Suboptimal Bowel Function after (Recto) Sigmoid Resection in Patients with Deep Infiltrating Endometriosis

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Abstract

Purpose: To investigate the postoperative outcomes regarding bowel functions in women and the pattern of symptoms after surgical treatment for deep infiltrating endometriosis in comparison with healthy subjects.

Methods: This cross-sectional study was designed as a single tertiary-level academic center. We included 130 female adult patients who had undergone (recto) sigmoid resection for deep infiltrating endometriosis between January 2005 and December 2015. Patients were randomly age-matched to two controls derived from the general population in the Netherlands. We measured the prevalence of constipation, fecal incontinence, Irritable Bowel Syndrome and the Low Anterior Resection Syndrome Score.

Results: The prevalence of constipation, fecal incontinence, and irritable bowel syndrome in the patients was significantly higher than in the controls (50.8% versus 26.2% and 15.4% versus 5.4%, and 14.6% versus 5.4%, respectively, P < 0.05 for each). The prevalence of constipation and fecal incontinence was lower in the patients who had undergone surgery longer than 24 months ago, in comparison with those who had undergone surgery less than 24 months ago (46.7% versus 69.9% and 15.0% versus 17.4%), which was still significantly higher in comparison to the control group. The low anterior resection syndrome score was significantly higher in the patients than in the controls.

Conclusion: The postoperative outcomes in patients treated for deep infiltrated endometriosis regarding constipation, fecal incontinence, and irritable bowel syndrome are suboptimal and do not come close to outcomes in the general female population in the Netherlands. These patients should be screened postoperatively and if necessary, treated for bowel functions.

Keywords: Defecation; fecal incontinence; constipation; irritable bowel syndrome; deep infiltrating endometriosis.

Introduction

Deep infiltrating endometriosis (DIE) is often associated with functional disorders of muscles and organs located in the pelvic floor [1-3]. Chronic pelvic pain, dyspareunia, infertility, increased pelvic floor muscle spasms, and altered bowel habits are common symptoms [4-6]. As a result of the overgrowth of endometriosis different physiological processes in the pelvic floor may also be impaired, leading to problems such as constipation, fecal incontinence (FI), and irritable bowel syndrome (IBS) [7-9]. Previous publications already showed that women with DIE report significant postoperative improvement of their bowel functions after surgical removal of the DIE [10, 11] in comparison to preoperative conditions. Such findings could, however, give patients the vain hope that their health will be restored to the same state as before they fell ill, especially when taking into account that most improvement is based on pain reduction. We know, however, that patients who underwent surgical treatment for DIE still tend to experience pelvic floor muscle tenderness [12] that can give rise to symptoms other than pain. A previous report stated that segmental bowel resection for DIE might be associated with an increased incidence of new bowel symptoms, as a result perhaps of abdominal pain and incomplete bowel movements [13]. Based on our clinical experience, we know that despite postoperative improvement of bowel functions, patients’ bowel functions are still far from optimal. The question is, how far.

To answer this question, we aimed to assess whether frequency and magnitude of defeatory disorders in patients who underwent (recto) sigmoid resection for DIE were comparable to women who never had DIE. We compared the prevalence and odd ratios of defeatory disorders and the spectrum and pattern of their symptoms in patients and women from the general Dutch population who had never undergone surgery and/or had no comorbidities that could influence defeation and fecal continence.
Method

Study design

This cross-sectional study was designed as a single-center study and was performed at the Department of Gynecology in cooperation with the Abdominal Surgery and the Anorectal Physiology Laboratory, both of the Department of Surgery at the University Medical Center of Groningen, the Netherlands.

Defec Questionnaire

The postoperative evaluation of the fecal problems was performed using the validated Groningen Defecation & Fecal Continence questionnaire (DeFeC) [14]. The questionnaire contains questions on demographic issues, symptoms related to constipation, FI and IBS, medical history, and diet. It also contains questions based on the Rome IV criteria for constipation, FI and IBS. The patients and the control group received the same DeFeC questionnaire.

Patient group

First, we screened the medical records of all patients diagnosed with endometriosis between January 2005 and December 2015 (Figure 1). The indications to operate women with DIE were unbearable abdominal and pelvic floor pain and problems with severe bleeding and/or fertility, and the fact that the patients could not have been helped with non-surgical treatment.

Figure 1. Study flow diagram.
Stage IV endometriosis was defined according to the guideline of the American Society for Reproductive Medicine (ASRM), which is “the presence of deeply invasive endometriosis with moderate to extensive adhesions between the uterus and the bowel” [15]. All patients (403) underwent either the pre-surgical Magnetic Resonance Imaging (MRI) at which (recto) sigmoid infiltration was evaluated by the radiologist or diagnostic laparoscopy in which endometriosis lesions in the (recto) sigmoid region were investigated, respectively. After multidisciplinary counseling, patients were subsequently seen in an outpatient appointment, at which point informed consent was taken, all the patients were explained the possible treatment options, their advantages and disadvantages. Optimal pre-surgical work-up was discussed at a multidisciplinary setting, including radiologist, colorectal surgeon and gynecologist. Furthermore, during surgical treatment, biopsies were taken from all patients and endometriosis was pathologically proven.

We initially excluded 221 women who had received endometriosis treatment other than (recto) sigmoid resection and one woman who had a permanent stoma. We invited 181 patients who had received laparoscopic (recto) sigmoid resection surgery at least a year before this study. Both segmental- and discoid (recto) sigmoid resections were included.

Out of the 181 patients, 145 agreed to participate. Of these, 132 patients filled out the DeFeC questionnaire. One woman suffered ulcerative colitis and one woman having Crohn’s disease were excluded. None of the patients reported other somatic diseases that could influence their bowel, such as Diabetes Mellitus, prolapse of the rectum, cerebral hemorrhage or infarction (stroke), neurological conditions such as paraplegia or slow transit constipation. None of the patients reported hereditary conditions such as anal atresia or congenital anorectal malformation, Hirschsprung’s disease, sacrococcygeal syndrome and spina bifida. Also patients who had previously undergone bowel surgery that may have affected their bowel function (e.g. perianal fistula, the anal sphincter or hemorrhoids), were excluded.

Finally, our patient group consisted of 130 women. We distinguished two subgroups: one consisted of the patients who had been treated less than 24 months ago (n=23) and the other of the patients who had been treated longer than 24 months ago (n=107).

**Control Group**

We used the database of the general Dutch population that had been compiled for our previous studies in 2015 [16]. We retrospectively used data on 680 women who had anonymously completed the digital DeFeC questionnaire. For this study, we chose to select a theoretically “healthy” control group by excluding 119 respondents who reported the aforementioned diseases that may influence the bowel function. Subsequently, our control group consisted of 561 women.

For the analysis, we randomly age-matched the patients with women in the control group at a 1 to 2 ratio. The final control group consisted of 260 women. Women who underwent vaginal or any other type of child delivery were not excluded, which we corrected for by using multivariate analysis.

**Data Analysis**

**Determination of constipation, fecal incontinence, Low-Anterior-Resection-Syndrome score and IBS**

Constipation was determined according to the Rome IV criteria that consist of the following items: >25% defecation straining, lumpy, or hard stools, incomplete evacuation, anorectal blockage, manual maneuvers to support defecation, <3 spontaneous bowel movements per week, loose stools are rarely present without prior use of laxatives and insufficient criteria for IBS. To meet the criteria for constipation the respondents had to comply with at least two of these criteria for the last three months with symptom onset at least six months prior to diagnosis [17].

FI was also determined according to the Rome IV criteria, i.e. recurrent involuntary passage of fecal material (solid or liquid stool), including soiling, which occurs at least two to four times during four weeks for the last six months [17]. We also determined certain types of FI. Soiling was characterized by staining of underwear or the loss of small chunks of feces. Urge FI was defined as involuntarily losing of some, or substantial amounts of stool once urge sensation had been reached, but incapable of reaching the toilet on time. Liquid stool FI was defined as involuntary loss of watery stools or diarrhea and solid stool FI as involuntary loss of large amounts of solid feces, irrespective of urge sensation.

In addition, we determined the patients’ Low-Anterior-Resection-Syndrome (LARS) score [18]. Where 0-20 score indicated no LARS, 21-29 indicated minor LARS and 30-42 indicated Major LARS.

We also used the Rome IV criteria to determine IBS according to the following items: recurrent abdominal pain, on average, at least one day a week during the last three months and associated with two or more of the following: defecation, a change in stool frequency, and a change in appearance of stool. Respondents had to comply with at least two of the aforementioned criteria to meet the criteria for IBS [17].

**Statistical Analysis**

IBM SPSS Statistics, Version 23.0 (Armonk, NY, USA: IBM Corp.) was used for statistical analysis. Descriptive statistics were used to characterize the respondents’ demographic characteristics and prevalences. We presented nominal variables as percentages and continuous variables as median and range. Comparisons were made using the chi-square test in case of categorical variables. Mann-Whitney U was used in case of continuous data. Univariate and multivariate regression analyses were used to determine the odds ratios (ORs) with the corresponding 95% CI. The level of statistical significance was set at a probability of <0.05. Microsoft Visio was used to create figures.

**Ethical Approval**

The study was approved by the Medical Ethical Committee of University Medical Center Groningen. All patients gave their written informed consent.

**Results**

**Characteristics of Patients and Control Group**

The median age of the patients at the time of completing the questionnaire was 39 years (range 27-52 years) and 41 years (range 24-55 years) for the control group (P = 0.083). The median time between the (recto) sigmoid resection and completing the questionnaire was 52 months (range 14 - 139 months). The prevalence of vaginal deliveries among the patients was significantly lower compared to the control group (27.7% versus 46.5%, P = 0.001). Out of the 130 patients, 103 (79.2%) had segmental (recto) sigmoid resection and 27 (20.8%) had discoid (recto) sigmoid resection. We found that the prevalence of constipation and FI was not significantly different in patients who had undergone either resection procedure (P = 0.577 and P = 0.492). The median LARS score did not differ either between the patients treated with segmental (recto) sigmoid resections in comparison to those who had discoid (recto) sigmoid (21.0 versus 22.0, P = 0.542). As a consequence, we did not distinguish between the two resection procedures for the rest of the analyses.

**Prevalence of Constipation and Its Symptoms**

The prevalence of constipation in the patients who had undergone (recto) sigmoid resection for DIE was significantly higher than in the control group (50.8% versus 26.2%, P <0.001), Table 1.
Regression analysis confirmed that the patients were almost three times more likely to have IBS than the control group. The OR was 6.846 (95% CI, 2.770-14.863, < 0.001). The prevalence of FI in both subgroups remained significantly higher than in the control group (17.4% versus 5.4%, P < 0.001). When looking at two forms of FI, we found that soiling FI and urge FI were significantly more frequent in the patient group than in the control group (P < 0.001 and P = 0.012), Table 1.

The Co-Occurrence of Constipation and Fecal Incontinence
The prevalence of FI in constipated patients was significantly higher in comparison to the constipated control group (9.2% versus 1.5%, P < 0.001), Table 1. Regression analysis confirmed this observation. The OR was 6.5, (95% CI, 2.056-20.605, P = 0.001).

Prevalence of Irritable Bowel Syndrome
The prevalence of IBS among patients after (recto) sigmoid resection for DIE was significantly higher than in the control group (14.6% versus 5.4%, P = 0.002), Table 1. Univariate regression analysis confirmed that the patients were at higher risk of having IBS than the control group. The OR was 3.0 (95% CI, 1.456-6.215, P = 0.003).

Low Anterior Resection Syndrome Score
The median LARS score was also significantly higher in the patients than in the healthy controls (21.5 versus 16, P < 0.001, Table 2).

| Patents n (%) | Control n (%) | P value | OR (95%CI) | P value* |
|--------------|--------------|---------|------------|---------|
| Total        | 130 (100.0)  | 260 (100.0) | Not applicable | Not applicable |
| Defecation frequency** | 11 (8.5) | 2 (0.8) | <0.001 | 11.924 (2.602-54.642), 0.001 |
| Constipation | 66 (50.8) | 68 (26.2) | <0.001 | 2.912 (1.873-4.527), < 0.001 |

| Symptoms*** | Straining | Hard stools | Incomplete evacuation | Anorectal blockage sensation | Manual maneuvers | <3 spontaneous bowel movements a week |
|-------------|-----------|-------------|-----------------------|-----------------------------|----------------|-----------------------------------|
|             | 88 (67.7) | 36 (27.7)   | 86 (66.2)             | 65 (50.0)                  | 22 (16.9)         | 8 (6.2)                           |
|             | 96 (36.9) | 35 (13.5)   | 83 (31.9)             | 61 (23.5)                  | 25 (9.6)          | 29 (11.2)                         |
|             |           |             |                      |                             |                  |                                   |
|             |           |             |                       |                             |                  |                                   |
|             |           |             |                       |                             |                  |                                   |
|             |           |             |                       |                             |                  |                                   |

Abbreviation: OR - odds ratio; CI – confidence interval
*For the ORs the control group was used as reference; ** > Five times a day for the last six months; ***Some patients suffered from a combination of specific subtypes. Statistically significant differences are indicated in bold font.

Table 1. Prevalence of Constipation, Fecal Incontinence and Irritable Bowel Syndrome, and the Symptoms or Subtypes of these Disorders.

Prevalence of Fecal Incontinence and Its Symptoms
We also found that the prevalence of FI after (recto) sigmoid resection for DIE was significantly higher than in the control group (15.4% versus 5.4%, P = 0.001), Table 1. Regression analysis confirmed that the women with DIE were three times more likely to have FI than the controls. The OR was 3.2 (95% CI, 1.557-6.557, P = 0.002). The prevalence of FI between the subgroup of patients treated less than 24 months ago and the subgroup treated longer than 24 months ago was comparable (17.4% versus 15.0%, P = 0.769). The OR was 1.197 (95% CI, 0.360-3.983, P = 0.769). The prevalence of FI in both subgroups remained significantly higher than in the control group (17.4% versus 5.4%, P < 0.001 and 15.0% versus 5.4%, P < 0.001) as was the likelihood of FI (OR = 1.197, 95% CI: 1.188-13.467, P = 0.052). When looking at two forms of FI, we found that soiling FI and urge FI were significantly more frequent in the patient group than in the control group (P < 0.001 and P = 0.012), Table 1.
| Patients n (%) | Control n (%) | P value |
|---------------|---------------|---------|
| Total         | 130 (100.0)   | 260 (100.0) |
| Total LARS score (median) | 21.50 | 16.00 | <0.001 |
| No LARS*       | 61 (46.9)     | 166 (63.8) | 0.002 |
| Minor LARS     | 37 (28.5)     | 61 (23.5) | 0.284 |
| Major LARS     | 32 (24.6)     | 33 (12.7) | 0.003 |

**Do you ever have occasions when you cannot control your flatus?**

|                      | Patients n (%) | Control n (%) | P value |
|----------------------|---------------|---------------|---------|
| No, never            | 32 (24.6)     | 69 (26.5)     | <0.001 |
| Yes, less than once a week | 51 (39.2) | 114 (43.8) | <0.001 |
| Yes, at least once a week | 47 (36.2) | 77 (29.6) | 0.008 |

**Do you ever have accidental leakage of liquid stool?**

|                      | Patients n (%) | Control n (%) | P value |
|----------------------|---------------|---------------|---------|
| No, never            | 104 (80.0)    | 216 (83.1)    | <0.001 |
| Yes, less than once a week | 24 (18.5) | 42 (16.2) | 0.029 |
| Yes, at least once a week | 2 (1.5)    | 2 (0.8)       | 1.000  |

**How often do you open your bowels?**

|                      | Patients n (%) | Control n (%) | P value |
|----------------------|---------------|---------------|---------|
| Less than once a day  | 36 (27.7)     | 98 (37.7)     | <0.001 |
| 1-3 times a day       | 58 (44.6)     | 152 (58.5)    | <0.001 |
| 4-7 times a day       | 25 (19.2)     | 8 (3.1)       | 0.005  |
| More than 7 times a day | 11 (8.5) | 2 (0.8) | 0.027 |

**Do you ever have to open your bowels again within one hour of the last bowel opening?**

|                      | Patients n (%) | Control n (%) | P value |
|----------------------|---------------|---------------|---------|
| No, never            | 25 (19.2)     | 116 (44.6)    | <0.001 |
| Yes, less than once a week | 73 (56.2) | 119 (45.8) | 0.001 |
| Yes, at least once a week | 32 (24.6) | 25 (9.6) | 0.355 |

**Do you ever have such a strong urge to open your bowels that you have to rush to the toilet?**

|                      | Patients n (%) | Control n (%) | P value |
|----------------------|---------------|---------------|---------|
| No, never            | 58 (44.6)     | 141 (54.2)    | <0.001 |
| Yes, less than once a week | 54 (41.5) | 107 (41.2) | <0.001 |
| Yes, at least once a week | 18 (13.8) | 12 (4.6) | 0.277 |

**Abbreviations:** LARS – Low Anterior Resection Syndrome.

* 0-20 no LARS; 21-29 minor LARS; 30-42 major LARS

**Table 2.** Comparison of the Low Anterior Resection Syndrome Score and its Symptoms between patients and controls.

The controls had a LARS score between 0–20, indicating no LARS, significantly more often than the patients (63.8% versus 46.9%, P = 0.002). More importantly, the prevalence of major LARS was significantly higher in the patient group (24.6% versus 12.7%, P =0.003). In addition, most of the symptoms characteristic of LARS were significantly more frequent in the patients than in the controls. The median LARS score was higher in the subgroup of patients treated less than 24 months ago in comparison with the subgroup treated longer than 24 months ago (24.0 versus 20.0, P = 0.245). There was no difference between major LARS in either subgroup (21.7% versus 25.2%, P = 0.203), however, absence of LARS was significantly more prevalent in the subgroup treated longer than 24 months ago (50.5% versus 30.4%, P = 0.041).

**Risk Factors Associated With Constipation and Fecal Incontinence**

Being a patient was the only significant factor associated with constipation, Table 3.
Discussion

In this study, we show that the postoperative outcomes regarding defecatory disorders, including constipation, FI, their co-occurrence, IBS, and associated symptoms are still far from optimal in patients who underwent (recto) sigmoid resection for DIE, as confirmed by comparison with a control group.

The clinical improvement of patients having surgery for DIE has already been reported before [10, 11]. We show however, that these patients, despite the treatment, still have significantly higher risks of suffering from constipation than women who had never experienced DIE. Consequently, also a broad spectrum of constipation-associated symptoms have been reported by at least half the patients. These include incomplete defecation, anal blockage, hard stools, and straining. Finally, relatively frequent manually supported defecation, or laxative use, also indicate suboptimal outcomes in the patients. Additionally, constipation is known to be a risk factor for FI [19], and indeed, the patients in the current study experienced FI approximately six times more often than non-patients. The high prevalence of different forms of FI, including soiling and urge FI in patients, is also notable, especially when we realize that it is approximately three times higher than in the control group.

Furthermore, it is known that the time of regeneration can contribute to improved postoperative outcomes [10, 11]. Indeed, patients who had undergone surgery more than 24 months before the survey have better outcomes in terms of constipation than patients treated less than 24 months before, albeit not in the case of FI. It seems thus that the period of postoperative regeneration of the pelvic floor may only contribute partially to the improvement of bowel functions.

IBS is also a known risk factor for FI [20-22], and our patients experience IBS more often than the non-patients. We did, however, find that patients who do not experience IBS, still have a more than two times higher risk of having FI than controls. This indicates that IBS is not the only factor that has contributed to the increased prevalence of FI in our patients.

It is known that after low anterior resection patients can develop LARS, and constipation or FI belong to the most typical symptoms of LARS [23-25]. As shown recently, LARS can also be present in the general population [26]. Nevertheless, patients from our study experience Major LARS significantly more often than controls. Vaginal delivery too is often considered a risk factor for developing FI [27-30]. Although we corrected for this cofactor in our analysis the outcomes regarding FI have not changed.

The findings we describe illustrate that although the postoperative outcomes of patients suffering from DIE are known to improve, the patients’ condition remains far from optimal compared to healthy controls.

Limitations

With this study, researchers were unable to establish the direct causes of the suboptimal postoperative outcomes regarding patients’ bowel functions. The defecatory disorders could already have existed before the patients developed DIE, because such disorders also occur in the ‘healthy’ population [26]. The causes could have developed or could have become progressively worse along with the growth of endometriosis. One might also imagine that the surgical intervention caused damage to the pelvic floor and that it influenced bowel functions negatively. Studies reporting on improved postoperative outcomes compared to the preoperative situations, allowed us to reject this possibility [10, 11].

That we did not use a preoperative baseline for our patients might also be seen as a limitation. Such studies, however, have already been performed. Moreover, the preoperative baseline would not have enabled us to answer our question about how far removed patients treated for DIE were from ‘normal women’, that is women who never suffered endometrioses. The ideal baseline would consist of patients before they had DIE, but this is rather difficult to determine. Different diagnostic tests should be performed to diagnose the possible functional causes of postoperative constipation, FI, or IBS. We think that symptoms related to defecatory disorders, including chronic abdominal pain [4], abdominal bloating, painful bowel movements, and painful defecation experienced before treatment for DIE, might in some patients have contributed to inadequate use of their pelvic floor muscles, resulting in dyssynergic defecation [31]. Surgery for DIE removed endometriosis, reduced pain, but it did not remove prior symptoms that, as we demonstrated, still occurred frequently in the patients after surgery. Thus, poor preoperative conditions could have contributed to suboptimal postoperative outcomes.
Conclusion

Patients who underwent (recto) sigmoid resection for DIE are at a significantly higher risk of suffering constipation, FI, and IBS than women who have never experienced DIE. Despite postoperative outcomes of patients treated for DIE improving after 24 months, patients are still far from optimal in comparison to controls. This finding should encourage medical specialists to postoperatively screen their patients for the possible bowel problems, offer adequate treatment when necessary, and in this way, offer a complete care. Moreover, although indirectly, this data adds to the knowledge regarding the cause of the abdominal pain, which belongs to the most frequent criteria to operate patients with DIE. Since constipation can present with a severe abdominal pain, it is possible that a certain cohort of patients diagnosed with DIE and operated due to the abdominal pain, had suffered from constipation already before the (recto) sigmoid resection. Consequently, it is possible that some of the patients might have been helped with non-surgical, conservative treatment for constipation. Following this rationale, we conclude that patients suffering from DIE and suffering severe abdominal pain, should be screened for bowel disease before the decision about surgery is taken.

Recommendations.

Patients should be advised by an experienced medical specialist to undergo diagnostic tests before making decision about surgery to exclude that certain symptoms, for instance abdominal pain, result from a pre-existing bowel dysfunction. Furthermore, medical specialist should take care of postoperative screening of bowel function of their patients, and when necessary, establish the cause of their suboptimal bowel functions and provide with suitable treatment.

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- Oral presentation at the meeting of the European Society for Gynaecological Endoscopy, 7-10 October 2018, Vienna, Austria.

Declarations

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Conflicts of interest: none

Author Contributions:

Study concept and design: Al-Saidi, Klinkert, Hofker, Trzpis, and Broens

Acquisition of data: Al-Saidi, Klinkert, Hofker, Trzpis, and Broens

Analysis and interpretation of data: Al-Saidi, Klinkert, Hofker, Trzpis, and Broens

Drafting the manuscript: Al-Saidi, Klinkert, Hofker, Trzpis, and Broens

Critical revision of the manuscript for important intellectual content: Al-Saidi, Klinkert, Hofker, Trzpis, and Broens

Statistical analysis: Al-Saidi and Trzpis

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