Received: 29 November 2018 | Revised: 27 March 2019 | Accepted: 4 April 2019

DOI: 10.1111/aogs.13619

ORIGINAL RESEARCH ARTICLE

AOGS Acta Obstetricia et Gynecologica Scandinavica

Conservative treatment of rectosigmoid endometriosis: A prospective study

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Funding information
The Graduate School of Health, Aarhus University, The Danish Endometriosis Society, and Knud og Edith Eriksens Mindefond funded this study.

Abstract

Introduction: Deep infiltrating endometriosis is a common cause of pelvic pain. However, some patients have limited problems that may be controlled by medical treatment, so avoiding the potentially severe complications of major surgery. This approach requires detailed knowledge on quality of life and clinical symptoms over time. The aim of the study was to monitor these parameters in patients with rectosigmoid endometriosis treated with oral contraceptives, oral gestagens, and/or the levonorgestrel-releasing intrauterine device. Moreover, nodule size measurements performed with transvaginal sonography were correlated to severity of symptoms.

Material and methods: Conservatively treated patients on oral contraceptives, oral gestagens, or the levonorgestrel-releasing intrauterine device underwent transvaginal sonography and answered a self-administered questionnaire regarding clinical symptoms and quality of life (Short Form 36 and Endometriosis Health Profile 30) at baseline, and 6 and 12 months later.

Results: Eighty women completed the follow up. Scores of quality of life were comparable to normative data for Danish women of similar age and did not change with time. No association between change in size of the rectosigmoid nodule and change in symptoms was seen.

Conclusions: This study supports that simple treatment with oral contraceptives, oral gestagens, or the levonorgestrel-releasing intrauterine device represents a viable therapeutic approach to rectosigmoid Deep infiltrating endometriosis, provided that proper selection of patients in need of surgery exists.

KEYWORDS

bowel endometriosis, deep infiltrating endometriosis, dysmenorrhea, endometriosis, medical therapy, oral contraceptives, pelvic pain, progestins

1 | INTRODUCTION

Deep infiltrating endometriosis (DIE) is a severe chronic disease leading to dysmenorrhea, intermenstrual pain, dyspareunia, dyschezia,[1-3] and impaired quality of life (QoL).[4] DIE is typically located in the posterior pelvic compartment, often affecting the bowel wall. Treatment is subject of discussion,[5,6] and much attention has been paid to the effect of laparoscopic local excision or segmental bowel resection.[7,8]

Abbreviations: DIE, deep infiltrating endometriosis; EHP-30, Endometriosis Health Profile 30 questionnaire; LNG-IUD, levonorgestrel-releasing intrauterine device; NSAID, nonsteroidal anti-inflammatory drugs; OC, oral contraceptives; OG, oral gestagens; QoL, quality of life; SF-36, Short Form 36 questionnaire; TVS, transvaginal sonography.

Data on medical treatment are limited, but oral contraceptives (OC), oral gestagens (OG), and the levonorgestrel-releasing intrauterine device (LNG-IUD) seem to reduce pain symptoms.[9,10] These treatment strategies are therefore used for long-term treatment.[11] In a study using historical data we found that >50% of women with bowel DIE could be treated for endometriosis in this way, and >80% continued the treatment on a long-term basis.[12] However, these women may face major problems. Conservative treatment implies a risk of disease progression ultimately leading to bowel obstruction,[13-16] so patients must be followed clinically[17] to detect worsening of pain and bowel symptoms. The impact of medical therapy on this process remains to be elucidated.

The aim of this prospective study was therefore to monitor QoL and clinical symptoms in women with rectosigmoid endometriosis treated with OCs, OGs, or LNG-IUD. Moreover, we investigated possible correlations between nodule size and severity of symptoms.

Key message

Quality of life, symptoms, and nodule size were assessed in a cohort of 80 patients on medical treatment due to bowel endometriosis. Mean scores suggest good quality of life in Short Form 36 and Endometriosis Health Profile-30.

2 | MATERIAL AND METHODS

This was a prospective clinical cohort of patients of reproductive age treated conservatively for rectosigmoid endometriosis without previous surgery for bowel DIE. Participants were recruited from the outpatient clinic at the Department of Obstetrics and Gynecology, Aarhus University Hospital, which is 1 of 2 tertiary referral centers for endometriosis in Denmark.

Standard clinical control of DIE in the rectosigmoid includes annual visits with transvaginal sonography (TVS) and discussion of symptoms. In our clinic, patients with rectosigmoid DIE are generally recommended long-term, low-risk medical treatment. Surgery is considered when pain cannot be controlled by these measures, but this is always a shared decision process, where the risk of complications is taken into account.

Enrolment of patients in the outpatient clinic took place from September 2014 to February 2016. Eligible patients already attending the clinic were invited to participate by letter. Identification of these patients was carried out in the hospital electronic record system by use of International Classification of Diseases 10 codes for DIE (N80.4 Endometriosis of rectovaginal septum and vagina, N80.4A Endometriosis of rectovaginal septum, N80.4B Endometriosis of vagina, N80.5 Endometriosis of intestine, N80.5A Endometriosis of large intestine, N80.5B Endometriosis of small intestine, N80.5C Rectosigmoid endometriosis).

Patients who did not respond to the letter, and newly referred patients were approached in the outpatient clinic. Inclusion criteria were rectosigmoid DIE that could be verified by TVS. The medical treatment was registered at study entry, and aimed at pain control and maintenance of amenorrhea. Continuous OCs, OGs, and/or the LNG-IUD were the primary treatment choices and were used in a shared decision process. In case of insufficient effect alone, these medications were used in combination. For women >35 years of age the LNG-IUD or OGs were proposed to minimize risk of thrombosis.[18] In case of pain during the study period, patients were counseled regarding adjustments of medical treatment, bowel habits, and laxatives. Gonadotropin-releasing hormone analogues (GnRH) with estrogen+gestogen add-back were used in case of insufficient symptom control, reflecting an unstable situation for the patient. In our center, need for long-term use motivates consideration of surgery.

Patients were not included when surgical treatment was scheduled, or when patients would discontinue the current treatment within a year (eg wish for pregnancy or treatment with GnRH analogues). Surgical treatment was scheduled when the patient had severe pain resistant to long-term medical treatment (as mentioned above), or severe pain and wish for pregnancy where hormonal treatment was not an option. Our study concerned patients who remained stable on a specific simple treatment with OC, OG, and/or the LNG-IUD. Need for GnRH analogues reflected exacerbation of symptoms despite this treatment, and these women were therefore excluded, as were patients in need of surgery. Patients who had rectosigmoid resection before the study, had a diagnosis of cancer, suffered from severe mental disorders or were unable to speak and understand Danish, were not included. Participants answered a self-administered questionnaire, and underwent TVS and pelvic examination at baseline, and 6 and 12 months later.

2.1 | Questionnaire data

Demographic data such as height and weight, number of previous deliveries, smoking habits, alcohol consumption, and educational level were self-reported. The Danish versions of the 30-item Endometriosis Health Profile (EHP-30) and Short Form 36 (SF-36) questionnaires were used to quantify QoL.[19,20] The EHP-30 (0-100) uses zero whereas the SF-36 (0-100) uses 100 as the best possible score. We evaluated similarities between SF-36 scores from this study against Danish SF-36 normative data for women in the age group (35-44 years).[20] A numerical rating scale 0-10[21] was used to investigate intensity of dysmenorrhea, intermenstrual pain and dyschezia both on average and when worst. Type and use of pain-relieving drugs were also self-reported.

2.2 | TVS

TVS of rectosigmoid DIE was performed on a Voluson® E8 (GE Healthcare, Milwaukee, WI) with a 6-12 MHz vaginal probe by the first author (A.G.E.) who had 5 years of experience with this technique. The examination included evaluation of the ovaries, uterus, and bladder

wall. The rectosigmoid nodule was located by following the thin hypoechoic line in close relation to the vaginal wall representing the muscular layer of the rectal wall starting from the anal sphincter and moving cranially until the nodule presented as an irregular thickening of this line >3 mm.[22] The nodule was measured in 3 orthogonal planes (length, depth, and width) as previously described[23] and shown in Figure 1. Our procedure also included 3-dimensional volume measurements by Virtual Organ Computer-aided Analysis (VOCAL) software, but results from our previous study on intra- and interobserver variability showed poor reproducibility of this method. These data were therefore not used in this study. No bowel preparation was used for TVS examinations.

After the TVS assessment, an abdominal probe (2-5 MHz) was used to evaluate the renal pelvis concerning the presence/absence of hydronephrosis. To ensure the quality of this evaluation, A.G.E. was trained by a subspecialized uro-radiologist (O.G.) to ensure the quality of this examination. The investigator was blinded to previous measurements of the bowel nodule during the course of follow up. Nodules in the posterior vaginal fornix were detected by palpation at pelvic examination. Data from existing MRI were all analyzed by the same subspecialized radiologist (E.M.) with 12 years of experience with MRI of endometriosis. When several MRI examinations were available, data from the most recent were used. Data on previous surgery for endometriosis were obtained from the patient records.

2.3 | Statistical analyses

To analyze changes in EHP-30, SF-36, and numerical rating scale scores during the follow-up, different statistical tests were performed as follows. Comparisons between scores at baseline, and at 6 and 12 months were performed using 1-way analysis of variance for continuous data, Friedman test for ordinal data, and chi-squared test for categorical data.

Stratified analysis was performed assigning patients to two groups (small and large nodules) according to the median value of measured dimensions (length, depth, and width) of the rectosigmoid nodule at baseline. Comparison between scores in the 2 groups was performed using *t* test, chi-squared test or Mann-Whitney *U* test as appropriate.

To assess the potential association between change in nodule size and pain, QoL and a number of treatment-related factors, nodule size was grouped into "no change", "regression", and "progression" for each of the measured dimensions in 2 dimensions, taking the intraobserver variability of the measurements into account (11 mm for length, 3 mm for depth and 5 mm for width of the nodule).[23] Similarly, symptoms were grouped. Comparisons between change in size and change in symptoms were performed using chi-squared test/Fisher's exact test or Kruskal-Wallis test.

In case of missing values in the questionnaires, imputation was performed by inserting the mean or median observation of the specific category. No more than three missing values were found in each of the variables: average/worst dysmenorrhea, average/worst dyschezia, frequency of pain-relieving drugs and the EHP-30 single questions. No more than 8 missing values were found in each of the variables for average/worst intermenstrual pain.

2.4 | Ethical Approval

All participants gave written informed consent, and the study was approved by The Central Denmark Region Committees on Health Research Ethics (no. 1-10-72-196-13) and the Danish Data Protection Agency (no. 1-16-2-657-15).

3 | RESULTS

Of 109 patients invited by letter, 20 accepted to participate. Of the remaining 89 patients, 25 later accepted to participate during scheduled visits to the outpatient clinic. Out of 82 patients further contacted in the outpatient clinic, 53 accepted to participate.

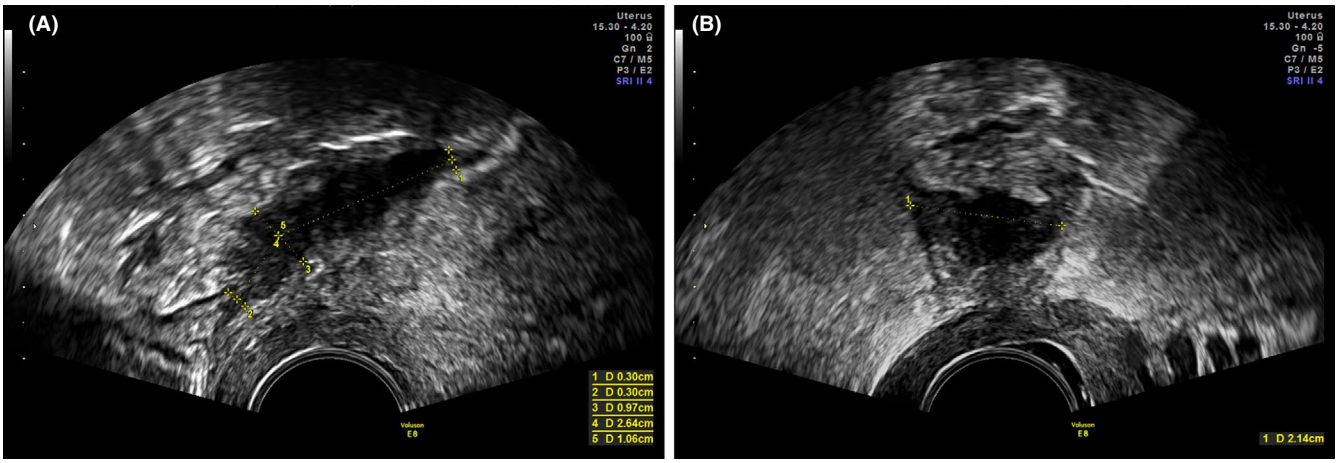

FIGURE 1 Measurement of a rectosigmoid nodule by transvaginal sonography. A, 1 and 2: Limits for measurement of length, where the muscular layer ≥3 mm. 3: infiltration depth. 4 + 5: measurement of length. B, 1: measurement of width [Color figure can be viewed at wileyonlinelibrary.com]

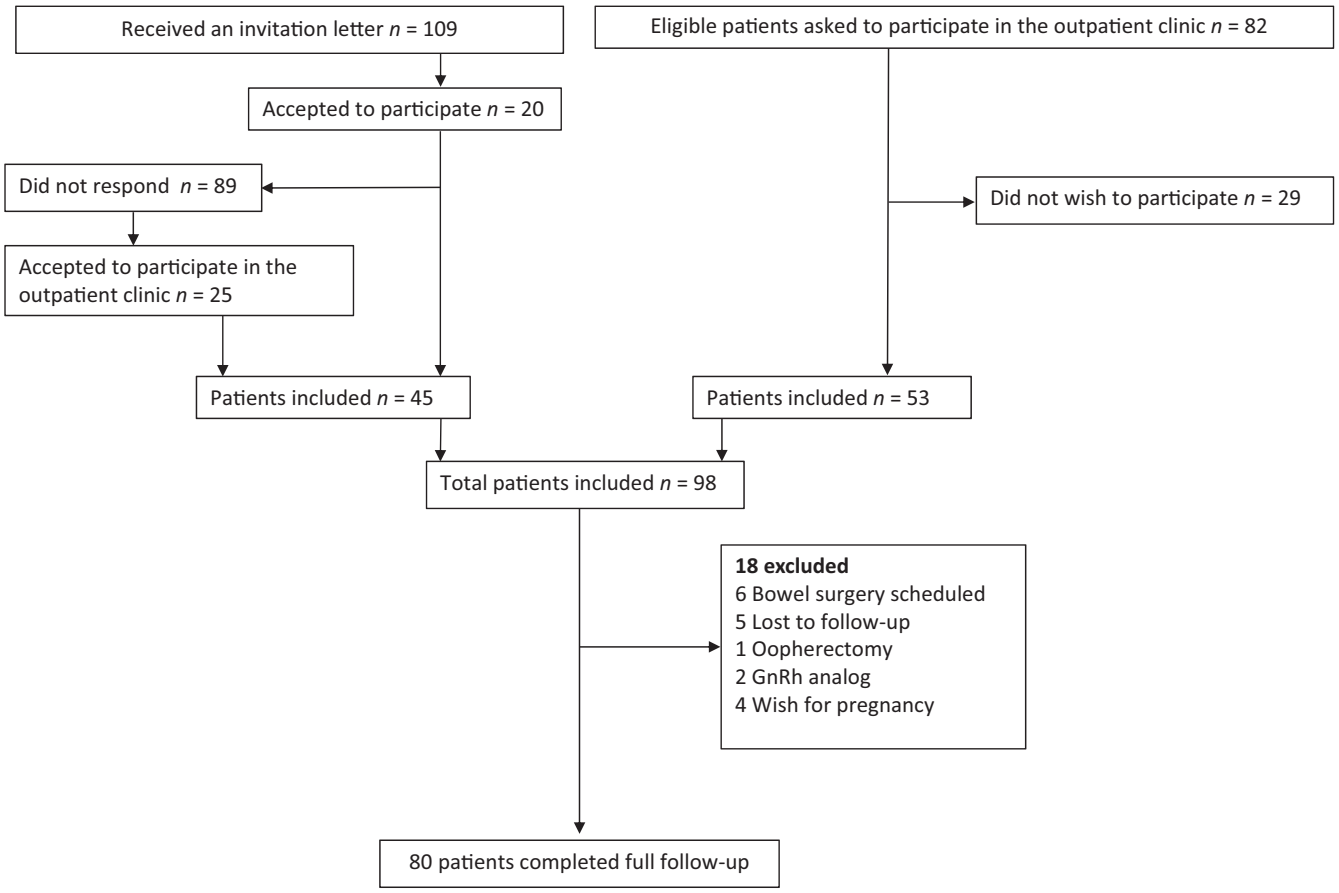

FIGURE 2 Flowchart for inclusion and exclusion of patients with rectosigmoid deep infiltrative endometriosis

Overall, 51% of the women who were contacted accepted to participate.

Ninety-eight participants were included and 80 (82%) completed the study with full follow-up (Figure 2). Eighteen patients were excluded during the study period: six had bowel surgery scheduled, one underwent oophorectomy, two were treated with GnRH analogues, four had a wish for pregnancy and five were lost to follow up.

In Table 1 demographic data on the participants are shown. The mean (SD) age was 38.6 (5.8) years. Mean time on medical treatment was 1.8 (2.5) years when entering the study. In nine patients, medical treatment was adjusted once, in seven patients it was adjusted twice, and in one patient it was adjusted four times during follow up. Ten patients used continuous OCs and two patients used sequential OCs. Sixty-two (78%) patients had an MRI scan for analysis, and mean time since the scan was 2.3 (1.7) years.

Table 2 displays the data from patients on medical treatment gathered at the three time-points.

The scores for SF-36 were similar to the Danish normative data for women in this age group.[20] In the EHP-30 none of the patients scored >19 in any of the items. In line with scores for dysmenorrhea "Pain" in the EHP-30 tended to improve during follow up, although not significantly so. Scores of dysmenorrhea improved from 4 to 1 ($P = 0.019$) in average pain and from 6 to 2 ($P = 0.006$) for worst pain. One patient had mild hydronephrosis at 12 months, which was unrelated to the endometriotic nodule at subsequent MRI. This patient was known to have a single kidney and urogenital malformations.

In Table 3 the patients are stratified into 2 groups depending on the infiltration length (≤26 and >26 mm) and depth (≤8 and >8 mm) measured by TVS at baseline. Patients with large nodule length scored higher on all items in the EHP-30 apart from social support and self-image, and lower on the item "Bodily pain" in the SF-36. Moreover, patients with large nodule length were significantly older and had higher scores of average dysmenorrhea. These differences were not found at 12 months of follow up (data not shown). At baseline, patients with large invasion depth (>8 mm) had worse score for the "Pain" item in EHP-30 and the "Bodily pain" item in SF-36 compared with patients with small invasion depth (<8 mm). Patients with large invasion depth had a significantly higher score of average dysmenorrhea and larger intake of pain-relieving drugs (paracetamol and nonsteroidal anti-inflammatory drugs [NSAID] in combination). Moreover, when stratifying analyses on width, patients with nodule width >12 mm consumed more paracetamol and NSAID in comparison with patients with narrower lesions (data not shown). These differences could not be found at 12 months follow up. Body mass index, educational status, smoking, or alcohol consumption were not related to size of the nodule (data not shown). Taking the intraobserver variability into account, 9, 0, and 6 rectosigmoid nodules

TABLE 1 Baseline characteristics of 80 women on medical treatment for rectosigmoid deep infiltrative endometriosis (DIE)

Age (years), mean (SD)	38.6 (5.8)
Body mass index (kg/m^2), mean (SD)	24.9 (4.4)
Parity	
Nullipara	20 (25.0)
Para	60 (75)
Higher education	
None or <3 y	30 (37.5)
3-4 y	36 (45.0)
>4 y	14 (17.5)
Smoking status	
Current smoker	10 (12.5)
Alcohol consumption	
>1 unit per week	28 (35.4)
Years since first visit in the outpatient clinic	
Mean (SD)	4.0 (3.4)
Previous surgery for endometriosis	
0	34 (42.5)
1	27 (33.8)
2	14 (17.5)
≥3	5 (6.3)
Years on current medical treatment	
Mean (SD)	1.8 (2.5)
Medical treatment	
Levonorgestrel-releasing intrauterine device	49 (61.3)
Oral contraceptives	12 (15.0)
Gestagens	9 (11.3)
Combinations of above	10 (12.5)
DIE in the posterior vaginal fornix	44 (55.7)
Rectosigmoid nodules[a]	
1	74 (92.5)
2	6 (7.5)
Endometriomas[a]	
Unilateral	20 (25)
Bilateral	2 (2.5)
Adenomyosis[b,c]	26 (41.9)
DIE in the uterosacral ligaments[b,d]	
Unilateral	34 (57.6)
Bilateral	11 (18.6)
Bladder endometriosis[b,c]	2 (3.2)

Numbers are given in n (%) unless otherwise specified.
[a]Ultrasonography findings.
[b]MRI findings.
[c]18 (23%) missing values.
[d]21 (26%) missing values.

progressed and 12, 3, and 3 regressed in length, depth, and width, respectively. However, no association was seen between changes in size and alterations in QoL or clinical symptoms.

4 | DISCUSSION

To our knowledge, this is the first study presenting prospective data on QoL and clinical symptoms along with monitoring of nodule size by TVS in women with rectosigmoid DIE treated with OCs, OGs, or the LNG-IUD. Results showed that only 6% of all participants needed surgery during the study period. Otherwise, patients had stationary symptoms and low EHP-30 scores. Moreover, SF-36 scores remained constant and comparable to the background population. With the reservation that the normative SF-36 data were collected >20 years ago, our results support the notion that treatment with OCs, OGs, or LNG-IUD of women with rectosigmoid DIE can be associated with satisfactory QoL.

It has been suggested that bowel endometriosis may be resistant to medical therapy due to the histology of the lesions.[24] However, Ferrari et al achieved results comparable to ours with respect to intermenstrual pain and dyschezia in their study of 26 women treated for 12 months with continuous OCs.[10] Our results are also similar to findings by Ferrero et al using norethisterone acetate for treatment in 40 women[9] where satisfactory SF-36 and EHP-30 levels were found during the study period. Finally, Vercellini et al reported that more than two-thirds of 50 women with colorectal endometriosis receiving low-dose OC or progestins remained satisfied with their treatment during follow up for 3 years.[25] This is in line with the present results and a previous study from our group.[12]

Recently, Riiskjaer et al reported on pelvic pain and QoL in 175 women undergoing bowel resection due to rectosigmoid endometriosis not responding to conservative treatment.[26] Before surgery, the authors found higher pain and lower SF-36 scores compared with our data. Surgery implied significant improvement but most postoperative parameters were still below the scores in the present study.

It might be argued that many of our patients had been stationary before entering the study. The stable QoL measures were therefore not unexpected, but our findings still indicate that a significant number of patients with bowel DIE can be treated with OCs, OGs, and/or LNG-IUD with satisfactory results. Further research including the use of long-term GnRH analogues[27] is needed to define the limits between the medical modalities and the surgical solutions.

When the measurements of nodule size were stratified according to size, significant differences emerged, with more severe symptoms in patients with larger nodules. This was especially seen for length of the lesion where EHP-30 values showed systematic differences in all items, except for social support and self-image. This could suggest that large nodules are associated with more pronounced problems, although the difference did not persist at 12 months follow up. It is possible that our patients improved with time, owing to continued medical treatment and counseling in bowel habits.

We found progression of length in 9 patients, and progression of width in six patients. These changes occurred without worsening of symptoms or QoL. We were therefore unable to confirm earlier findings that growth of rectosigmoid endometriosis should be accompanied by pain as suggested in previous reports.[16,28]

TABLE 2 Data on 80 women with rectosigmoid endometriosis gathered at baseline, and at 6 and 12 months

	Baseline	6 mo	12 mo	*P*-value	Danish normative data[a]
SF-36, mean (SD)					
Physical functioning	94.5 (9.7)	94.2 (10.1)	93.8 (12.6)[b]	0.920	91.7 (15.1)
Role physical	87.1 (20.6)	89.0 (19.1)	90.4 (16.8)[b]	0.540	87.0 (28.0)
Bodily pain	72.0 (23.8)	72.6 (22.5)	76.4 (21.9)[b]	0.418	75.9 (24.5)
General health	73.2 (20.8)	72.5 (21.1)	74.4 (22.1)	0.851	79.1 (18.8)
Vitality	58.4 (21.9)	59.2 (23.1)	62.0 (23.3)	0.567	67.9 (19.7)
Social functioning	85.8 (19.9)	84.8 (20.7)	87.8 (18.7)	0.625	90.6 (16.9)
Role emotional	88.6 (17.5)	86.7 (20.2)	88.8 (17.8)	0.727	86.3 (27.2)
Mental health	79.9 (14.4)	76.9 (16.3)	80.3 (15.1)	0.319	79.6 (16.3)
EHP-30, mean (SD)					
Total	18.9 (20.0)	15.3 (19.1)	13.8 (17.8)	0.213	
Pain	13.4 (16.5)	9.6 (15.3)	7.6 (12.9)	0.051	
Control and powerlessness	17.9 (20.5)	15.4 (20.9)	13.0 (20.1)	0.329	
Emotional well-being	16.2 (19.0)	14.1 (19.2)	13.8 (18.3)	0.690	
Social support	16.9 (23.4)	13.3 (19.7)	11.4 (18.3)	0.235	
Self-image	17.2 (24.4)	15.3 (21.7)	17.9 (23.5)	0.765	
Nodule dimensions 2D, mean (SD)					
Length	27.4 (11.8)	26.4 (10.6)[b]	26.8 (12.7)	0.871	
Depth	8.4 (2.3)	8.5 (2.5)[b]	8.1 (2.4)	0.648	
Width	12.7 (4.1)	12.7 (3.8)[b]	13.3 (4.1)	0.492	
Dysmenorrhea, median (range)					
Average pain 0-10	4 (0-10)	0 (0-9)	1 (0-8)	0.019	
Worst pain 0-10	6 (0-10)	0 (0-10)	2 (0-10)	0.006	
Intermenstrual pain, median (range)					
Average pain 0-10	0 (0-9)	0 (0-7)	1 (0-8)	0.426	
Worst pain 0-10	0 (0-10)	0 (0-9)	0 (0-9)	0.252	
Dyschezia, median (range)					
Average pain 0-10	1 (0-9)	0 (0-7)	1 (0-8)	0.418	
Worst pain 0-10	4 (0-10)	0 (0-10)	2 (0-10)	0.363	
Unilateral hydronephrosis, n (%)					
No	80 (100)	80 (100)	79 (100)	0.383	
Yes	0	0	1		
Painkillers due to pelvic pain, n (%)					
None	35 (43.8)	37 (46.3)	38 (47.5)	0.625	
<2 d a week	34 (42.5)	31 (38.8)	33 (41.3)		
≥2 d a week	6 (7.5)	10 (12.5)	8 (10.0)		
Every day	5 (6.3)	2 (2.5)	1 (1.3)		

The EHP-30 uses zero whereas SF-36 uses 100 as the best possible score.
Abbreviations: EHP-30, Endometriosis Health Profile 30 questionnaire; SF-36, Short Form 36 questionnaire.
[a]Danish women age 35-44 y.[20]
[b]1 missing value.

Our data on size and growth of rectosigmoid nodules should, however, be considered in light of the intraobserver variability associated with TVS measurement of rectosigmoid DIE,[23] where large intra- and interobserver variations have been shown in a recent study. Still, the present results suggest a low risk of progression and bowel obstruction; however longer follow up on larger study groups is needed to assess the occurrence of this complication.

This series represented a subgroup of all patients with rectosigmoid DIE referred to our center. Participants had been followed

TABLE 3 Stratified analysis for infiltration length and depth of rectosigmoid DIE

	Length of rectosigmoid DIE			Infiltration depth of rectosigmoid DIE		
Baseline	**Small (≤26 mm)**	**Large >26 mm**	***P*-value**	**Small (≤8 mm)**	**Large >8 mm**	***P*-value**
n	42	38		49	31	
Average size, mean (SD)	19.0 (4.8)	36.7 (10.2)	—	7.0 (1.1)	10.7 (1.8)	—
Age, mean (SD)	37.1 (6.3)	40.2 (4.8)	0.017	37.6 (6.2)	40.0 (4.9)	0.070
Dysmenorrhea, median (range)						
Average pain 0-10	1.5 (0-10)	4.5 (0-10)	0.009	2 (0-10)	4 (0-10)	0.035
Worst pain 0-10	3 (0-10)	7 (0-10)	0.027	4 (0-10)	7 (0-10)	0.087
Intermenstrual pain, median (range)						
Average pain 0-10	0 (0-9)	1 (0-8)	0.152	0 (0-8)	1 (0-9)	0.196
Worst pain 0-10	0 (0-10)	2 (0-10)	0.235	0 (0-10)	3 (0-10)	0.196
Dyschezia, median (range)						
Average pain 0-10	1 (0-9)	1.5 (0-7)	0.907	1 (0-8)	2 (0-9)	0.164
Worst pain 0-10	3 (0-10)	4 (0-10)	0.800	1 (0-10)	4 (0-10)	0.187
Painkillers due to pelvic pain, n (%)						
None	23 (54.8)	12 (31.6)	0.100	27 (55.1)	8 (25.8)	0.002
<2 d a week	16 (38.1)	18 (47.4)		18 (36.7)	16 (51.6)	
>2 d a week	1 (2.4)	5 (13.2)		0	6 (19.4)	
Every day	2 (4.8)	3 (7.9)		4 (8.2)	1 (3.2)	
Type of pain-relieving drug, n (%)						
Paracetamol only	9 (21.4)	8 (21.1)	0.967	12 (24.5)	5 (16.3)	0.373
NSAID only	1 (2.4)	3 (7.9)	0.258	2 (4.1)	2 (6.5)	0.636
Combination of paracetamol and NSAID	9 (21.4)	14 (36.8)	0.128	8 (16.3)	15 (48.4)	0.002
Morphine	2 (4.8)	1 (2.6)	0.616	2 (4.1)	1 (3.2)	0.844
EHP-30, mean (SD)						
Total	14.0 (19.7)	24.4 (19.1)	0.018	16.3 (20.1)	23.2 (19.3)	0.134
Pain	9.3 (16.2)	17.9 (16.0)	0.018	9.5 (15.3)	19.5 (16.8)	0.008
Control and powerlessness	12.9 (19.4)	23.4 (20.5)	0.022	14.7 (20.3)	22.8 (20.0)	0.083
Emotional well-being	11.0 (15.3)	21.9 (21.1)	0.009	15.5 (19.6)	17.2 (18.2)	0.709
Social support	12.9 (22.7)	21.2 (23.7)	0.115	16.2 (24.3)	17.9 (22.3)	0.748
Self-image	14.9 (24.7)	19.7 (24.2)	0.377	16.5 (25.8)	18.3 (22.3)	0.752
SF-36, mean (SD)						
Physical functioning	94.5 (10.0)	94.5 (9.6)	0.982	95.0 (9.5)	93.7 (10.2)	0.567
Role physical	87.6 (22.0)	86.5 (19.1)	0.807	88.1 (19.2)	85.5 (22.8)	0.578
Bodily pain	78.4 (23.2)	64.8 (22.5)	0.010	79.1 (20.9)	60.6 (23.9)	<0.001
General health	74.2 (22.4)	72.1 (19.0)	0.649	74.5 (21.4)	71.1 (19.9)	0.473
Vitality	61.6 (20.9)	54.8 (22.8)	0.165	59.6 (22.5)	56.5 (21.3)	0.540
Social functioning	89.9 (17.5)	81.3 (21.5)	0.052	88.5 (18.7)	81.5 (21.1)	0.122
Role emotional	90.9 (13.1)	86.2 (21.2)	0.234	88.6 (15.6)	88.7 (20.5)	0.980
Mental health	82.0 (12.8)	77.6 (15.9)	0.176	79.6 (15.1)	80.5 (13.5)	0.790

Abbreviations: DIE, deep infiltrative endometriosis; EHP-30, Endometriosis Health Profile 30 questionnaire; NSAID, nonsteroidal anti-inflammatory drugs; SF-36, Short Form 36 questionnaire.

for a mean of 4 years (Table 1) and were therefore in a stable situation. This may account for the limited changes in clinical parameters and nodule size, and for the low number of patients referred for surgical treatment. Moreover, the mean age of our patients was 38 years, as opposed to the younger patients undergoing surgery in our previous study.[12] This probably reflects that surgery is needed in aggressive endometriosis causing severe symptoms earlier in younger women.

Strengths of the present study include the prospective design, and the fact that TVS was performed by one observer blinded to previous examinations, so minimizing information bias.[29] Limitations include that nodule size was stratified into large and small lesions according to the median value. With the large intraobserver variation in mind,[23] nondifferential misclassification may have affected our results[29] but this would imply a bias toward no association. Moreover, differences found at baseline could not be found at 12 months, possibly through misclassification. We did not control for potential confounders such as body mass index, education, smoking, or alcohol consumption, because there were no differences between the 2 nodule-size groups with respect to these variables. Apart from these aspects, limitations of the present data include the missing information on dyspareunia. The question was included in the questionnaire later and could not be included in the present data set.

Only 18% of women accepted to participate after receiving an invitation letter. Although the inclusion was greater when eligible participants were contacted in the outpatient clinic, selection bias[30] may have played a role in our study. Moreover, women with more pronounced symptoms and less energy may have been more likely to decline participation. These aspects may affect extrapolation of our results.

5 | CONCLUSION

This study supports that simple treatment with OCs, OGs, or LNG-IUD represents a viable therapeutic approach to rectosigmoid DIE, provided that proper selection of patients in need of surgery exists. With reservation for study size and the variability inherent in TVS measurements of DIE, no compelling evidence was found that change in size of rectosigmoid DIE correlates to clinical symptoms. We are still in need of knowledge on the natural history of endometriosis and its growth pattern in relation to symptoms.

CONFLICT OF INTEREST

None.

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How to cite this article: Egekvist AG, Marinovskij E, Forman A, Kesmodel US, Graumann O, Seyer-Hansen M. Conservative treatment of rectosigmoid endometriosis: A prospective study. *Acta Obstet Gynecol Scand*. 2019;98:1139–1147. https://doi.org/10.1111/aogs.13619