

# Fertility outcomes in women experiencing severe complications after surgery for colorectal endometriosis

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**STUDY QUESTION:** What are the fertility outcomes in women wishing to conceive after experiencing a severe complication from surgical removal of colorectal endometriosis?

**SUMMARY ANSWER:** The pregnancy rate (PR) among women who wished to conceive after a severe complication of surgery for colorectal endometriosis was 41.2% (spontaneously for 80%, after ART procedure for 20%).

**WHAT IS KNOWN ALREADY:** While the long-term benefit of surgery on pain and quality of life is well documented for women with colorectal endometriosis, it exposes women to the risk of severe complications. However, little is known about fertility outcomes in women experiencing such severe postoperative complications.

**STUDY DESIGN, SIZE, DURATION:** This retrospective cohort study included women who experienced a severe complication after surgery for colorectal endometriosis between January 2004 and June 2014, and who wished to conceive. A total of 53 patients met the inclusion criteria. The fertility outcome was available for 48 women, who were therefore included in the analysis. The median follow-up was 5 years.

**PARTICIPANTS/MATERIALS, SETTING, METHODS:** All the women underwent complete removal of colorectal endometriosis. Postoperative severe complications were defined as grades III–IV of the Clavien–Dindo classification. Fertility outcomes, PR and cumulative pregnancy rate (CPR), were estimated.

**MAIN RESULTS AND THE ROLE OF CHANCE:** Most women experienced a grade IIIb complication (83.3%). Of 48 women, 20 became pregnant (overall PR: 41.2%); spontaneously for 16 (80%) and after ART procedure for 4 (20%). The median interval between surgery and first pregnancy was 3 years. The live birth rate was 14/48 (29.2%). The 5-year CPR was 46%. A lower CPR was found for women who experienced anastomotic leakage (with or without rectovaginal fistula) ( $P = 0.02$ ) or deep pelvic abscess (with or without anastomotic leakage) ( $P = 0.04$ ).

**LIMITATIONS REASONS FOR CAUTION:** Due to a lack of information, no sub-analysis was done to investigate other parameters potentially impacting fertility outcomes.

**WIDER IMPLICATIONS OF THE FINDINGS:** The PR for our population was slightly lower to that observed in the literature for women who experience such surgery without consideration for the occurrence of complications. However, 'severe complications' covers a

range of conditions which are likely to have a very different impacts on fertility. Even if the PR and CPR appear satisfactory, septic complications can negatively impact fertility outcomes. Rapid ART may be a good option for these patients.

**STUDY FUNDING/COMPETING INTEREST(S):** No funding was required for the current study. Pr H. Roman reported personal fees from Plasma Surgical Inc. (Roswell, GA, USA) for participating in a symposium and a masterclass, in which he presented his experience in the use of PlasmaJet<sup>®</sup>. None of the other authors declared any conflict of interest.

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**Key words:** endometriosis / colorectal resection / surgery / complication / fertility / assisted reproductive technology / pregnancy outcomes

## Introduction

It is now well established that deep infiltrating endometriosis (DIE) with colorectal involvement is a major source of chronic pelvic pain with an altered quality of life (Dunselman et al., 2014). Even if medical treatment is the first therapeutic option, surgery including removal of colorectal endometriosis is an option for selected patients, especially when medical treatment is ineffective or associated with side effects (Alabiso et al., 2015). Moreover, this surgery exposes women to the risk of severe complications, such as rectovaginal fistula (1.8–4.5%) (De Cicco et al., 2011; Roman and FRIENDS group (French coloRectal Infiltrating ENDometriosis Study group), 2017), that could alter fertility. However, little is known about fertility outcomes in women experiencing severe postoperative complications.

Hence, the aim of this retrospective multicenter study was to report fertility outcomes for women who experienced severe complications after surgery for colorectal endometriosis and who wished to conceive.

## Materials and Methods

### Women

From January 2004 to June 2014, data from 900 women with DIE with colorectal involvement were retrospectively extracted from prospectively maintained databases at three French referral centres: Tenon University Hospital (Paris), Rouen University Hospital and Lille University Hospital. We included women who underwent colorectal surgery for DIE and who experienced a major postoperative complication ( $\geq$ grade III according to the Clavien–Dindo classification (Dindo et al., 2004)). Diagnosis of DIE was based on physical examination, transvaginal sonography and magnetic resonance imaging (Bazot et al., 2009). In case of colorectal involvement, rectal endoscopic sonography or computed tomography based colonoscopy was performed depending on expertise in the centre. We excluded women who had a history of hysterectomy, those who underwent hysterectomy associated with the colorectal resection, those who underwent bilateral salpingectomy and those not wishing to conceive after surgery.

### Data collection

The women were contacted by phone between February and September 2016 and were asked to answer a standard questionnaire including questions about: (i) their desire to conceive after surgery; (ii) whether they became pregnant after surgery; (iii) the number of pregnancies; (iv) how they conceived (spontaneous or after ART); (v) the time between surgery and pregnancy; and (vi) the pregnancy outcome. Clinical pregnancies were

only taken into account if they were confirmed on vaginal ultrasound examination.

### Surgery

All the women had undergone complete removal of colorectal endometriosis. To determine the best surgical approach, we used the following parameters: (i) size of the colorectal lesion (more or <3 cm in diameter); (ii) the extent of bowel circumference involvement (more or <30–40%); (iii) the depth of the lesion; and (iv) the degree of colorectal stenosis (Abrão et al., 2015).

### Complications

Complications that occurred during the first month after surgery were recorded based on the Clavien–Dindo classification. We only analysed fertility outcomes among women who experienced at least one severe complication ( $\geq$ grade III).

### Statistical analysis

Statistical analysis was based on the Student's *t* test or ANOVA test, as appropriate for continuous variables, and the Chi-square test or Fisher's exact test, as appropriate for categorical variables. Values of  $P < 0.05$  were considered to denote significant differences. Fertility outcomes, pregnancy rate (PR) and cumulative pregnancy rate (CPR), were estimated. Kaplan–Meier method was used to estimate the CPR, and comparisons of CPR were made using the log-rank test according to different types of complications. Data were analysed using R 3.0.1 software, available online.

### Ethical approval

Prospective recording of the data was approved by the French authority CCTIRS (Advisory Committee on Information Processing in Healthcare Research). All the women gave their informed consent.

## Results

### Epidemiological and surgical characteristics of the population

Among the 900 women who underwent surgery for colorectal endometriosis, 53 (5.9%) met the inclusion criteria. We were unable to contact five of them. Hence, 48 women (90%) were included in the analysis. The epidemiological characteristics of the study population are summarized in Table I.

Surgical procedures are presented in Table II. One of the women was managed for an isolated sigmoid nodule. A protective

**Table I** Epidemiological characteristics of the population.

Characteristics	Population n = 48
Age <sup>a</sup> (years) (range)	32 (21–39)
BMI (kg/m <sup>2</sup> ) <sup>a</sup> (range)	21.6 (16.2–39.0)
ASRM score <sup>a</sup> (range)	82 (11–154)
Infertility, n (%)	26 (54.2%)
Primary	19 (39.6%)
Secondary	7 (14.6%)
History of prior surgery for endometriosis, n (%)	25 (52.1%)
Pregnancy before surgery, n (%)	11 (22.9%)
Live birth before surgery, n (%)	7 (14.6%)
Prior ART, n (%)	17/26 (65.4%)

ASRM, American Society of Reproductive Medicine.

<sup>a</sup>Median.

defunctioning stoma was performed for 18 women (37.5%) during the primary surgical procedure, including 16 with associated partial colectomy.

## Complications

Overall, 11 women (22.9%) experienced a rectovaginal fistula, 9 (18.8%) had an anastomotic leakage, 10 (20.8%) had a deep pelvic abscess, 4 (8.3%) had ureterohydronephrosis, 4 (8.3%) had a urinary fistula, 3 (6.3%) experienced bowel obstruction and 7 (14.6%) had another type of complication (two cases of rectorrhagia, one case of ileostomy bleeding, one case of parietal abscess, one case of intra-abdominal bleeding, one case of vaginal suture line breakdown, and one case of hernia through the stoma scar). All women who experienced a rectovaginal fistula and anastomotic leakage underwent a secondary protective defunctioning stoma. Forty women (83.3%) experienced a grade IIIb complication and six (12.5%) a grade IIIa complication. The remaining two women had a grade IV complication requiring further surgery and management in an intensive care unit.

## Fertility outcomes

The median follow-up was 5 years (range: 1–12). Twenty women became pregnant, giving an overall PR of 41.2%. Four women became pregnant at least twice, giving 26 pregnancies in all. Sixteen of the women (80%) conceived spontaneously. Of the 17 women who underwent an ART procedure, 4 (23.5%) became pregnant. The median time between surgery and the first pregnancy was 3 years (range: 1–6). Overall, no pregnancy was obtained beyond 6 years after surgery or 4 years after an ART procedure. The PR was 66.7% after grade IIIa complications and 40% after grade IIIb complications. Neither of the women with a grade IV complication became pregnant. The live birth rate was 14/48 (29.2%): six women had an early miscarriage and none had an ectopic pregnancy.

The 5-year CPR was 46% (Fig. 1a). We found no difference in CPR according to the type of pregnancy (spontaneous vs ART) ( $P = 0.12$ ), fertility status ( $P = 0.3$ ) or age (<35 vs ≥35) ( $P = 0.6$ ). A trend toward

**Table II** Surgical procedures.

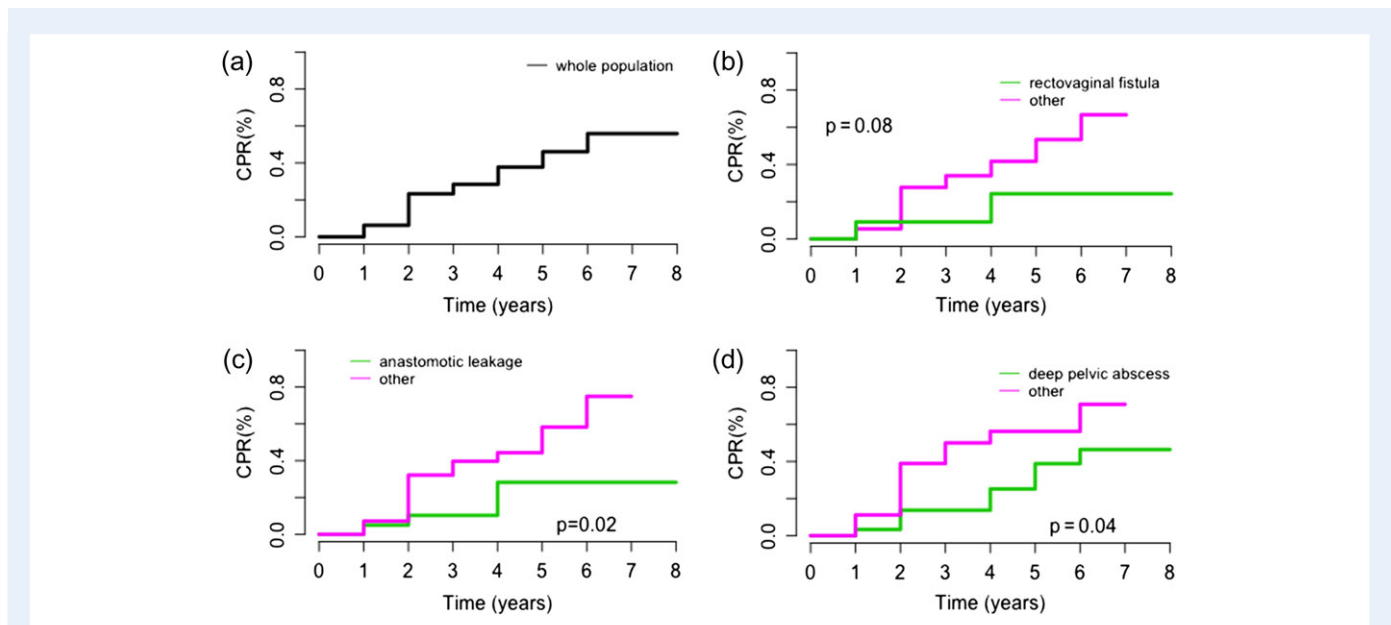
Surgical characteristics	Population n = 48
Surgical route, n (%)	
Laparoscopy	40 (83.3)
Robot-assisted	2 (4.2)
Laparotomy or conversion to laparotomy	6 (12.5)
Rectal procedure, n (%)	
Segmental resection	42 (87.5)
Discoid resection	3 (6.2)
Deep shaving	3 (6.2)
Torus or uterosacral ligament resection, n (%)	44 (91.7)
Parametrial resection, n (%)	8 (16.7)
Ovarian cystectomy or ablation, n (%)	7 (14.6)
Partial colectomy, n (%)	27 (56.3)
Sigmoid resection, n (%)	24 (50)
Ileo-caecal resection, n (%)	3 (6.3)
Appendectomy, n (%)	5 (10.4)
Partial bladder resection, n (%)	4 (8.3)
Ureteral resection, n (%)	2 (4.2)
Protective defunctioning stoma after primary surgical procedure, n (%)	18 (37.5)

a lower CPR was found for women who experienced a rectovaginal fistula ( $P = 0.08$ ) (Fig. 1b). A lower CPR was found for women who experienced an anastomotic leakage (with or without rectovaginal fistula) ( $P = 0.02$ ) and those who experienced a deep pelvic abscess (with or without anastomotic leakage) ( $P = 0.04$ ) (Fig. 1c and d).

## Discussion

Our study shows that women experiencing a severe complication after surgery for colorectal endometriosis and wishing to conceive have relatively satisfactory fertility outcomes. Moreover, we found that 80% of pregnancies were obtained spontaneously. Finally, the occurrence of a rectovaginal fistula, anastomotic leakage and deep pelvic abscess negatively impact fertility outcomes.

Despite the occurrence of a grade III complication according to Clavien–Dindo classification, the present study demonstrates that one-third of the total patients became pregnant spontaneously. Moreover, an overall PR of 41.2% (spontaneous pregnancies in 80% of cases) and a 5-year CPR of 46% were observed. Although slightly lower, our PR is close to that reported in a recent review (Daraï *et al.*, 2016) on colorectal resection for endometriosis showing that the overall PR in patients with proven infertility was 51.1% (spontaneous PR of 31.4% (95% IC = 28–34) and 19.8% (95% CI = 17–22) after ART). However, the PR was not analysed according to the occurrence of the surgical complications. Interpretation of our results might suggest that the occurrence of a severe postoperative complication has little impact on fertility outcomes. However, in a prospective study, Meuleman *et al.* (2014) reported a spontaneous PR rate of 40% after colorectal resection in patients with at least one functional Fallopian



**Figure 1** Cumulative pregnancy rate (CPR), comparison between subgroups. (a) CPR in the whole population; (b) impact of rectovaginal fistula on CPR; (c) impact of anastomotic leakages ( $\pm$ rectovaginal fistula) on CPR; and (d) impact of deep pelvic abscess ( $\pm$ anastomotic leakage) on CPR.

tube and an overall PR of 78% after ART. When compared to our results, these data from prospective studies in women irrespective of postsurgical complications concur to suggest a negative impact of severe postoperative complications on fertility.

Another issue is the type of grades III–IV complication that could impact fertility outcomes. In the current study, a lower CPR was found in patients experiencing a digestive complication (rectovaginal fistula or anastomotic leakage) compared to those with other grades III–IV complications. Similarly, a lower CPR was observed in patients experiencing a deep pelvic abscess regardless of the occurrence of an anastomotic leakage or rectovaginal fistula, suggesting that a pelvic abscess per se is a negative determinant of fertility outcome. However, our results should be interpreted with caution as ‘severe complications’ covers a range of conditions including anastomotic leakage with pelvic abscess as well as a hernia through the stoma scar which is likely to have a very different impact on fertility. Moreover, we found that no women became pregnant after 6 years and that 65% of the pregnancies occurred during the first 3 years, suggesting that all efforts should be made to obtain a pregnancy during the first few years following the initial surgery. It would thus appear to be crucial to identify women who have a low chance of a spontaneous pregnancy after a grades III–IV complication, so as to offer ART as soon as possible.

To our knowledge, only one study has previously focused on PR after major complications following surgery for DIE (Kondo *et al.*, 2011). In this series including 23 women (of whom 91% underwent a colorectal surgery), Kondo *et al.* reported a PR of 47.8%, which is in agreement with our results. However, the study population was quite different as it did not focus exclusively on women requiring colorectal surgery and the rate of rectovaginal fistula was 56.5% as opposed to 22.9% in the current study. Moreover, we found that the CPR was lower in women who experienced a deep pelvic abscess (with or without anastomotic leakage) and those with anastomotic leakage (with or without rectovaginal fistula). Indeed, these are the most severe and

morbid complications with intra-abdominal inflammatory processes, often requiring multiple surgical procedures. Nevertheless, it is important to point out that among the 26 women with proven infertility before surgery, 10 became pregnant (spontaneously in seven cases and after ART procedure in three), leading to a PR of 38.5% and raising the issue of the impact of surgical removal of colorectal endometriosis on fertility even in the event of a severe postoperative complication.

Our study has several limitations. First, we cannot exclude a bias due to its retrospective nature. However, data were collected from prospectively maintained databases after directly contacting all the women to correct or complete the data. Second, due to a lack of information, no sub-analysis was done to investigate parameters potentially impacting fertility outcomes, such as serum anti-Müllerian hormone levels, sonographic antral follicle count, postcomplication evaluation of tubal patency or the presence of associated adenomyosis.

Our results confirm that the PR and CPR appear satisfactory, however septic complications still appear to significantly impact postoperative fertility. While 80% of the pregnancies were spontaneous, further studies including parameters of poor fertility outcomes are required to better select the women who may benefit from rapid ART procedures.

## Authors' roles

C.F.: Participation in study design, execution and analysis, article drafting and critical discussion. H.R.: Study execution, article drafting and critical discussion. Y.A.: Study execution and critical discussion. E.M.: Critical discussion. S.B.: Article drafting and critical discussion. N.M.: Study execution. M.P.: Study execution. C.R.: Critical discussion. P.C.: Study execution and critical discussion. E.D.: Participation in study design and analysis, article drafting and critical discussion. M.B.: Participation in study design, execution and analysis, article drafting and critical discussion.

## Funding

No funding was required for the present study.

## Conflict of interest

H.R. reported personal fees from Plasma Surgical Inc. (Roswell, GA, USA) for participating in a symposium and a masterclass, in which he presented his experience in the use of PlasmaJet®. None of the other authors declared any conflict of interest.

## References

- Abrão MS, Petraglia F, Falcone T, Keckstein J, Osuga Y, Chapron C. Deep endometriosis infiltrating the recto-sigmoid: critical factors to consider before management. *Hum Reprod Update* 2015;**21**:329–339.
- Alabiso G, Alio L, Arena S, Prun AB, di, Bergamini V, Berlanda N, Busacca M, Candiani M, Centini G, Di Cello A *et al.* How to manage bowel endometriosis: the ETIC Approach. *J Minim Invasive Gynecol* 2015;**22**:517–529.
- Bazot M, Lafont C, Rouzier R, Roseau G, Thomassin-Naggara I, Daraï E. Diagnostic accuracy of physical examination, transvaginal sonography, rectal endoscopic sonography, and magnetic resonance imaging to diagnose deep infiltrating endometriosis. *Fertil Steril* 2009;**92**:1825–1833.
- Daraï E, Cohen J, Ballester M. Colorectal endometriosis and fertility. *Eur J Obstet Gynecol Reprod Biol* 2016;**209**:86–94.
- De Cicco C, Corona R, Schonman R, Mailova K, Ussia A, Koninckx P. Bowel resection for deep endometriosis: a systematic review. *BJOG Int J Obstet Gynaecol* 2011;**118**:285–291.
- Dindo D, Demartines N, Clavien P-A. Classification of surgical complications. *Ann Surg* 2004;**240**:205–213.
- Dunselman G a. J, Vermeulen N, Becker C, Calhaz-Jorge C, D'Hooghe T, De Bie B, Heikinheimo O, Horne AW, Kiesel L, Nap A *et al.* ESHRE guideline: management of women with endometriosis. *Hum Reprod Oxf Engl* 2014;**29**:400–412.
- Kondo W, Daraï E, Yazbeck C, Panel P, Tamburro S, Dubuisson J, Jardon K, Mage G, Madelenat P, Canis M. Do patients manage to achieve pregnancy after a major complication of deeply infiltrating endometriosis resection? *Eur J Obstet Gynecol Reprod Biol* 2011;**154**:196–199.
- Meuleman C, Tomassetti C, Wolthuis A, Van Cleynenbreugel B, Laenen A, Penninckx F, Vergote I, D'Hoore A, D'Hooghe T. Clinical outcome after radical excision of moderate-severe endometriosis with or without bowel resection and reanastomosis: a prospective cohort study. *Ann Surg* 2014;**259**:522–531.
- Roman H, FRIENDS group. (French coloRectal Infiltrating ENDometriosis Study group). A national snapshot of the surgical management of deep infiltrating endometriosis of the rectum and colon in France in 2015: a multicenter series of 1135 cases. *J Gynecol Obstet Hum Reprod* 2017;**46**:159–165.