

# Modern treatment of the bowel endometriosis

PhD thesis

**Dr. Péter Lukovich**

Doctoral School of Clinical Sciences  
Semmelweis University



Supervisor: Attila Bokor, PhD, assistant professor

Official reviewers: Pál Ondrejka, PhD, professor  
Zsanett Szigeti, MD, PhD, head of department

Head of the Complex Examination Committee:  
Ferenc Paulin, PhD, professor

Members of the Final Examination Committee:  
István Szabó, PhD, assistant professor  
Zsolt Csapó, PhD, head of department

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## Introduction

The endometriosis is a chronic disease, an endometrium-like glandular- and stroma tissue proliferation outside of the hollow of the uterus. The exact etiology is unknown, the frequency is about 6-10% at the reproductive age females. Separate entity is the deep infiltrating endometriosis (DIE), where the endometriotic tissue infiltration is more than 5 mm from the peritoneum, and about 30% of the all cases. DIE is frequently encountered at the posterior part of the pelvis minor (sacrouterine ligament, rectovaginal spatium) but affects the anterior region of the minor pelvis: can appear on the vesicouterine plica, and can infiltrate the muscle of the bladder, and the disease, which infiltrates the lateral part of the pelvis, can also affects the somatic nerves (hypogastric inferior plexus) which are running there. The endometriosis can appear everywhere in the abdominal cavity, and - although the organs of the minor pelvis are affected most often, - it can appear in the upper part of the abdominal cavity. Therefore not so rare the endometriosis on the diaphragm, removal of the endometrioma is also happened from the stomach and the liver, and lung endometriosis was confirmed in the background of the haemoptysis respectively, which was spread into the tissue of the lung intravascularly like the tumour cell spreading.

The disease affects the urological organs in 14% and the gastrointestinal organs in 12-45% besides the gynaecological organs in the abdominal cavity. The most common signs are the pain in the pelvis (73,4%), dysmenorrhea (76,9 %) which increase in time, dyspareunia at cases the endometriosis infiltrate the vagina, haematochezia caused by the infiltration of the bowel, stool passage difficulties, dysuria and haematuria at the cases endometriosis affects the urological organs and ureter compression. Beside these signs the endometriosis associates with infertility: at 50% of the women with fertility problem has endometriosis.

Making of the diagnosis of the endometriosis usually late for years. From the first signs it is need usually 10 years in Germany and Austria, 6 years in Norway, and only 3.9 years in Hungary. The early diagnosis should be important, because the often really severe complains caused by the deep infiltrating endometriosis affects the quality of life of the patients unfavourably. Economic importance of the disease according to the data of the literature - beside the medical expenses - is impaired health and decreased ability to work.

The diseases became more frequent in the last two decades, and the number of the operated patients also increased significantly. Because the disease infiltrate not only the

gynaecological organs at 10-40% of the cases, but the bowels and/or the urological organs too, the strict, long-term and systematic cooperation with other professions is required in the surgical treatment: the multiorgan operation in one course is less loading for the patient, rational and suggested in financial view, too. Therefore multidisciplinary teams are developed more places all over the world to the treatment of the disease.

The laparoscopic surgery of all the three affected specialization (gynaecology, urology, surgery) had significant evolution in the last decades, and nowadays all the affected organs could be operated by minimal invasive technique, with the help of the experts of the laparoscopic surgery.

## Aim of the study

The aim was to involve a new diagnostic procedure into the preoperative check-up, which has higher specificity and sensitivity at the infiltration of the bowel needs resection than the previous methods. For this the colonoscopy was chosen, which is suggested firstly to the large bowel diseases.

### **The aim of the study:**

1. Definition of the endoscopic signs of the bowel endometriosis
2. Definition of the frequency of the endoscopic signs
3. Comparing the results of the sigmoidoscopy and the intraoperative situation
4. Comparing the results of the sigmoidoscopy with the histology
5. Definition the sensitivity and specificity of the sigmoidoscopy in the diagnosis of the bowel endometriosis

### **The aim of the study of the laparoscopic operation:**

1. Measuring the operating time decrease at the operation with the same assistant

**Further aim was the examination of the applicability of the newest minimal invasive method, the NOSE in the surgical treatment of the bowel endometriosis.**

1. Development of the safety steps of the transrectal specimen extraction
2. Definition of the complication of the transrectal specimen extraction
3. The effect of the transrectal specimen extraction on the operating time

## Method

On 14th of July, 2009 a multidisciplinary team (gynaecologist, surgeon, urologist) was formed for the purpose of treating patients with deep infiltrating endometriosis at Semmelweis University.

Before the operation bimanual gynaecological examination, transvaginal ultrasound, MRI, and - at the suspicion of bladder endometriosis – cystoscopy was made.

The verification of the bowel endometriosis by sigmoidoscopy was approved by the Institutional Ethical and Review Board of Semmelweis University for the protection of human subjects (No: 162/2016)

Our study protocol on the transrectal specimen extraction was approved by the Institutional Ethical and Review Board of Semmelweis University for the protection of human subjects (No: 58723-4/2016/EKU)

## Results

### Sigmoidoscopy in the diagnosis of the endometriosis infiltrate the bowel

Between 20th August of 2009 and 1st of October 2014 in a prospective study routine sigmoidoscopy was made to confirm of the bowel infiltration at 383 patients treated by endometriosis.

During the examination the signs of the bowel endometriosis were observed.

The success rate of the full sigmoidoscopy, the number and the distance of the lesion(s) from the anus were also examined.

### **Endoscopic signs and causes of the endometriosis infiltrate the bowel**

The endometriosis infiltrate the deeper layers of the bowel from the peritoneum, therefore the subperitoneal, muscular layer (64%) affected most often, a the submucosal layer infiltrated at 25%, but only at 11% affected the mucosa, -and appear – and histologically certify – in the lumen obviously.

Therefore we should lean only the secondary signs at 95-97% of the cases during the colonoscopy.

The endometriosis on the surface of the peritoneum of the bowel fixes the bowel to the surrounding tissue, and the affected, clinically scary area loses its flexibility. These two facts lead to the secondary signs that should be visible during the colonoscopy.

The following differences have been found during the examination:

1. intraluminal endometriosis,
2. secondary signs of the endometriosis infiltrating the bowel
  - rigidity of the wall.
  - impression,
  - kinking,
  - submucosal suffusion,
  - and pain at the examination made without narcosis.

## **Endoscopic signs of the bowel endometriosis**

### *Kinking*

The endometriotic nodule is not affected the lumen concentrically. The wall of the bowel is not able to expand at the infiltrated area, and will be fixed, while the wall on the opposite side the wall will expand. Because of this the normally concentric folds converge to the direction of the endometriosis, and develops significant kinking. This counteracts in a part of the cases to lead up the instrument through this area.

### *Impression*

The reason for the impression during the examination is that the scary part of the bowel is not able to expand either crosswise and longitudinally so much than the not affected part during the examination, which has been detected as an impression during the colonoscopy. Of course the nodule itself looks like an impression on the screen.

### *Rigidity of the wall*

The instrument could be led by the positioning the tip. The wall became rigid on the area where the endometriosis infiltrate the wall of the bowel therefore the tip of the instrument cannot turn in the correct direction, the lumen cannot see, the instrument jams at the affected area. The endometriotic nodule causes „S” curve, and although the flexibility of the instrument is enough to turn the first bend, the second one exceeds the flexibility of the instrument. In these cases – when the assistant leads the instrument – already the assistant feels, that the instrument cannot move on the ordinary way. Because the endometriotic nodule infiltrate the

surrounding tissues (sacrouterin ligament, vagina) too, the traction of the region should be painful for the patient.

#### *Submucosal suffusion*

The submucosal suffusion should be the consequence not only the endometriosis. The preparation of the bowel for the colonoscopy should make small suffusions, too. But together with the other signs – especially, if there is blood in the lumen at the same time – should be a pathological sign.

#### *Intraluminal endometriosis*

The histology of the specimens of the bowel resected because of endometriosis confirmed that endometriosis infiltrate the mucosa only in 2-4%. The endometriosis can be seen usually as a nodular, bloody, foreigner tissue at the examination, and the affected area is soft when taking biopsy. The histology will be also positive if the disease is intraluminal.

#### *Pain during the examination*

There are no nociceptors in the bowel. The patients have no any pain during taking biopsy or polypectomy. But there are baroreceptors in the wall of the bowel, which cause pain for the patients at strain. The intensified insufflation because of the difficult leading of the instrument caused by the kinking, and the tension of the wall caused by the instrument are painful for the patient. There should be role of the baroreceptors in the pain in the dysmenorrhea when the hormonal effects make oedema in the wall of the bowel, and in the pain in the rectum during the menstruation.

#### *Other findings*

Although the risk of the other diseases is small, there should be come to light other differences. These were polyps most frequently. When polyps were detected during the sigmoidoscopy (4 cases) colonoscopy was made instead of sigmoidoscopy, and the polyp was removed.

One of our examination draw the attention the importance of the sigmoidoscopy, where the diagnostic examination was made at a patient who had earlier a resection of the sigmoid bowel because of endometriosis in another hospital. They were not able to explore the infraperitoneal region during the operation, therefore there was not detected the intraluminal endometriosis in the rectum, which was removed later by our team laparoscopically.

### **Result of the sigmoidoscopy**

Histology of the surgically resected bowel proved infiltration of the mucosa at 11 cases (100%), infiltration of the submucosal layer 80/97 cases, and 16/97 cases muscular layer, and 1/97 cases only the subserosal layer, but it affected a long segment of the rectosigmoid bowel.

The median age at diagnosis was 32.7 years, with a range of 19 to 41 years.

In 224 of the 383 cases (58.49%) bowel endometriosis has been diagnosed based on the colonoscopy findings.

The endoscopic signs frequency were the next:

Intraluminal endometriosis – soft, nodular mass in the lumen - had been identified only in 11 patients (4.91%).

The incidence of secondary signs were: kinking 57.14% (Figure 2.), stenosis-impression 45.54%, wall rigidity 38.39%, pain – when examination was performed without narcosis - 26.06%), and suffusion 3.82%.

The complete sigmoidoscopy was feasible only in 34.7%. The unsuccessful examination was due to the significant kinking, stenosis or pain.

Multilocular recto-sigmoid endometriosis were found at 14.73% of the patients at sigmoidoscopy.

The segments affected by endometriosis were: distal rectum (0-10 cm) 17 patients, middle part of the rectum (10-15 cm) 65 patients, recto-sigmoid junction (15-20 cm) 68 patients, aboral sigma colon (20-25 cm) 44 patients, proximal part of the colon (25-50 cm) 62 patients.

Until the completion of the study, 108 patients underwent multidisciplinary surgery from the endoscopically positive cases. (Some patients of positive cases is still on waiting list or there was no indication of operation or they refused the surgery.) In the operated patients the deep bowel infiltration required colonic resection at 103 cases. In the other 5 cases there was an ovarian carcinoma with peritoneal carcinosis (Douglas metastasis), postoperative adhesions was found due the previous operations at 2 cases, whereas in the remaining 2 cases the bowel endometriosis was removable with only shaving technique.

From the endoscopically negative cases overall 135 patients underwent gynaecological surgery; the endometriosis infiltrated the deeper layers, and was not suitable for shaving at 8 patients.

The sensitivity and specificity of the sigmoidoscopy was 92.8% and 96.2% respectively.

There were appendicular and coecum endometriosis in 2-2 patients respectively among the 238 patients who underwent laparoscopic surgery. In these cases appendectomy and coecum excision were performed.

Only the  $\frac{1}{4}$  of the circumference of the resected bowel was infiltrated by the endometriosis at more than 80% of the cases (most frequently the anterior wall, beside the vagina), which caused usually significant signs. The reason is not only the impression caused by the nodule, but he lost flexibility of the part of the bowel infiltrated by the endometriosis.

## **Results of the laparoscopic operations**

### *Results of laparoscopic operation with traditional and NOSE technique specimen extraction*

There were operated on 1240 patients with endometriosis between 2015 January and 2017 January. There were detected endometriosis at 256 patients, and there were segmental resection at 90 patients. There were enough rectal shaving or discoid resection at the remainder 166 patients.

The transrectal NOSE technique was practiced at the first 30 patients, and after the next 30 NOSE patients data was compared prospectively with the next 60 patient was operated traditionally, with transabdominal specimen extraction.

The average age of the patient were 32 years (24-48) at the time of the operation in the traditional group and 33 years (25-45) in the transrectal group. All patient have got hormone therapy (oral contraceptive or dienogest) before the operation and there was no significant difference in the BMI of the patients. There were earlier laparotomy because of endometriosis at 10% of the patients in the traditional group, while there were 6% of this value in the NOSE group.

There was no any significant difference in the white blood cell number at the operated patients on the 1st and 2nd day. (Kolmogorov Smirnov test, Mann-Whitney test:  $p=0.359$ , unpaired t-probe  $p=0.208$ )

### *Location of the endometriosis in the pelvis*

The average, median and range of the revised American Fertility Society scores which is used for the division of the operated endometriosis patient are summarized in the Table 3. Endometriosis was present in areas other than the colorectal region in most cases, most commonly, these were found in the rectovaginal septum, pelvic peritoneum, and the ovaries



Eight patients (13%) in the traditional group and two (7%) in the transrectal group required vaginal resection because of transmural vaginal involvement.

The bladder was infiltrated in 18% of the traditional and 20% of the transrectal group ( $p = .85$ ). Ureteral endometriosis was present in 18.7% of the transrectal and 10% of the traditional group ( $p = .32$ )

The anastomosis line was between 5 and 8 cm from the anal verge at more than 50% of the cases at both group. ( $p=0.65$ ).

A single nodule was detected during histologic examination in 56% in the NOSE group and 58% in the traditional group ( $p = .88$ ). Multifocal (2 or more) lesions were diagnosed in 44% of the specimens from the NOSE colectomy group and 42% in the traditional group.

The length of the resected bowel section varied from 5 to 29 cm; the average length was 10 cm in the traditional group and 7 cm in the transrectal group ( $p = .31$ )

### *Surgical complications*

There was anastomosis insufficiency at two patients (3,3%) in the traditional group, while there was no in the transrectal group. ( $p=0,55$ ) In one of the previous two cases a rectovaginal fistula has been also developed (1,7%, 1/60 cases), In this case at the resection of the endometriotic nodule infiltrate the whole wall the vagina opened. In total serious complication (Clavien-Dindo IIIb or more) was 3,3% in the transrectal group.

At the detection of the rectovaginal fistula re-laparoscopy and sigmoideostomy was made immediately. Three months later, after check-up the closure of the fistula gynecologically and colonoscopically the stoma was closed by laparoscopic way.

Laparoscopic suturing and making stoma deviation was made at the other case with anastomosis insufficiency.

At one patient in the traditional group bleeding was the detected from the place of the umbilical port, which stopped with conservative therapy.

Temporary bladder dysfunction (bladder retention) was at 2 patients in the traditional group (3.3%) and at 1 patient (3%) in the tranrectal group ( $p=1$ ). Per oral pyridostigmine (3x60mg/day) treatment have got all the patients in both groups, and complains were disappear in maximum 7 days.

There were no significant difference in the blood loss, too ( $p=0.82$ ).

In the traditional group recidiv disease was detected at a patient as a late complication (1.7%) in spite of the postoperative ovarium suppression and continuous oral anticoncipient

taking. Another infraperitoneal nodule has been found 5 cm aborally from the previous anastomosis line which was removed a discoid resection during a laparoscopic operation.

There was no recidiv endometriosis in the NOSE group.

### *Histologic results*

Histologic examination confirmed bowel endometriosis infiltrating the muscular layer in 81 of 90 cases, and in 9 (10%) cases the mucosal layer was also involved.

### *Staying in hospital*

The patients were admitted a day before the operation routinely, the preparation (purgation) for the operation was on the operation. The patients went home after the first stool. The median length of hospital stay in the CG was 7 days (95% confidence interval [CI], 5–13) days, whereas in the TRG it was 6 days (95% CI, 3–11). Both groups postoperative hospital stay was one day shorter, because the patients were admit a day before the operation. Patients in the NOSE group had a shorter time of hospitalization compared with the CG ( $p < .001$ ).

## **Changing in the operation time**

There was a good possibility to measure how change of the operation time, because all the analysed operation was made same surgeon with the same assistant.

There was 8 years' experience with the gynaecologist in the laparoscopic surgery of the endometriosis and the surgeon made laparoscopic large bowel resection for 6 years at the formation of the multidisciplinary team – that is, both of them had significant experience in the laparoscopic surgery. In spite of this there was significant improvement in the operation time of the traditional, transabdominal specimen extraction. While the average operation time at the first 20 operation was 300 minutes (min: 180 minutes / max: 560 minutes), until there was 110 minutes (min: 60 minutes / max: 160 minutes) the operation time at the last 20 cases.

While the operating time at laparoscopic cholecystectomy – at the end of the learning curve – decrease only with 40% based on the literature, at the endometriosis operation made by us it reached the 60%. There was role in this – beside the characteristics of the disease – the multidisciplinary cooperation, which needs compromise from both persona at the beginning (other instrument, other place of the trocar, other assistant). Acquiring the operation and getting together the members of the team, the operating time decrease significantly.

Comparing the transabdominal and transrectal specimen extraction the facts increase and decrease the operating time must review.

- **Increase the operating time** the ligation of the bowels and insertion of the purse string suture.
- **The operation time is shorter** with the time of the laparotomy and the closure of the incision.

There was a statistically significant difference between the duration of surgeries in the conventional (CG) when compared with the transrectal TRG (CG: median = 121 minutes [range, 85–205 minutes] and TRG: median = 96 minutes [range, 60–190 minutes);  $p = .005$ ).

## Conclusions

**Based on results can be declared with the examination of the endometriosis, that:**

1. Sigmoidoscopy is a useful diagnostic tool in the preoperative examination of the bowel endometriosis
2. 98% of the nodules (55-60 cm from the anus) can be detected by sigmoidoscopy. The affected proximal part of the bowel was less than 2% in our series.
3. Besides the sigmoidoscopy is more time- and cost effective, and less stressful for the patient than the colonoscopy.
4. The endometriosis appear only 2-4 % in the lumen, because the endometriosis infiltrate the wall of the bowel from outside. Therefore endometriosis can be concluded based on the secondary signs in more than 95% of the cases.
5. The secondary signs of the endometriosis infiltrated by the endometriosis in frequency order are the next: rigidity, impression, kinking, suffusion
6. The examination is painful for the patient, because the rigidity of the wall of the bowel, the kinking and stretching the surrounding tissues by the ligaments of the minor pelvis infiltrated by the endometriosis.
7. Sigmoidoscopy – done by experienced gastroenterologist - is a high specificity and sensitivity diagnostic examination at the endometriosis which involve the large bowel.

**Stated about the NOSE technique first time applied by us:**

1. The transrectal specimen extraction – used the technique developed by us – is a safety surgical procedure
2. A transrectal specimen extraction operating time is shorter than the traditional, transabdominal specimen extraction

3. More than 50% decrease can achieve in the operating time at complex, long operation with accustomed team.
4. The postoperative hospital stay is significantly shorter after NOSE procedure

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