

Laparoscopic treatment of bowel endometriosis in infertile women

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BACKGROUND: The purpose of the study was to determine the influence of bowel endometriosis on fertility, and to study whether its removal improves fecundity in women with endometriosis-associated infertility.

METHODS: Three groups of infertile patients were included in the study. Group A (60 women) consisted of patients who underwent surgery for endometriosis with colorectal segmental resection. In group B, 40 patients with evidence of bowel endometriosis underwent endometriosis removal without bowel resection. Group C consisted of 55 women who underwent surgery for moderate or severe endometriosis with at least one endometrioma and deep infiltrating endometriosis but without bowel involvement. The women were clinically evaluated before laparoscopy and then at 1 month, at 6 months and at each year up to 4 years after surgery. Main outcome measures were surgical complications as well as post-operative pregnancy rate, time to conception and monthly fecundity rate.

RESULTS: The monthly fecundity rates (MFR) in groups A, B and C were 2.3, 0.84 and 3.95%, respectively. The difference in the MFR between groups was significant ($P < 0.05$).

CONCLUSIONS: The presence of bowel infiltration by endometriosis seems to negatively influence the reproductive outcome in women with endometriosis-associated infertility. The complete removal of endometriosis with bowel segmental resection seems to offer better results in terms of post-operative fertility.

Key words: bowel endometriosis / infertility / pregnancy rates / laparoscopy / segmental bowel resection

Introduction

Endometriosis is characterized by the presence of the endometrial glands, and stroma outside of the uterine cavity. It primarily affects women of fertile age, and represents a relevant clinical issue as it causes pain (Koninckx *et al.*, 1991; Fauconnier *et al.*, 2002) and infertility (Pouly *et al.*, 1996; Fauconnier *et al.*, 2002). The incidence of the disease seems to have increased in recent years, but it is not easy to distinguish whether it really affects the population more frequently, or whether the diagnosis is more frequent because of the diffusion of diagnostic tools such as ultrasound and laparoscopy. Endometriosis affects about 5–15% of the general population while the incidence in infertile women is as high as 48% (Starthy *et al.*, 1982; The Practice Committee of ASRM, 2004). The monthly fecundity has been reported to be reduced (Akande *et al.*, 2004) by up to 50% in the presence of the disease (Hughes *et al.*, 1993).

The mechanism of infertility is not clear (Pritts and Taylor, 2003), however surgical treatment in early-stage endometriosis (rASRM

stage I–II) increases the pregnancy rate (Marcoux *et al.*, 1997; Jacobson *et al.*, 2002; Kennedy *et al.*, 2005). In moderate and severe endometriosis (rASRM stage III–IV), infertility may be caused by distorted pelvic anatomy and in these patients as well, surgical treatment confers benefit (Donnez *et al.*, 2002; Suginami *et al.*, 2002).

The incidence of bowel infiltration among women with endometriosis is between 6 and 12% (MacAfee and Hardy Greer, 1960; Weed and Ray, 1987; Jerby *et al.*, 1999; Chapron *et al.*, 2003). The most frequently affected sites are the rectum and rectosigmoid junction which account for up to 93% (Coronado *et al.*, 1990; Bailey *et al.*, 1994; Tran *et al.*, 1996) of all intestinal endometriosis lesions. Recent studies suggest that complete excision of deep endometriosis with bowel resection leads to a reliable and persistent relief of pain symptoms and improvement of quality of life (Canis *et al.*, 1996; Duepree *et al.*, 2002; Abbott *et al.*, 2003; Kavallaris *et al.*, 2003; Ford *et al.*, 2004; Thomassin *et al.*, 2004; Fleisch *et al.*, 2005; Dubernard *et al.*, 2006; Landi *et al.*, 2006; Ferrero *et al.*, 2008), however, little data are available on fertility and pregnancy outcome after bowel resection

for endometriosis (Jerby *et al.*, 1999; Possover *et al.*, 2000; Redwine and Wright, 2001; Darai *et al.*, 2005; Mohr *et al.*, 2005), and particularly after such treatment in infertile women.

The aim of the present study was to determine the influence of bowel endometriosis on fertility, and to study whether its removal improves fecundity in women with endometriosis-associated infertility.

Methods

Patients and treatments

Three groups of patients were included in the study. All of them suffered from infertility for at least 1 year and underwent laparoscopic surgery between May 2000 and May 2005 in our referral centre for endometriosis. Indication for endometriosis surgery was severe pelvic pain refractory medical treatments or severe bowel or ureteral stenosis due to endometriosis. All cases referred to our centre during the study period and who fit the entry criteria were considered for this study and a prospective follow-up was carried out.

Group A (60 women) consisted of patients with endometriosis who underwent laparoscopy with colorectal segmental resection because of the strong pain often associated with an relevant bowel stenosis, as diagnosed through double-contrast barium enema (Landi *et al.*, 2004; Faccioli *et al.*, 2008). In group B, all 40 patients underwent laparoscopic endometriosis eradication without bowel resection, due to the lack of the patient's consent, despite the presence of colorectal endometriosis. Group C consisted of 55 women affected by moderate or severe endometriosis (rASRM stage III–IV) with at least one endometrioma and deep infiltrating endometriosis but without bowel involvement. Patients older than 40 or women who underwent surgery for bowel endometriosis other than segmental resection (discoid resection, mucosal skinning and superficial excision) were not included in the study. In all cases, endometriosis presence was confirmed by histology.

Preoperative evaluation included a careful detailed history, and an assessment of pain using a visual analogue scale (10 point rating scale: 0 = absent, 10 = unbearable) for four components of endometriosis-related pain: dysmenorrhea, non-menstrual pelvic pain, dyspareunia and dyschezia. Rectovaginal examination, transvaginal pelvic ultrasound scan, double-contrast barium enema and ultrasonography of the urinary tract were also performed in all cases.

Investigation of fertility problems included a semen analysis for the partner. No tests for tubal patency were performed before surgery, but the tubal factor was evaluated intraoperatively through a dye-test. No preoperative hormonal therapy was given for at least 4 months before surgery. All women were counselled regarding the potential benefits and risks of the surgical procedure and each gave written informed consent.

Data on patients' parity, infertility history, previous abdominal laparoscopic and laparotomic surgery for endometriosis or other problems, operating time and intra- or early post-operative complications were prospectively recorded in a database.

In all cases, surgery was performed by laparoscopy. Each procedure was performed using a 10 mm laparoscope in the umbilical position and three 5 mm trocars. At the beginning, an accurate check of pelvic and abdominal organs was performed and successively adnexal adhesions, when present, were removed. If endometriomas were present, steeping and temporary ovarian suspension was performed. Complete excision of all visible endometriosis lesions from healthy tissue was performed using 5 mm bipolar scissors working from the retroperitoneal, according to technique described by Redwine (2004), and the pre- and post-operative management has already been reported in previous studies performed in our centre (Landi *et al.*, 2006, 2008; Mereu *et al.*, 2007). The intestinal

surgery was performed by a specialist colorectal surgeon, and the T–T colorectal anastomosis was done transanally with a 28–32 mm circular stapler. Colorectal resections were classified as very low (less than 4 cm from the anus), low (4–8 cm from the anus) or high (more than 8 cm from the anus). All patients who were candidates for IVF were given post-operative GnRH analogues for 6 months.

All women were clinically evaluated at 1 month, at 6 months and at each year up to 4 years after surgery. Follow-up consisted of a rectovaginal examination, transvaginal ultrasonography to evaluate endometriosis recurrence and a careful questionnaire about infertility treatments, pregnancies, changes in bowel, urinary and sexual function and any further surgery. At every follow-up, an evaluation of pain score was made using a visual analogue scale (the same as before surgery) for dysmenorrhea, dyspareunia, dyschezia and pelvic pain. All subjects participated in the follow-up study.

Statistics

Data were collected in the Microsoft Excel 2001 for Macintosh datasheet.

Continuous variables were expressed as arithmetic mean \pm SD; in case of quantitative variables extremely asymmetric, the indicators were associated with the median and interquartile ranges. Categorical variables were expressed as distributions of absolute or relative frequencies.

The variance analysis by *F* test or Welch and Brown–Forsythe test was used, and the Leven test was applied when heteroskedasticity was present or when appropriate.

The analysis of cooperation of categorical variables was evaluated by the χ^2 Pearson test and the force of cooperation was measured by the coefficient of contingency.

The distribution of pregnancies during follow-up time was studied by the Kaplan–Meier curve and the differences were compared by the log-rank Mantel–Cox test.

To analyse mean changes of symptomatology, the analysis of variance was applied (*F* test and Welch and Brown–Forsythe test).

All statistic tests and confidential intervals were created with 5% level of significance. The data analysis were performed with SPSS version 14.0.

Results

The patient surgical history in the three groups was similar (Table 1). Most (62.5%) of the patients had already been operated for endometriosis.

Preoperative bowel enema was positive in 59 patients (98%) in group A and in 49 (95%) in the group B, while the mean bowel stenosis was of 49 and 23%, respectively. Most patients with stenosis <20% refused to undergo bowel surgery. The mean length of the stenotic tract was 3.78 ± 2.18 cm in group A and 2.75 ± 0.53 cm in B group. In all cases in group A, the presence of bowel endometriosis was confirmed by histology. Four patients of this group had endometriosis nodules in two different sites of the bowel tract, and five patients had a monolateral hydronephrosis. Additional surgical procedures in group A were: resection of cecum (4 cases), ileal resection (5), vaginal resection for endometriosis (8), bladder endometriosis resection (5), enucleation of bilateral (10) or monolateral (23) endometriomas, appendectomy (1), monolateral parametrectomy (4) and monolateral salpingectomy (2).

In all cases of group B, the presence of bowel endometriosis was confirmed at laparoscopy and in all of them it involved the rectosigmoid tract. One patient of this group also had endometriosis of the ileum and it was not resected. The other sites of endometriosis

Table I Characteristics of patients trying to conceive

All patients	Group A (bowel resection) N = 60	Group B (residual bowel endometriosis) N = 40	Group C (no bowel involvement) N = 55	Statistic analysis
Previous laparotomy for endometriosis	12 (20%)	9 (23%)	5 (9%)	NS
Previous laparoscopy for endometriosis	33 (55%)	12 (40%)	16 (29%)	NS
Patients trying to conceive	Group A (bowel resection) N = 48	Group B (residual bowel endometriosis) N = 39	Group C (no bowel involvement) N = 46	Statistical analysis
Previous infertility (years) mean \pm SD	2.48 (\pm 2.173)	2.79 (\pm 1.641)	2.41 (\pm 1.613)	NS
Tubal occlusion	2/48	2/39	2/46	NS
Male infertility factor	2/48	2/39	2/46	NS
Peritubal adhesions mono- and bilateral	37.5%	46.2%	19.6%	NS
	33.3%	33.3%	41.3%	
Secondary infertility	8.3%	23.1%	8.7%	NS
BMI (mean \pm SD)	21.34 (\pm 3.84)	22.46 (\pm 3.19)	20.99 (\pm 2.36)	NS
Age (mean \pm SD)	31.67 (\pm 3.61)	33.48 (\pm 4.59)	32.35 (\pm 3.82)	NS

Table II Pregnancies obtained spontaneously, or with IUI or IVF, performed after surgery

Post-operative treatment	Group of patients	Number of patients who conceived	Number of miscarriages
IVF	A (segmental resection) N = 13	5	1
	B (residual bowel endometriosis) N = 13	1	0
	C (no bowel endometriosis) N = 6	4	0
IUI	A (segmental resection) N = 5	0	0
	B (residual bowel endometriosis) N = 3	0	0
	C (no bowel endometriosis) N = 6	4	1
Spontaneous conception	A (segmental resection) N = 30	12	0
	B (residual bowel endometriosis) N = 23	7	1
	C (no bowel endometriosis) N = 34	24	4 + 1 extrauterine pregnancy

which were not removed during surgery were: the vaginal wall (one case), and the parametrium in another two cases. Additional surgical procedures in this group were: 16 monolateral and 8 bilateral enucleations of endometriomas and two monolateral salpingectomies. In one patient, endometriosis was also present at the scar of a previous laparoscopy.

In group C, the procedures performed were: bladder resection (1 patient), monolateral parametrectomy (1 patient), monolateral salpingectomy, monolateral (37) or bilateral (18) enucleations of endometriomas and one asportation of endometriosis at the abdominal wall scar. In seven women, vaginal wall endometriosis was resected. The most frequent symptoms were dysmenorrhoea (98% in group A, 98% in group B, 65% in group C), dyspareunia (72%, 65%, 64%, respectively) and dyschezia (72%, 33%, 42%, respectively). Other symptoms included non-menstrual pelvic pain (52%, 53%, 35%) and dysuria (20%, 5%, 9%). Five patients of group A suffered from rectorrhagia before bowel resection.

The clinical characteristics of patients who tried to conceive during the follow-up period were similar in all groups (Table I). All patients suffered from infertility before surgery. In Table I, we reported

patients who after surgery, during the follow-up period, tried to conceive. Some patients did not try to conceive because of different reasons such as a change of the partner, occurrence of health problems in the patient (e.g. breast cancer) or the partner (e.g. chemotherapy for lymphoma) or a change of plans (e.g. adoption). Also patients who had a clear indication for IVF (male or tubal factor) and who refused IVF treatment were considered as not trying to conceive.

The mean infertility duration in all groups was more than 2 years and there were no differences between the incidence of primary and secondary infertility. Only two patients in each group presented a tubal occlusion, and two couples in each group had severe male factor infertility. There were no differences in age, BMI or peritubal adhesions found during surgery.

The mean follow-up period was 26.9 months. In group A, 17 (35%) conceived after surgery, in group B, 8 (21%) conceived and in group C, 32 (70%) conceived ($P = 0.03$).

There was extrauterine pregnancy, as well as seven miscarriages, while the other conceptions resulted in term pregnancies (Table II). Most of the pregnancies were obtained spontaneously. None of the

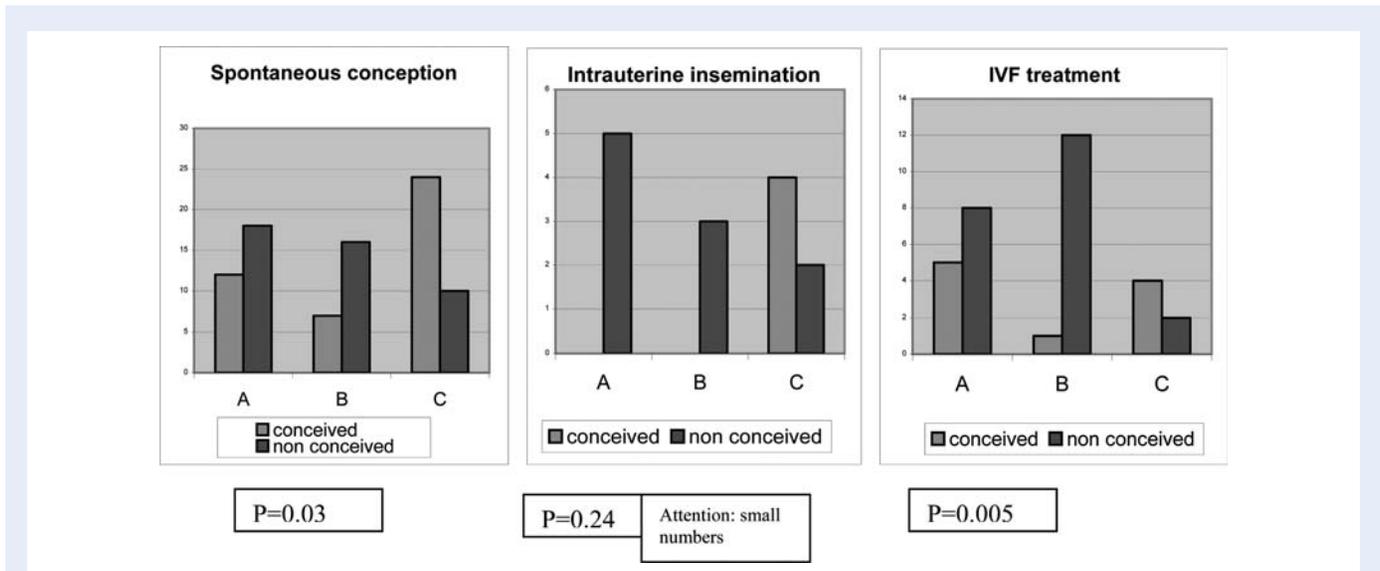


Figure 1 Pregnancies obtained spontaneously, with IUI, and with IVF treatment performed after surgery. Group A: bowel resection, Group B: residual bowel endometriosis, Group C: no bowel endometriosis.

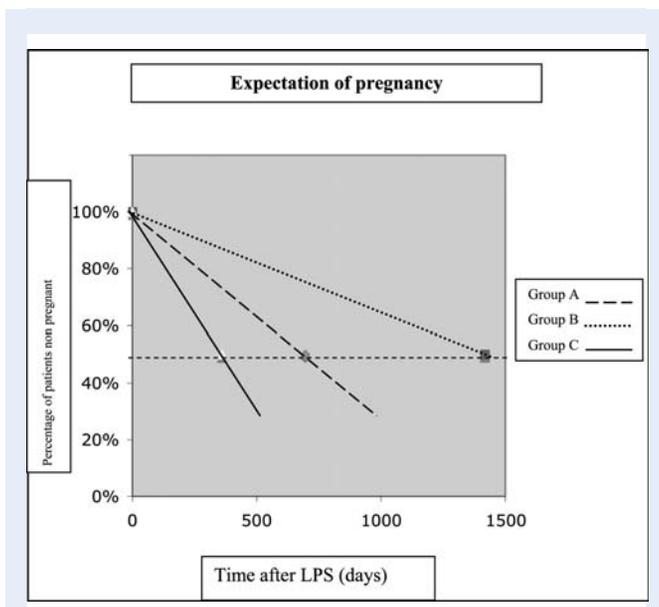


Figure 2 Time passing from surgery to the moment of obtaining half of pregnancies in three groups.

In group A (bowel resection) half of pregnancies were obtained after 696 days, in group B- after 1417 days and in group C- after 361 days from surgery.

patients with bowel endometriosis (group A or B) who underwent intrauterine insemination (IUI) conceived, although the numbers in these groups were small.

Among patients who tried to conceive spontaneously, the pregnancy rate was lower if bowel endometriosis was present (group A or B compared with group C). There was a strong association ($P = 0.005$) between the classification of patients into groups (A, B, C)

and spontaneous fertility (Fig. 1). Among women with bowel endometriosis, the reproductive outcome was better if bowel resection was performed ($P = 0.03$).

After the first pregnancy, one patient in group A, four in group B, and eight in group C tried to conceive, and one, one and six in each group, respectively, conceived again.

The differences in reproductive outcome between groups are evident not only for the cumulative pregnancy rate but also in terms of the time necessary to conceive. Fig. 2 shows the time necessary to obtain half of pregnancies in every group. In group A, this time was shorter (696 days) than in group B (1417 days). In group C only 361 days were necessary to obtain half of pregnancies. The difference in interval-to-conception between groups was significant ($P < 0.05$). The monthly fecundity rates (MFR) in groups A, B and C were: 2.3, 0.84 and 3.95%, respectively. The difference in the MFR between groups was significant ($P < 0.05$).

Fig. 3 shows the distribution of pregnancies using the Kaplan–Meier curve. The best results were obtained in the group without bowel endometriosis (group C). If bowel endometriosis was present, its removal improved the post-operative fertility. The long-rank Mantel–Cox test confirmed that the distribution of survival is statistically different ($P = 0.03$), so there was a difference in the post-operative fecundity between the three groups.

There were no cases with surgical evidence of recurrence in group C, while in group B the surgical evidence of recurrence was more frequent (15%) than in group A (7%, $P = 0.03$).

The main surgical complications which occurred in group A were two anastomotic fistulas (3.2%), both after a very low bowel resection. The other early (before a month after surgery) post-operative complications in group A were: ureteral lesion (1.6%), bladder lesion (1.6%), bowel occlusion (1.6%) or severe blood loss (12.8%) treated by hemotransfusion (6.4%) or autotransfusion (6.4%).

Urine retention for less than 1 month was present in 15 patients (25%) in group A, and the mean time of autocatheterization after

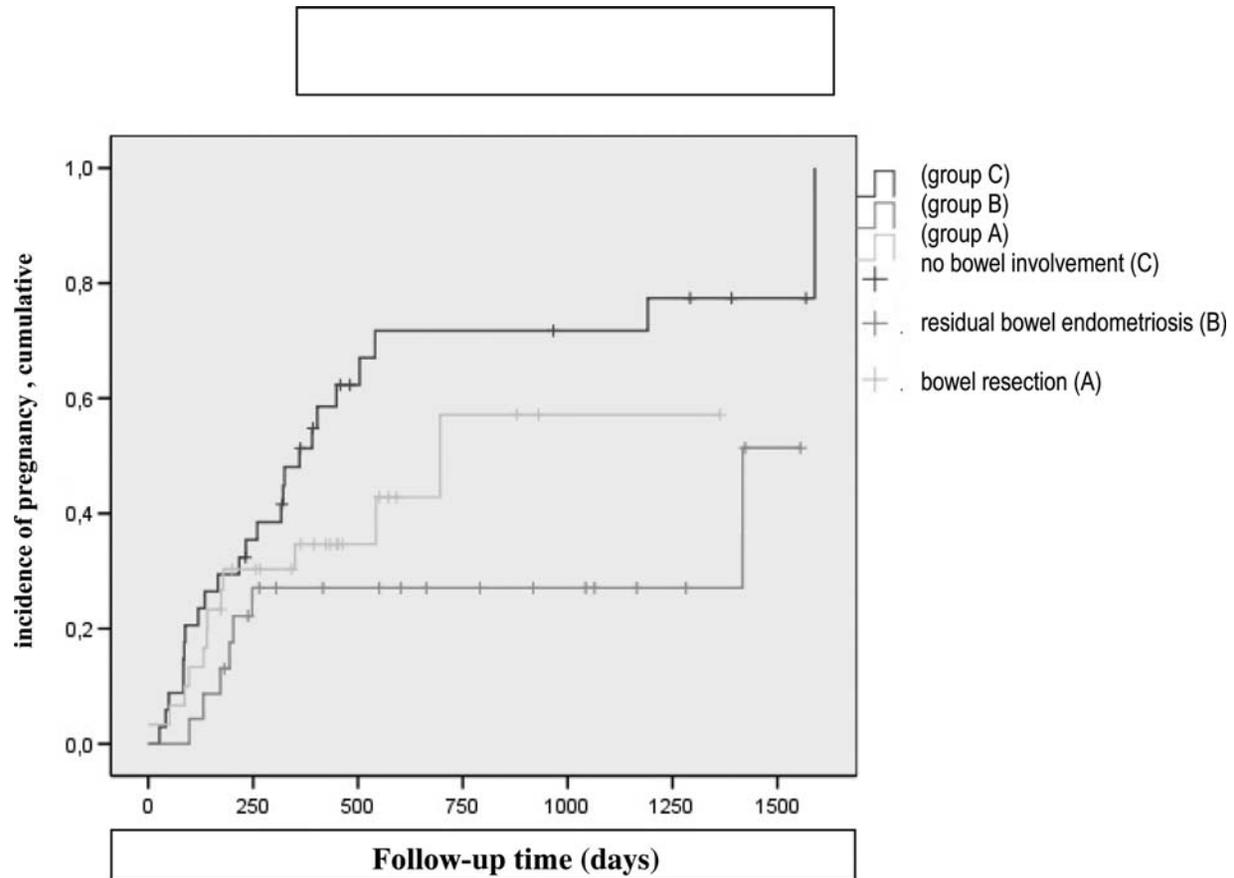


Figure 3 Distribution of pregnancies in time after surgery in three groups (Kaplan–Meier curve).

surgery was 2.4 days. Urine retention after bowel resection for more than 1 month was present in three patients (5%).

The other late complications (after a month) in group A were: urine incontinence (1.6%), constipation (1.6%) and one case of premature ovarian failure (POF) (1.6%).

Discussion

Our findings suggest that the presence of bowel endometriosis negatively influences fecundity. Among women with bowel endometriosis, the post-operative fertility was improved if segmental bowel resection was performed. A comparison with patients affected by endometriosis without bowel involvement (group C) showed that bowel endometriosis impairs fertility, perhaps due to involvement and obliteration of the pouch of Douglas.

These data are of relevance in clinical practice, because at present, the decision to perform bowel segmental resection, especially in patients wishing to conceive, is still controversial.

There are some data in literature describing reproductive outcome after bowel surgery for endometriosis. The percentage of patients who conceived after bowel resection in our study (the cumulative pregnancy rate of 35% for spontaneous pregnancies) is comparable to that reported by other authors. Darai *et al.* (2005) reported 5 pregnancies in 12 infertile patients, and Mohr *et al.* (2005) reported

2 pregnancies in 11 women. In the study of Possover *et al.* (2000), 8 out of 15 patients conceived after vaginal resection of endometriosis assisted by laparoscopy, but it is not specified whether the pregnancies were spontaneous or medically induced.

Besides the clear advantage of pain relief, and a decreased recurrence rate (Fedele *et al.*, 2004; Darai *et al.*, 2005; Dubernard *et al.*, 2006), the 'price to pay' of segmental bowel resection is presented by possible complications (Varol *et al.*, 2003; Kaloo *et al.*, 2006; Slack *et al.*, 2007), which means that it should be performed in selected cases.

The indication for bowel resection in infertile women may be represented by important bowel stenosis and severe pelvic pain, with mandatory preoperative counselling.

In our study, we observed cases of anastomotic fistulae in two patients (3.2%), both after a very low bowel resection. The incidence of bowel fistula is comparable to that in literature: Darai reported 9% (Darai *et al.*, 2005) and 8% (Darai *et al.*, 2007) incidence of fistulae, while Dubernard *et al.* (2006) and Jerby *et al.* (1999) reported 10 and 14%, respectively. In the study of Redwine and Wright (2001), there were no fistulas after six bowel resections, while Possover *et al.* (2000) describes two cases of anastomotic dehiscence in 34 patients, both of which did not require reintervention. Mereu *et al.* (2007) reported data from our centre, and in 192 bowel resections, four anastomotic leakages and five rectovaginal fistulae occurred.

The risk of complications depends on the clinical conditions such as the level of bowel stenosis (Ret Dávalos *et al.*, 2007), opening of the vaginal wall, the extension of endometriosis infiltration and the surgeon's experience. During recent years, the surgical techniques have significantly evolved, and the post-operative outcome has improved.

One case of POF after surgery occurred in our study. The patient with POF underwent surgery twice for bilateral endometriomas in the past, and she presented with bilateral endometriomas, important bowel stenosis and a very strong pelvic pain refractory to any medical treatment. The risk of POF after repeated surgery treatments for ovarian cysts has already been reported in the literature (Reich and Abrao, 2006).

In our study, the incidence of endometriosis recurrence was higher if bowel endometriosis was not resected. Anaf *et al.* (2000) suggested that in such cases, ovarian stimulation could induce a bowel occlusion, but there were no cases of such complications in our study. Surgical recurrence in group B was required more frequently if successive IVF or IUI had been performed (4 cases in 16 patients versus 2 cases in 24 patients with no IUI or IVF). However the results are not informative because of the small number of patients. The incidence of sonographic recurrence did not significantly differ after ovarian stimulation (4 cases in 16 women) than without such treatment (5 in 24 patients). In a recent study, D'Hooghe *et al.* (2006) reported that ovarian stimulation did not enhance the incidence of recurrence of endometriosis.

Our study, no doubt, has some limits due to the nature of the study (retrospective cohort study with longitudinal evaluation of clinical outcomes), and needs confirmation with a randomized clinical trial, but the results suggest that the presence of bowel endometriosis negatively influences fertility outcome. However while there were no differences between groups regarding the characteristics important for fertility outcome, such as age, presence of male factor infertility or tubal adhesions, it is important to underline that there were differences in symptomatology. Patients in group A had more severe symptoms than those in group B, and that is why they decided for a bowel surgery, even if it was not free of possible complications. Another difference between groups is the incidence of endometriomas. In all 55 patients of group C, endometriomas were present, while in group A they were present 55% (33/60) and in group B in 60% (24/40). Nevertheless this did not influence the post-operative fertility, which was best in the group C. The poorest fertility outcome occurred in the group B, that is in patients who underwent incomplete surgery for endometriosis, and had a residual bowel nodule. This result could be explained by a negative influence of obliteration of the pouch of Douglas on fertility, and it confirmed advantages of the complete removal of endometriosis.

It is important to underline that the results of the study does not indicate that all infertile women with bowel endometriosis should undergo segmental bowel resection. Our results may not apply to infertile patients with bowel endometriosis who do not have pain symptomatology. This kind of surgery is not free of severe complications, so it should be performed only in selected patients.

Despite the limits of this study, it reports the largest series of bowel surgery for endometriosis in infertile women. All cases were treated in a single centre and the longitudinal follow-up for 4 years was performed by the same team. This data suggest the importance of pre-operative bowel evaluation in infertility patients affected by severe

endometriosis. Our study offers some new aspects to be considered in the decision-making process for therapeutic treatment, when evaluating possible risks and benefits of surgery in such cases.

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Submitted on November 12, 2008; resubmitted on March 6, 2009; accepted on March 13, 2009