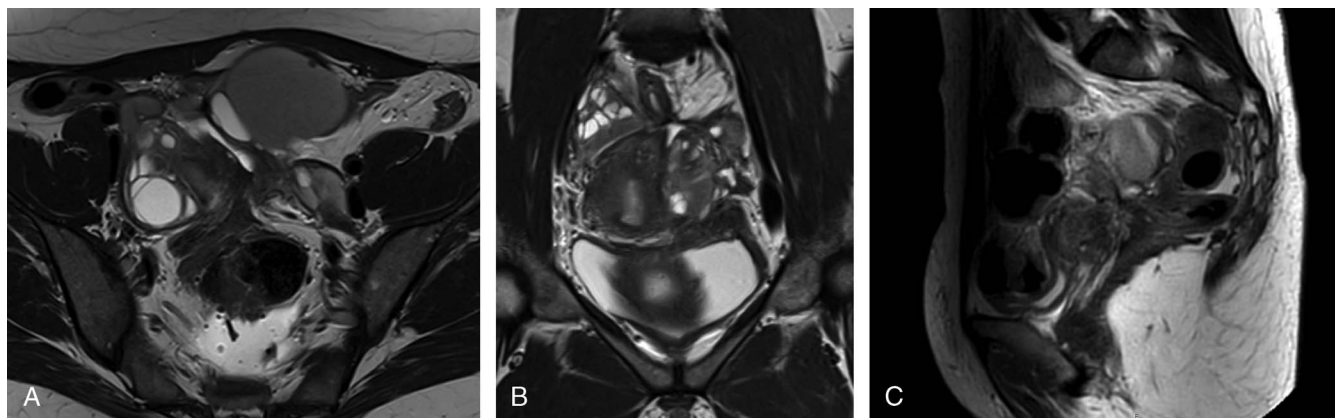
Of the operations in the cloverleaf group, 79% took more than 300 minutes (correlation coefficient between cloverleaf sign/operation time  $\geq 300$  minutes, 0.50). Operation times of 90 minutes or less correlated only moderately with noncloverleaf group of patients (correlation coefficient, 0.28).

In the entire study population, a bowel resection was done in 22% of cases (23/103). Where rectum endometriosis showed on the MRI, bowel resection was done in 36% of the patients (17/47), and in the case of depicting sigmoid endometriosis on MRI, in 53% of the patients (9/17). Of the patients with the cloverleaf sign, 41% underwent bowel resection (14/34). In the patient group without the cloverleaf sign, bowel resection was done in 13% (9/69) of these cases.

The presence of the cloverleaf sign was associated with significantly longer operation time (median of 248 vs 145 minutes) and intraoperative blood loss (median of 125 vs 50 minutes). In contrast, in the patients without the cloverleaf sign, short operation times did not show a strong correlation. For patients with operation times under 90 minutes and without the cloverleaf sign on MRI, the correlation coefficient was 0.28.

Figure 2 shows the MRIs with the cloverleaf sign of 2 patients with the longest operation times of the study population (540 and 570 minutes, respectively). Extragenital extrapelvic endometriosis was diagnosed on MRIs in 3 patients (3/103 = 2.9%), in diaphragmatic,





**FIGURE 2.** MRIs showing the cloverleaf signs of the patients with most longer-lasting operation times. Operation time, 570 minutes; cloverleaf with 4 leaves: rectum, both ovaries, and endometrioma. A, T2W transaxial plane. B, T2W coronal plane. Notice, in coronal plane, almost 5 leaves were detectable. Operation time, 540 minutes. C, T2W sagittal plane, the cloverleaf sign with 4 leaves, the rectum, endometrioma, and uterus. No vaginal and rectal filling in an outer house MRI.

inguinal, and abdominal wall sites. None of these patients with extragenital endometriosis showed a cloverleaf sign on the MRI. All extragenital endometriosis cases were resected and histopathologically proven. The main results are described in the Table 3 and Figures 3 to 6.

## DISCUSSION

The cloverleaf sign in DIE is a new MRI sign, introduced in the current study for the first time. This sign correlates significantly with longer operation times. Accordingly, Minelli et al<sup>10</sup> reported long operation times in laparoscopic colorectal resections of DIE patients (median, 300 minutes; range, 85–720 minutes); operation times without bowel resection were not reported. Significantly longer operations were also observed in patients with the sonographic “kissing ovaries” (KO) sign.<sup>13</sup> Most recently, Guerriero et al published an interesting observational study of 333 patients with ultrasonographic “soft markers.” The absence of a sonographic sliding sign and the presence of KO could be enough to screen patients with clinical suspicion of rectosigmoid endometriosis to be then referred to “second-level” ultrasonography with a low rate of false-negatives.<sup>14</sup> Sonographic soft markers (missing sonographic sliding sign with KO) could possibly indicate a presence of an MRI graphic cloverleaf sign, meaning that patients with sonographic soft markers may profit from further MRI diagnostic to ensure an accurate staging of the severe class of endometriosis. However, studies comparing US and MRI would be required in the future. Due to the definition of the cloverleaf pattern, kissing ovaries are not a criterion

for a cloverleaf sign, even if they may indicate the sign's being present. In the current study, we observed one patient with clear KO on the MRI but without fulfilling the criteria for the cloverleaf sign. Even if US will remain inferior in terms of the magnitude of FOV, it will remain the first-line imaging diagnostic in DIE. When planning future studies, comparison of, and learning from, both the US and MRI findings in DIE is crucial, possibly leading to faster and more accurate diagnosis of severe endometriosis in unequivocal cases.

As mentioned, the symptoms often do not correlate with the severity of DIE. The purpose of the rASRM and the ENZIAN scores is to estimate the burden and severity of endometriosis. Until now, the scores are given intraoperative or postoperative by gynecologists. Most recently, an MRI-based ENZIAN score was found to correlate with intraoperative DIE findings. This score was considered as a promising tool in DIE diagnostics enabling better planning of the surgical procedure for patients and physicians.<sup>15</sup> However, the study did not include a correlation with operation outcome, operation time, blood loss, or bowel resection rate. In the future, it could be of interest to compare the power of the cloverleaf sign with the MRI-based ENZIAN or rASRM score as a predictor of more complicated endometriosis operations. In our study, the detection of peritoneal DIE and bowel endometriosis was higher in the cloverleaf group than in the noncloverleaf group (100%/68% and 74%/32%, respectively). Weighing the risks and benefits of the surgery is crucial, especially in evaluating the need of a bowel resection. In the current study, bowel resection was performed in 22% of all patients, clearly more often in patients with the cloverleaf sign on a preoperative MRI (41% vs 13%).

**TABLE 3.** Study Results

	Cloverleaf Sign on MRI (n = 34)	No Cloverleaf Sign on MRI (n = 69)
Operation time (IQR), min	248 (165–330)*	145 (90–210)*
Intraoperative blood loss (IQR), mL	125 (100–300)†	50 (50–100)†
Bowel resection (patients)	14 (41%)	9 (13%)
Prescan vaginal/rectal gel filling (patients)	15 (44%)	32 (46%)
Peritoneal DIE on MRI (patients)	34 (100%)	47 (68%)
Rectum DIE of all layers on MRI (serosa, muscularis propria, mucosa)	25 (74%)	22 (32%)
Rectum DIE of deep layers on MRI (muscularis propria, mucosa)	14 (41%)	8 (12%)
Sigmoid colon DIE on MRI	12 (35%)	5 (7%)

\* $P < 0.0000$ , † $P < 0.0000$ , 2-sample Wilcoxon rank-sum (Mann-Whitney *U*) test.

MRI indicates magnetic resonance imaging; DIE, deep infiltrating endometriosis; IQR, interquartile range (25%–75%).

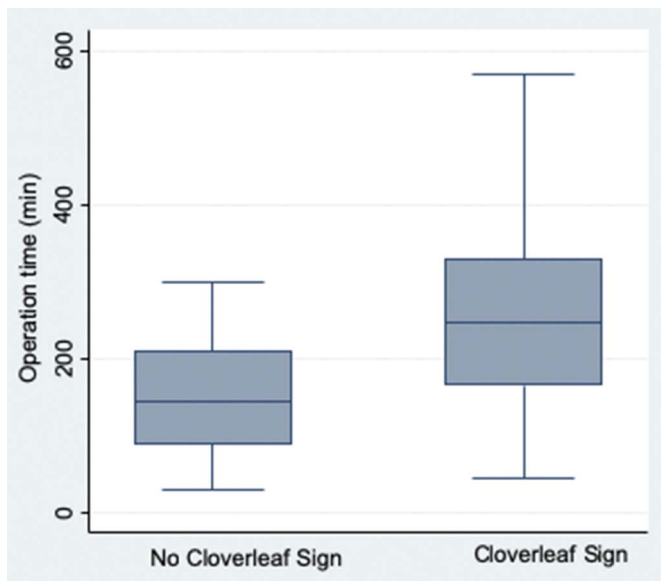


FIGURE 3. Operation time in cloverleaf (n = 34) and noncloverleaf (n = 69) patient groups (median and IQR, minutes);  $P < 0.001$ .

Perandini et al<sup>9</sup> defined a method to predict the probability of rectum resection before DIE surgery. The method was based on measuring the largest diameter of the rectum DIE and the impact angle on the MRI (n = 52). The depth of the rectum DIE infiltration was not analyzed nor used in their algorithm. Compared with an algorithm method, the presence of a cloverleaf sign on an MRI offers a fast and frugal and cost-effective method, by visually depicting the cloverleaf figure and then verifying that the criteria for its definition are met. It is known that the evaluating endometriosis MRIs needs experience on the part of the radiologist, not only in estimating the depth of the intestinal DIE invasion but also in simply depicting T2W hypointense DIE lesions. The cloverleaf sign may have the potential to sensitize less experienced radiologists to the need to look for severe DIE.

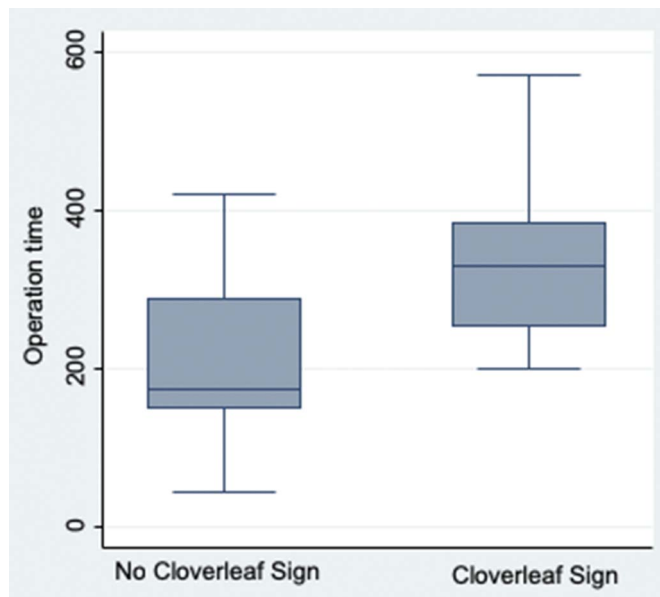


FIGURE 5. Operation time of the patients with bowel resection with or without cloverleaf sign on MRI preoperative (median and IQR, minutes);  $P = 0.001$ .

We could not determine that vaginal and rectal gel filling caused the cloverleaf sign per se. On the contrary, a small minority of the patients in the cloverleaf group had received the filling (15 vs 19). The BMI of the patients did not differ between the groups, and there were no reoperated patients in the cloverleaf group, so that the factors of obesity or reoperation could not be considered to influence the difference in operation times or blood loss between the groups. Furthermore, we do not assume the use of contrast media having an impact in the detection of the cloverleaf sign. Contrast media was used in 66% of the external MRIs, representing a big contrast to our in-house endometriosis MRI protocol done without contrast media. One reason for this could be that

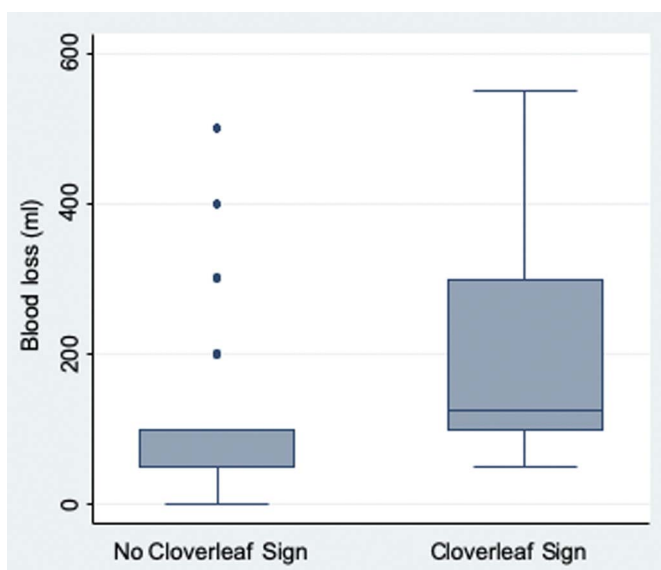


FIGURE 4. Intraoperative blood loss in cloverleaf (n = 34) and noncloverleaf (n = 69) patient groups (median and IQR, milliliters);  $P < 0.001$ .

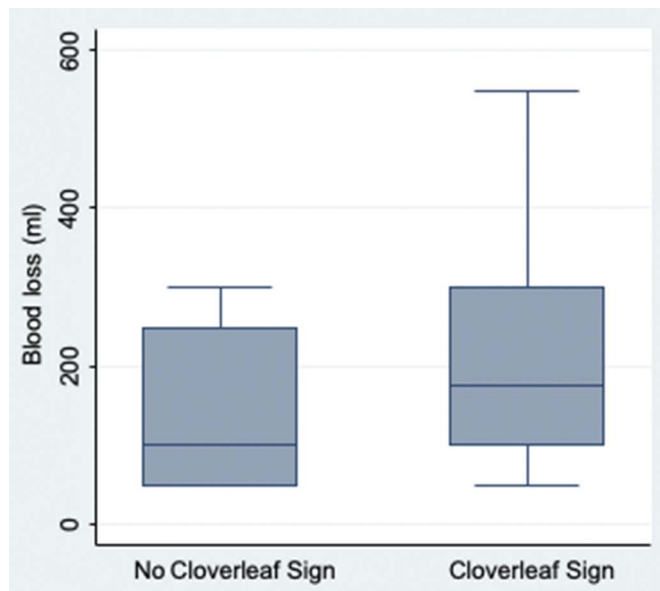
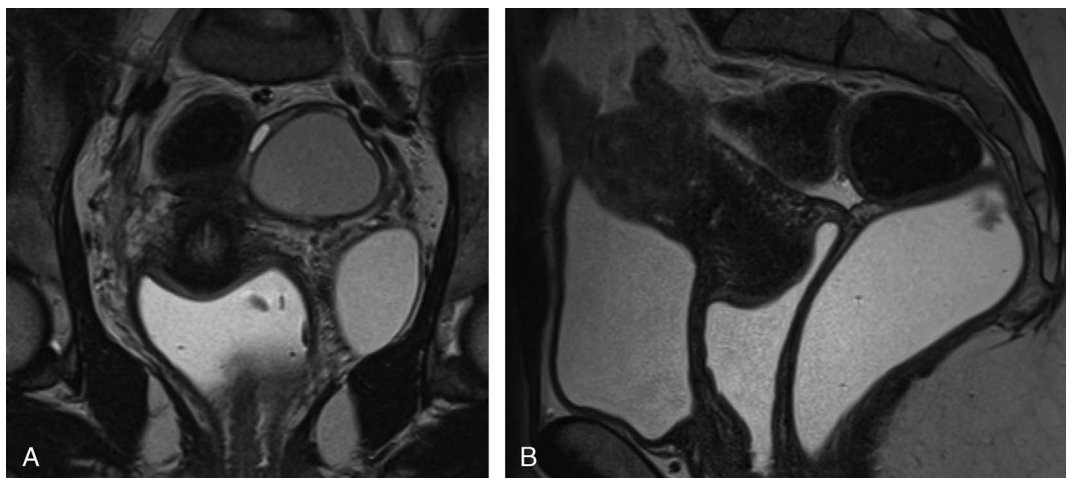


FIGURE 6. Intraoperative blood loss of the patients with bowel resection with or without cloverleaf sign on MRI (median and IQR, mL);  $P = 0.222$ .



**FIGURE 7.** On MRI in T2W coronal plane, a cloverleaf sign was diagnosed (A) assuming 3 leaves in it, the bowel, endometrioma, and cervix. This case presented a “false-positive cloverleaf” with a short operation time of 45 minutes. The T2W sagittal plane shows a relatively free Fossa Douglas (B).

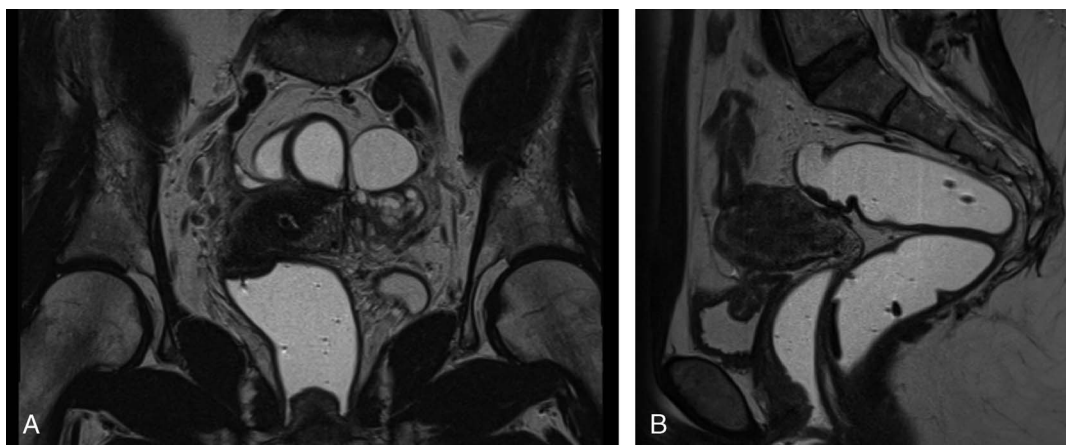
our in-house scanned patients were in the majority referred by our endometriosis-center gynecologists, who focus on endometriosis without questioning other unequivocal adnexal lesions. In cases of unexpected unclear adnexal lesions, we make use of diffusion-weighted imaging. A diffusion-restricted adnexal or any pelvic lesion that cannot be explained by hemorrhagic endometriosis lesions or that does not appear to be a typical corpus luteum requires further definition, for example, by power Doppler ultrasound or by the contrast-enhanced female pelvic MRI protocol. In our study population, we did not observe any indeterminate adnexal lesions suspicious of malignancy; diffusion-weighted sequences were not the focus of the current study. The frequent use of contrast media in external endometriosis MRI protocols raises the question of the responsibility in education and information exchange between expert centers and peripheral hospitals. During the last few years, there have been severe safety concerns with linear gadolinium-based contrast agents.<sup>16</sup> Even if macrocyclic contrast agents are well established today, their usage should be indicated only if critical for disease diagnosis. The European Society of Urogenital Radiology guidelines for endometriosis MRI<sup>5</sup> do not include a recommendation regarding the routine use of gadolinium in the evaluation of DIE and recommend gadolinium as an “option” in the case of indeterminate adnexal endometriosis. Onbas et al<sup>17</sup> proposed a dynamic MRI as

useful to detect abdominal wall endometriosis (AWE). In the current study, 1 of the 3 detected extragenital DIE was located in the abdominal wall. This 26-mm lesion was located subcutaneously in the abdominal wall adjacent to the rectus abdominis muscle showing both T1W fat-sat and DWI hyperintensity.

Accordingly, Genc et al showed the utility of diffusion-weighted imaging in AWE diagnostic. In addition, they observed the ADC values showing similar cyclical changes close to uterine endometrium suggesting a possible differentiation of AWE from the other disease entities in the abdominal wall.<sup>18</sup>

Due to the retrospective nature of our study, the gynecologic surgeons were not aware of the new cloverleaf sign at the time of the operation, so that they were not biased in terms of operating more bowel resections in the presence of the cloverleaf sign. The gynecologic surgeons plan going forward to do more frequent bowel resections in patients with MR-graphic cloverleaf sign remains to be investigated. Patients may benefit from radical primary treatment, if indicated, leading to less recurrent symptoms and recurrent DIE.

There are several limitations in our study, its retrospective nature among others. However, all patients (103) were operated in our university endometriosis center, which routinely includes high-quality intraoperative photo and video documentation, allowing for the correlation



**FIGURE 8.** The figure is showing the coronal and sagittal T2W MRI planes of the patient. The coronal plane shows clearly a cloverleaf-like formation, the left ovary, bowel loops, and uterus making the leaves (A). The sagittal T2W image shows a small 6-mm deep infiltrating endometriosis (DIE) lesion between the sigmoid colon and fundal uterus. Notice, the thin hypointense layer, the deep infiltrating endometriosis in the anterior wall of the sigmoid colon.



between preoperative and intraoperative findings to be as gapless as possible. For example, in one patient case, the cloverleaf sign was depicted on the MRI, but no cloverleaf (intraoperative conglomerate) was reported in the operation report, in photo, or in video documentation. The operation time in this case was 45 minutes, which speaks for the right intraoperative observation “no cloverleaf.”

The MRI of this case is shown in Figure 7. A further limitation to mention is the heterogeneity of the imaging quality between in-house and external MRI images; however, this heterogeneity will remain in a daily clinical routine, because any highly specialized endometriosis center will receive external MRIs to be viewed and evaluated by in-house radiologists for the preoperative planning. As mentioned in our results, the majority of the external MRI protocols matched with our in-house protocol with regard to the sequences analyzed.

No data are available on the number of patients for whom the decision to do a bowel resection was made preoperatively or on the criteria for making these decisions. In the future, prospective studies may show whether the presence of the cloverleaf sign on the preoperative MRI influences the decision to do a bowel resection.

Another challenge is the potential confounding factors that are inherent in retrospective studies, especially in endometriosis, since this disease presents a very inhomogeneous group: different surgeons with different levels of experience and different gynecologic histories, for example, pregnancy or prior operative procedures.

For radiologists reading endometriosis MRIs, the cloverleaf sign is detectable in basic anatomic T2W sequences in sagittal, coronal, and axial planes. Contrast-enhanced sequences are not required. It is important to read the T2W sequences very carefully in each plane, because the cloverleaf sign is not always seen clearly in all 3 planes; even very small DIE lesions can cause constrictive adhesions as the example in Figure 8 shows. To depict the cloverleaf sign, it is crucial to remain attentive to the 3 criteria of the definition: (1) detectable DIE, (2) constrictive adhesions forming the “cloverleaf,” and (3) at least 3 organs included among the leaves. After introducing the cloverleaf sign in our daily clinical routine, a fast learning curve and interest among the residents to identify the sign was noticed, as well as among the gynecologists. An MR-graphic sign known to be associated with challenging, longer-lasting operation with an increased risk of bowel resection could be a more powerful message for the referring clinicians, compared with several listed DIE findings in the radiological report. In addition, structured reporting might have a beneficial effect on interdisciplinary communication, also in endometriosis imaging. For example, the visceral surgeons found that structured reporting was more likely to have sufficient information needed for surgical planning than the free text reports.<sup>19</sup> For radiologists, the cloverleaf sign is simple and visual and is a reminder of the importance of a thorough search for DIE when reading MRIs. Taking into account that most smaller hospitals do not have a specialized gynecologic radiologist, the cloverleaf sign may have the potential of improving the diagnostic performance in detecting DIE.

In conclusion, the cloverleaf sign on endometriosis MRI is associated with more complex surgery, with significantly longer operation

times, and with higher intraoperative blood loss. Its presence therefore suggests better preoperative planning and patient counseling.

## REFERENCES

- Gordts S, Koninckx P, Brosens I. Pathogenesis of deep endometriosis. *Fertil Steril*. 2017;108:872–885.e1.
- Chapron C, Fauconnier A, Dubuisson JB, et al. Deep infiltrating endometriosis: relation between severity of dysmenorrhoea and extent of disease. *Hum Reprod*. 2003;18:760–766.
- Haas D, Chvatal R, Habelsberger A, et al. Comparison of revised American Fertility Society and ENZIAN staging: a critical evaluation of classifications of endometriosis on the basis of our patient population. *Fertil Steril*. 2011;95:1574–1578.
- Savelli L. Transvaginal sonography for the assessment of ovarian and pelvic endometriosis: how deep is our understanding? *Ultrasound Obstet Gynecol*. 2009;33:497–501.
- Bazot M, Bharwani N, Huchon C, et al. European society of urogenital radiology (ESUR) guidelines: MR imaging of pelvic endometriosis. *Eur Radiol*. 2017;27:2765–2775.
- Bazot M, Stivalet A, Darai E, et al. Comparison of 3D and 2D FSE T2-weighted MRI in the diagnosis of deep pelvic endometriosis: preliminary results. *Clin Radiol*. 2013;68:47–54.
- Kruger K, Behrendt K, Niedobitek-Kreuter G, et al. Location-dependent value of pelvic MRI in the preoperative diagnosis of endometriosis. *Eur J Obstet Gynecol Reprod Biol*. 2013;169:93–98.
- Scardapane A, Lorusso F, Scioscia M, et al. Standard high-resolution pelvic MRI vs. low-resolution pelvic MRI in the evaluation of deep infiltrating endometriosis. *Eur Radiol*. 2014;24:2590–2596.
- Perandini A, Perandini S, Montemezzi S, et al. Defining probabilities of bowel resection in deep endometriosis of the rectum: prediction with preoperative magnetic resonance imaging. *J Obstet Gynaecol Res*. 2018;44:292–297.
- Minelli L, Fanfani F, Fagotti A, et al. Laparoscopic colorectal resection for bowel endometriosis: feasibility, complications, and clinical outcome. *Arch Surg*. 2009;144:234–239; discussion 239.
- Balla A, Quaresima S, Subiela JD, et al. Outcomes after rectosigmoid resection for endometriosis: a systematic literature review. *Int J Colorectal Dis*. 2018;33:835–847.
- Abo C, Moatassim S, Marty N, et al. Postoperative complications after bowel endometriosis surgery by shaving, disc excision, or segmental resection: a three-arm comparative analysis of 364 consecutive cases. *Fertil Steril*. 2018;109:172–178.e1.
- Ghezzi F, Raio L, Cromi A, et al. “Kissing ovaries”: a sonographic sign of moderate to severe endometriosis. *Fertil Steril*. 2005;83:143–147.
- Guerriero S, Ajossa S, Pascual MA, et al. Ultrasonographic ‘soft’ markers for the detection of rectosigmoid endometriosis. *Ultrasound Obstet Gynecol*. 2019. doi: 10.1002/uog.20289.
- Burla L, Scheiner D, Samartzis EP, et al. The ENZIAN score as a preoperative MRI-based classification instrument for deep infiltrating endometriosis. *Arch Gynecol Obstet*. 2019;300:109–116.
- Runge VM. Dechelation (transmetalation): consequences and safety concerns with the linear gadolinium-based contrast agents, in view of recent health care rulings by the EMA (Europe), FDA (United States), and PMDA (Japan). *Invest Radiol*. 2018;53:571–578.
- Onbas O, Kantarci M, Alper F, et al. Nodular endometriosis: dynamic MR imaging. *Abdom Imaging*. 2007;32:451–456.
- Genç B, Solak A, Sahin N, et al. Diffusion-weighted imaging in the evaluation of hormonal cyclic changes in abdominal wall endometriomas. *Clin Radiol*. 2014;69:130–136.
- Nörenberg D, Sommer WH, Thasler W, et al. Structured reporting of rectal magnetic resonance imaging in suspected primary rectal cancer: potential benefits for surgical planning and interdisciplinary communication. *Invest Radiol*. 2017;52:232–239.