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Pregnancy and delivery outcomes in women with rectovaginal endometriosis treated either conservatively or operatively

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Objective: To study reproductive outcomes, and pregnancy and delivery complications after conservative or operative treatment of rectovaginal endometriosis during long-term follow-up.

Design: Retrospective cohort study.

Setting: University hospital.

Patient(s): Women with rectovaginal endometriosis referred to hospital due to any indication from 2004 to 2013 (N = 543) who were treated initially either conservatively (group CONS, n = 183), or operatively (OPER, n = 360) either with resection of rectovaginal nodule (RVR, n = 192) or with concomitant bowel resection (BR, n = 132).

Intervention(s): Conservative or operative management.

Main Outcome Measure(s): Clinical pregnancy rate, live-birth rate, and assessment of the complications during pregnancy and delivery.

Results(s): Between women in the CONS group or OPER group, no differences were found in either clinical pregnancy rate (56%, n = 102 vs. 50%, n = 181) or live-birth rate (48%, n = 87 vs. 42%, n = 153). Of the pregnancies, 64% (n = 65) and 49% (n = 89), respectively, started after medically assisted reproduction. No differences emerge in the subanalysis of women <40 years-old who wished to conceive. The most common pregnancy complication was preterm birth: 15% (n = 13) in the CONS group and 20% (n = 30) in the OPER group. The cesarean delivery rate also was high (46%, n = 40 vs. 49%, n = 76). Complications emerged in 21% (n = 10) versus 29% (n = 23) of vaginal deliveries and 45% (n = 18) versus 53% (n = 40) of cesarean deliveries. The most common delivery complication was excessive bleeding. The follow-up period was 4.9 years in the CONS group and 5.6 years in the OPER group.

Conclusion(s): Women with rectovaginal endometriosis have comparable and good reproductive prognosis regardless of the treatment method. (Fertil Steril® 2021;115:406-15. ©2020 by American Society for Reproductive Medicine.)

El resumen está disponible en Español al final del artículo.

Key Words: Delivery complication, fertility, pregnancy complication, rectovaginal endometriosis

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Rectovaginal endometriosis (RVE) is a severe form of deep endometriosis (DE) associated with pain and infertility (1). Several guidelines are available on the man-

agement of endometriosis pain using medical or surgical treatments (2-6), but the decisions concerning optimal management of endometriosis-associated infertility are much more

complex (7). The evidence for the management of infertility associated with DE has been unclear. The options include expectant management, medically assisted reproduction (MAR), or surgery (8-11). The choice of first-line treatment is individual and may be influenced by many factors such as age, the patient's preferences, the duration of infertility, pain, possible previous surgery, ovarian function, and possible concomitant male factor infertility.

Studies comparing reproductive outcomes after expectant management or surgical treatment of RVE are sparse.

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In a study by Vercellini et al. (12), surgical treatment of RVE by means of laparotomy in infertile women failed to improve the reproductive prognosis when compared with expectant management. More recently, Maggiore et al. (13) assessed the effect of expectant management compared with surgical treatment on spontaneous fertility in women with RVE without a history of infertility. They concluded that during the 1 year of follow-up the spontaneous pregnancy rate was lower in the women treated with expectant management compared with surgical treatment (cumulative spontaneous pregnancy rate 23.8% vs. 39.5%). Over the past few years, several studies have suggested that surgical treatment of colorectal endometriosis improves pregnancy rates (14–17), but the risk of repeated surgeries and severe complications should be considered (8, 18–20). Studies have also shown that some of the pregnancy and delivery complications such as preeclampsia, placenta previa, and preterm birth are associated with endometriosis (21–23). Nevertheless, knowledge on the association between specifically RVE and pregnancy or delivery complications remains limited (24–26). Our retrospective study was designed to investigate long-term pregnancy and delivery outcomes in all women with RVE who underwent either conservative or operative treatments.

MATERIALS AND METHODS

Study Population and Protocols

We identified all 925 women treated for RVE (International Classification of Diseases version 10 code N80.4) at the Department of Obstetrics and Gynaecology of Helsinki University Hospital in Finland from 2004 to 2013. The department is a tertiary referral center for severe endometriosis and MAR with good collaboration between the operative and infertility clinics. We defined RVE as the form of DE invading the rectovaginal septum. The diagnosis of RVE was set by a senior consultant experienced in endometriosis care. The diagnosis was based on clinical examination with typical findings, transvaginal ultrasound or magnetic resonance imaging, and/or findings from a previous operation. The exclusion criteria were incorrect diagnosis, endometriosis lesions located only in uterosacral ligaments not infiltrating the rectovaginal septum, an inability to conceive (history of hysterectomy, bilateral oophorectomy, sterilization of either the woman or spouse, or age >45 years), a history of rectovaginal resection or bowel resection, or having been operated on before 2004 or after 2013, or operated on in another hospital.

Finally, 543 eligible women formed the two study groups, and they were classified according to the initial treatment plan: women who were treated conservatively without surgery (CONS, $n = 183$) and those who were treated operatively (OPER, $n = 360$) with or without bowel resection. The index day was the day when the decision on the treatment plan was made (Fig. 1). Treatment-plan decisions were made clinically by the doctor together with the patient, and they were based on individual symptoms and patient preferences. Women with rectovaginal endometriosis are most commonly referred to our hospital either due to pain or infertility or both. Those referred for ureter or bowel stenosis are few, and they

undergo surgery. If the main indication for referral is pain and the patient has no active wish for pregnancy, medical treatment is offered as the first-line treatment. In conservative care, various combined oral contraceptive pills, progestin-only pills, levonorgestrel-releasing intrauterine system, and gonadotropin-releasing hormone analogues with or without add-back as oral contraceptives or estrogen are used. Together with hormone therapy, the pain medication included nonsteroidal anti-inflammatory drugs, paracetamol, and if needed paracetamol combined with codeine or tramadol. Additionally, neuropathic pain medication such as gabapentin could be administered to treat severe pain. If conservative methods proved inadequate or inappropriate, surgery would be considered. Operatively treated patients are observed up until the symptoms have stabilized. If the patient has no active wish for pregnancy, she is advised to continue medical treatment and to contact the hospital in case of later infertility. Otherwise, MAR is recommended individually after surgery.

When a woman is referred for infertility and has tolerable symptoms without hormone medication, initially a 6-month wait for a spontaneous pregnancy is recommended for cases with infertility of less than 2 years' duration, ovulatory cycles, open fallopian tubes, and normospermia in the male partner. Afterward, MAR is offered and individually planned. Primarily the first MAR treatment is ovulation induction with or without intrauterine insemination one to three times, depending on the response in cases of infertility of <3 years' duration and a woman younger than 35 years. Secondarily, in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) are suggested up to three treatment cycles after ovulation induction with or without intrauterine insemination, or immediately if a woman is older than 35 years. If the symptoms are intolerable, then surgery or immediate IVF-ICSI will be discussed and individually chosen (Supplemental Fig. 1, available online).

The data concerning symptoms, diagnosis, hospital visits, surgery, MAR, pregnancies, deliveries, and complications were gathered retrospectively by two researchers (A.Tu., L.S.) from the electronic and paper patient records of the hospital. Additionally, we posted a questionnaire concerning fertility, complications, possible endometriosis operation(s), and MAR in private clinics during the follow-up period. To complete the data gathered from the patient records, in the questionnaire we specifically inquired about the wish to conceive. The questionnaire was sent before study's onset to all women with RVE who spoke Finnish or Swedish, including those who had moved to another hospital district during the study period. A reminder letter was sent once.

The questionnaire was sent to 175 (95.6%) women in the CONS group and 344 (95.6%) women in the OPER group. Altogether 85 (48.6%) women in the CONS group and 231 (67.2%) in the OPER group answered the questionnaire. If only the year of the first delivery was reported in the questionnaire, then July 1 was used as a date of the delivery (CONS $n = 2$; OPER $n = 4$). The follow-up period continued until the end of 2016, the date of the first delivery, or the date of moving to another hospital district, whichever came first. If the questionnaire was answered, the follow-up period was extended

until the end of 2016, and the extension was also applied to those who had moved. If a hysterectomy or bilateral oophorectomy was performed after the index day, the follow-up period ended on the day of the procedure.

Conservative Treatment Group (CONS)

Women in the CONS group were treated by expectant management and received no surgery primarily because their pain was tolerable and could be managed by conservative means. Hormone therapy was also used according to individual treatment plan (Supplemental Fig. 1).

Operative Treatment Group (OPER)

Women in the OPER group received surgery mainly because of severe pain. Operations were performed either by laparoscopy or laparotomy. The goal of the surgical treatment was to excise or ablate all visible endometriotic lesions, including ovarian, peritoneal, and deep endometriosis. Cystectomy was a method of choice in treating endometriomas. The main procedure was resection of RVE lesion with or without vaginal resection and concomitant bowel resection, if needed. At the time of our study, the primary method of bowel surgery was segmental resection. Anastomosis was performed with a circular stapler, and prophylactic ileostomy/colostomy was performed only if there was an air leakage during the air-fluid test or if anastomosis was very low (less than 6 cm from the anal canal). Discoid resections were not performed during the study period, but shaving was an option if the rectovaginal lesion did not infiltrate the muscular layer of the bowel wall. Shaving is not registered as bowel resection.

The surgical treatments were performed mainly by one gynecologist (P.H.) who is experienced in advanced laparoscopy. The operations were conducted together with a gastrointestinal surgeon if a bowel resection was performed and with a urologist in cases of ureteroneocystostomy. There were altogether three consulting colorectal surgeons and two urologists, all acquainted with endometriosis during the study period. We classified the surgical complications using the Clavien-Dindo classification (27) and included severe complications (grade III: complication requiring reintervention; grade IV: life-threatening complication; and grade V: death) in our analysis.

Definitions of Study Outcomes

Spontaneous pregnancy was defined as a naturally conceived pregnancy with no infertility treatment. We considered MAR to apply to all methods of infertility treatment: induction of ovulation, intrauterine insemination, IVF, and use of donor oocyte or sperm. Clinical pregnancy was defined as a pregnancy diagnosed by means of ultrasound examination with visualization of one or more gestational sac(s). Live birth was defined as a delivery resulting in a live neonate.

Pregnancy complication was defined as requiring a referral to specialist health care (excluding uncomplicated twin pregnancy or uncomplicated pregnancies with breech presentation). Because there is a strong tradition of independent midwifery in Finland, we defined complicated vaginal

delivery as one that needed the intervention of an obstetrician during delivery (e.g., retained placenta or gr III perineal rupture). In addition, individual complications were recorded. Bleeding that exceeded 500 mL was considered a complication. Operative vaginal deliveries were addressed separately. A complicated cesarean delivery was defined as an abnormal course of a routine procedure resulting in excess use of surgical interventions (e.g., severe adhesions, urinary bladder laceration). In cesarean deliveries, bleeding that exceeded 1,000 mL was considered a complication.

Statistical Analysis

The data were analyzed on an intention-to-treat basis. In the OPER group, we conducted subanalyses of women who underwent rectovaginal resection-only compared with those who had a concomitant bowel resection (BR). Additionally, we constituted subanalyses of women, who were younger than 40 years at the beginning of the follow-up period and had an active wish to conceive.

The normality of continuous variables was evaluated visually using histograms. According to the data distribution, the comparisons between groups in continuous baseline characteristic variables were done with two-sample *t*-test or Mann-Whitney test. Categorical baseline characteristic variables were compared with chi-square test or Fisher exact test according to the sample size. The differences in the dichotomous outcomes between groups were examined using univariable and multivariable logistic regression analysis. Crude odds ratio with 95% confidence intervals was calculated for all outcomes, and adjusted *P* value for the main outcome variables.

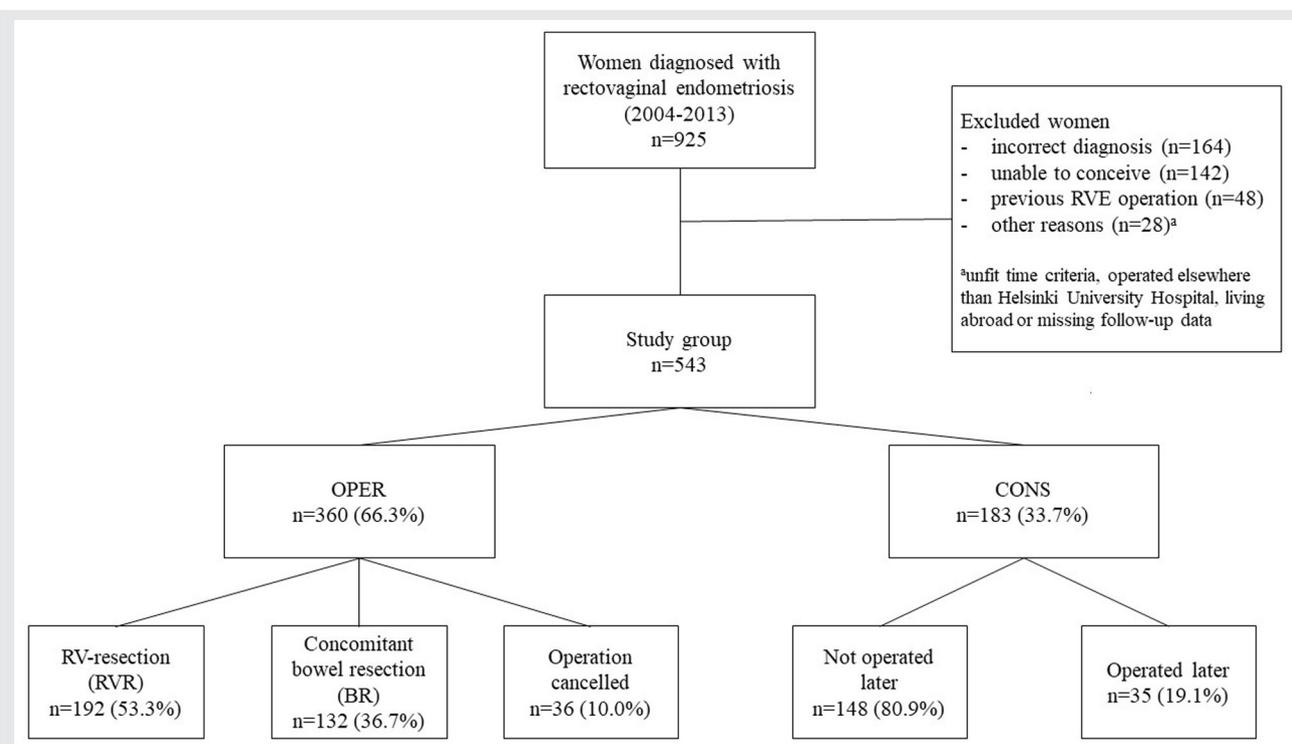
Adjusted factors varied between the analyses. With continuous outcome variables, the differences between groups were analyzed with two-sample *t*-test for follow-up time and with Mann-Whitney *U*-test for time to delivery. Hodges-Lehman estimate was used to calculate median difference with 95% CI for time to delivery. Analysis of covariance (ANCOVA) was used to calculate adjusted mean difference with 95% CI for continuous outcomes. Time to delivery values were natural log-transformed for ANCOVA analysis due to skewed distribution.

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM, Inc.). *P* < .05 was considered statistically significant, and two-sided tests were used. We obtained study approvals from the Ethics Committee of the Hospital District of Helsinki and Uusimaa (HUS/1381/2016) as well as from the institutional review board (21.3.2013, 25.5.2015 and 25.01.2016).

RESULTS

The study population consisted of 925 women who formed the cohort (Fig. 1). After exclusion, 543 of them were included in the final study. Altogether 183 (33.7%) women were included in the CONS group, and 360 (66.3%) women were in the OPER group. In the OPER group, 192 (53.3%) women underwent resection of RVE (RVR, rectovaginal resection) and a concomitant bowel resection together with resection of RVE was performed in 132 (36.7%) women (BR, bowel

FIGURE 1



Cohort of women with rectovaginal endometriosis (RVE).

Tuominen. RVE and pregnancy outcome. *Fertil Steril* 2020.

resection). The follow-up period was slightly longer in the OPER group: 4.9 (± 3.3) years for the CONS group versus 5.6 (± 3.6) years for the OPER group ($P=.02$).

There was also a proportion of 35 (19.1%) women assigned to the CONS group who underwent operative treatment later during the follow-up period because of insufficient symptom relief during conservative treatment. In the OPER group, 36 women (10%) cancelled the operation, of whom 19 (5.3%) conceived while waiting for the operation.

The demographic characteristics of the study participants are shown in Table 1. The most common reason for referral was pain, or pain with concomitant infertility: 64.0% in the CONS group and 95.8% in the OPER group. Similarly, infertility as the sole indication or with associated pain symptoms differed between the groups: 47.0% in the CONS group and 34.4% in the OPER group. The groups also differed regarding their wish to conceive. Grade III–IV surgical complications were experienced by 22 (6.1%) women in the OPER group, and four of the 35 women (11.4%) who underwent surgery later in the CONS group.

There were no statistically significant differences between the CONS and OPER groups concerning clinical pregnancy rate (CPR) (adjusted $P=.71$, adjusted for age, body mass index, smoking, previous endometriosis operation, history of delivery, history of MAR, MAR during the follow-up period, presence of endometrioma, follow-up time) or live-birth rate (LBR, adjusted $P=.50$) (Table 2). Medically assisted

reproduction as used more often in the CONS group (adjusted $P=.03$). The cumulative LBRs were similar in the CONS and OPER groups, even in the OPER subgroups with or without bowel resection (Fig. 2). The time to delivery and follow-up time were statistically significantly longer in the OPER group (adjusted $P=.03$ and adjusted $P=.04$, respectively).

The rates of pregnancy and delivery complications were elevated in both groups (Table 2). However, no statistically significant differences were seen between the groups. Preterm birth (<37 gestational weeks) was the most common pregnancy complication. The rate of cesarean delivery was high, with no difference between the groups. The most common indication for elective cesarean delivery was placenta previa in both of the groups (41.7% in the CONS group and 30.4% in the OPER group); in emergency cesarean deliveries, the most common indication was failure of labor progress (28.6% and 24.5%) together with fetal distress (25.0% and 32.1%). Excessive bleeding was the most common delivery complication regardless of the method of delivery. None of the women had to undergo surgery for endometriosis-related complications during pregnancy.

Subanalyses

In the first subanalysis, we focused on women <40 years old who wished to conceive in the OPER versus CONS groups. The only statistically significant difference in the baseline

TABLE 1

Baseline characteristics of the women with rectovaginal endometriosis treated either conservatively or operatively.

| Characteristic | CONS (n = 183) | OPER (n = 360) | P value |
|---|-----------------|-----------------|---------|
| Age (y), mean \pm SD | 31.9 \pm 5.16 | 31.5 \pm 4.74 | .32 |
| BMI (kg/m ²), median (IQR) ^a | 22.5 (4.6) | 22.9 (3.8) | .31 |
| Smoking ^b | 25 (14.0) | 61 (16.9) | .37 |
| Indication for referral | | | < .0001 |
| Infertility | 39 (21.3) | 4 (1.1) | |
| Pain | 70 (38.3) | 225 (62.5) | |
| Infertility and pain | 47 (25.7) | 120 (33.3) | |
| Other ^c | 27 (14.8) | 11 (3.1) | |
| History | | | |
| Endometriosis operation | 65 (35.5) | 132 (36.7) | .79 |
| Delivery | 24 (13.1) | 40 (11.1) | .49 |
| Cesarean delivery | 8 (4.4) | 13 (3.6) | .66 |
| MAR | 18 (9.8) | 36 (10.0) | .95 |
| Presence of endometrioma | 58 (31.7) | 125 (34.7) | .48 |
| Wish to conceive | 129 (70.5) | 209 (58.1) | .01 |

Note: Values are number (percentage) unless otherwise indicated. BMI = body mass index; CONS = conservatively; IQR = interquartile range; MAR = medically assisted reproduction; OPER = operatively; SD = standard deviation.

^a Data not available: CONS n = 6; OPER n = 2

^b Data not available: CONS n = 4

^c Most commonly an asymptomatic woman with rectovaginal endometriosis (n = 21). Other individual reasons in this category were bleeding of the vaginal endometriotic tissue, recurrent miscarriage, urinary or nervous system symptoms together with rectovaginal endometriosis and suspicion of malignancy.

Tuominen. RVE and pregnancy outcome. *Fertil Steril* 2020.

characteristics was the indication of referral—namely, infertility dominated in the CONS group. No difference was seen in CPR or LBR (adjusted $P = .94$ and adjusted $P = .50$, respectively) (Supplemental Table 1, available online). The cumulative LBRs are shown in Figure 2.

Similarly, in the second subanalysis we focused on OPER women younger than 40 years who wished to conceive in according to their type of operation, RVR versus BR (Supplemental Table 2, available online). In baseline characteristics, there were statistically significant differences in presence of endometrioma, use of laparoscopy, and ovarian status after operation between the groups. However, CPR and LBR (adjusted $P = .95$ and adjusted $P = .27$)—adjusted for age, body mass index, smoking, history of endometriosis operation, history of MAR, MAR during follow-up, presence of endometrioma, laparoscopy, ovarian status after operation, major complication during operation—did not differ between the subgroups. The cumulative LBRs are shown in Figure 2.

DISCUSSION

This study was designed to investigate the long-term pregnancy and delivery outcomes in women with RVE treated either with conservative or operative means at our tertiary clinic. We found no statistically significant differences in CPR or LBR between the women managed either conservatively or surgically. In addition, we conducted a subanalysis on the women younger than 40 years who wished to conceive and who were managed operatively and had only resection of RVE versus those who also had bowel resection. The CPR and LBR results did not differ in these subanalyses either.

Our results differ in part from previous studies that compared expectant management versus surgical treatment of RVE. Although the results are in line with the previous study from Vercellini et al. (12), the comparison is weakened

by the use of open surgery in their older study, whereas laparoscopic surgery dominated in our study. Our results are in line with the study by Maggiore et al. (13), which reported a higher spontaneous pregnancy rate after operative treatment of RVE but in our study no differences were found in total CPR or LBR between the groups. However, unlike previous studies, our study population was heterogenous and consisted of both noninfertility and infertility patients, and included various infertility treatments, not only IVF.

There are different views on the role of bowel surgery as a fertility-enhancing procedure (8, 11, 16). Analogously, we found no difference in the reproductive outcomes after conservative management, the operative treatment with resection of RVE only, or concomitant bowel resection. By contrast, a recent retrospective cohort study from Bendifallah et al. (9) reported better fertility outcomes after first-line surgery preceding assisted reproductive technology (assisted reproduction via ICSI-IVF) compared with first-line assisted reproduction in infertile women with colorectal endometriosis. Still, there is controversy regarding whether surgery should precede MAR or vice versa, and the lack of published randomized controlled trials limits clinical recommendations.

Endometriosis is associated with several pregnancy complications caused by placental insufficiency, such as increased risk of preterm birth, preeclampsia, small for gestational age babies, and placenta previa (21–23, 28). According to studies from Exacoustos et al. (25) and Vercellini et al. (24), RVE is associated with the same pregnancy complications. In Finland, the rate of preterm birth (<37 weeks) has been 5% to 6% in recent years (www.thl.fi). In our study the most common pregnancy complication was preterm birth with no difference between the CONS and OPER groups: both had high figures (15%–20%) compared with national perinatal statistics.

TABLE 2

Outcomes of pregnancy and the first delivery of the women with rectovaginal endometriosis treated either conservatively or operatively.

| Outcome | CONS (n = 183) | | OPER (n = 360) | | OR (95% CI) |
|--|----------------|------|----------------|------|------------------------|
| | n | % | N | % | |
| MAR during follow-up | 89/183 | 48.6 | 149/360 | 41.4 | 1.34 (0.94–1.92) |
| CPR | | | | | |
| Total | 102/183 | 55.7 | 181/360 | 50.3 | 1.25 (0.87–1.78) |
| Spontaneous | 37/102 | 36.3 | 92/181 | 50.8 | 0.55 (0.34–0.91) |
| LBR ^a | | | | | |
| Total | 87/183 | 47.5 | 153/360 | 42.5 | 1.23 (0.86–1.75) |
| Spontaneous | 34/87 | 39.1 | 82/153 | 53.6 | 0.56 (0.33–0.95) |
| Time to delivery (y), median (IQR) | 2.2 (2.3) | | 2.4 (2.3) | | –0.11 (–0.29 to 0.06) |
| Follow-up time (y), mean ± SD | 4.9 ± 3.3 | | 5.6 ± 3.6 | | –0.74 (–1.36 to –0.11) |
| Pregnancy complications | | | | | |
| Women with complication(s) | 46/88 | 52.3 | 89/155 | 57.4 | 0.81 (0.48–1.37) |
| Preterm birth <37 wk | 13/86 | 15.1 | 30/150 | 20.0 | 0.71 (0.35–1.45) |
| Preterm birth <32 wk | 0/88 | — | 6/148 | 4.1 | — |
| Gestational hypertension | 2/88 | 2.3 | 9/155 | 5.8 | 0.41 (0.09–2.00) |
| Preeclampsia | 6/88 | 6.8 | 11/155 | 7.1 | 1.09 (0.38–3.17) |
| Placenta previa | 8/88 | 9.1 | 19/155 | 12.3 | 0.80 (0.32–1.99) |
| Gestational diabetes | 14/88 | 15.9 | 12/155 | 7.7 | 2.90 (1.21–6.96) |
| Unspecified abdominal pain | 6/88 | 6.8 | 16/155 | 10.3 | 0.70 (0.25–1.94) |
| Unspecified vaginal bleeding | 7/88 | 8.0 | 9/155 | 5.8 | 1.64 (0.57–4.73) |
| Preterm contractions and term delivery | 3/88 | 3.4 | 5/155 | 3.2 | 1.20 (0.27–5.26) |
| Placental abruption | 1/88 | 1.1 | 2/155 | 1.3 | 0.99 (0.09–11.20) |
| Stillbirth | 1/88 | 1.1 | 2/155 | 1.3 | 0.99 (0.09–11.20) |
| Other ^b | 7/88 | 8.0 | 16/155 | 10.3 | 0.84 (0.32–2.22) |
| Mode of delivery | | | | | |
| Vaginal | | | | | |
| Total | 48/88 | 54.5 | 79/155 | 51.0 | 1.15 (0.68–1.96) |
| Operative | 9/88 | 10.2 | 14/155 | 9.0 | 1.07 (0.42–2.71) |
| Cesarean | | | | | |
| Total | 40/88 | 45.5 | 76/155 | 49.0 | 0.87 (0.51–1.46) |
| Emergency | 28/87 | 32.2 | 53/154 | 34.4 | 0.95 (0.40–2.23) |
| Delivery complications | | | | | |
| Vaginal | | | | | |
| Women with complication(s) | 10/48 | 20.8 | 23/79 | 29.1 | 0.64 (0.27–1.50) |
| Bleeding >500 mL | 8/45 | 17.8 | 19/70 | 27.1 | 0.84 (0.13–5.56) |
| Manual evacuation of the placenta | 2/48 | 4.2 | 5/79 | 6.3 | 0.90 (0.14–5.66) |
| Perineal rupture grade III | 1/48 | 2.1 | 1/79 | 1.3 | 2.44 (0.14–43.47) |
| Other ^c | 0/48 | — | 2/79 | 2.5 | — |
| Caesarean section | | | | | |
| Women with complication/s | 18/40 | 45.0 | 40/76 | 52.6 | 0.72 (0.33–1.55) |
| Bleeding >1,000 mL | 12/35 | 34.3 | 29/74 | 39.1 | 0.83 (0.25–2.72) |
| Severe adhesions | 4/40 | 10.0 | 16/76 | 21.1 | 1.25 (0.29–5.37) |
| Difficulty delivering the neonate | 6/40 | 15.0 | 5/76 | 6.6 | 3.60 (0.93–13.95) |
| Urinary bladder laceration | 2/40 | 5.0 | 2/76 | 2.6 | 2.44 (0.32–18.83) |
| Uterine rupture | 1/40 | 2.5 | 1/76 | 1.3 | 2.35 (0.14–39.84) |
| Relaparotomy ^d | 1/40 | 2.5 | 3/76 | 3.9 | 0.75 (0.07–7.69) |
| Other ^e | 5/40 | 12.5 | 7/76 | 9.2 | 1.87 (0.50–6.95) |

Note: Data presented as n/n of women with available data (unless stated otherwise); individual follow-up period starting from index day until the end of year 2016, first delivery, or moving outside the hospital district without responding the questionnaire. CI = confidence interval; CONS = conservatively; CPR = clinical pregnancy rate; LBR = live birth rate; IQR = interquartile range; MAR = medically assisted reproduction; OPER = operatively; OR = odds ratio; SD = standard deviation.

^a This does not include stillbirth deliveries: CONS n = 1; OPER n = 2.

^b Hyperemesis (OPER n = 3), diagnosed/suspected fetal anomaly (CONS n = 1, OPER n = 3), intrauterine growth retardation (CONS n = 1, OPER n = 1), fetal macrosomia (OPER n = 1), oligo/polyhydramnion (CONS n = 1, OPER n = 4), fetal transverse presentation (CONS n = 2, OPER n = 1), fear of childbirth (OPER n = 1), hepatosteatorrhea (CONS n = 1), minor abdominal trauma during pregnancy (CONS n = 1), hypothyroidism after autoimmune thyroiditis (OPER n = 1), Non-Hodgkin's lymphoma diagnosed during pregnancy (OPER n = 1).

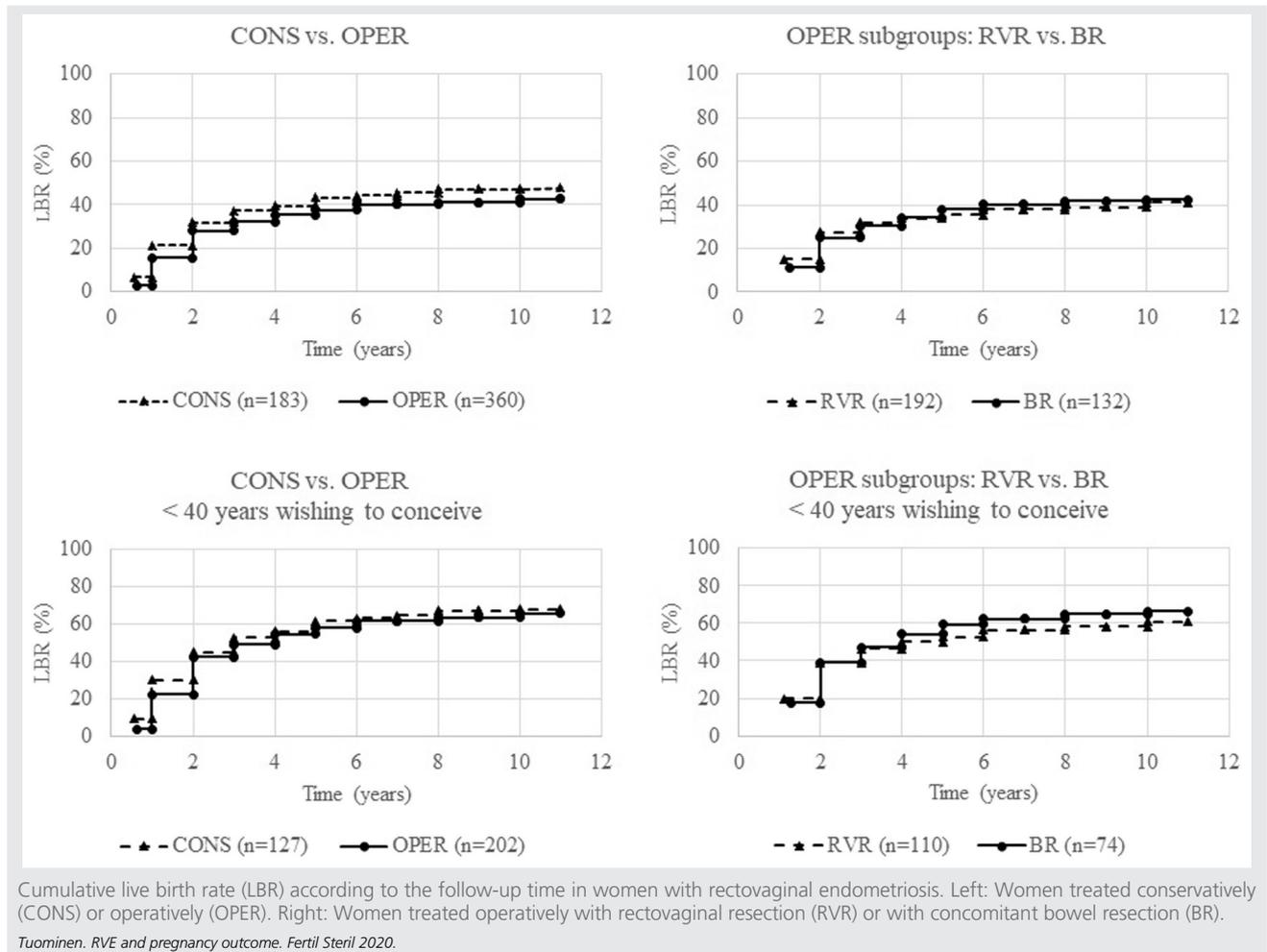
^c Abnormal pain during delivery regardless of effective epidural/spinal analgesia (OPER n = 2).

^d Two relaparotomies (OPER) were performed due to immediate postoperative hemorrhage, and the other needed further embolization. One relaparotomy (CONS) was performed due to postoperative infection 23 days after cesarean delivery, and 48 days afterward further hysterectomy was performed.

^e Difficult hemostasis because of oozing (OPER n = 3), difficulties delivering the placenta (CONS n = 1, OPER n = 1), uterine atony without bleeding >1,000 mL (CONS n = 2, OPER n = 1), perioperative diagnosis of placenta accreta resulting in hysterectomy (OPER n = 1), postoperative Sheehan's syndrome (OPER n = 1), and postoperative infection demanding hospitalization (CONS n = 2).

Tuominen. RVE and pregnancy outcome. *Fertil Steril* 2020.

FIGURE 2



We found excessive bleeding to be the most common delivery complication. Especially considering the cesarean deliveries, the rate of postpartum hemorrhage was high and occurred in more than one-third in both groups. In contrast, a previous large Danish cohort study (21) and a systematic review and meta-analysis (23) found no association between endometriosis and postpartum hemorrhage (defined as bleeding >500 mL). Moreover, the postpartum hemorrhage in women with RVE or DE was not increased in either a recent retrospective study (29) or case-control study (30). A retrospective cohort study examined obstetric hemorrhage after assisted reproductive therapies and found an elevated risk among a subgroup of women with endometriosis (31). In our study, the high rate of bleeding could be associated in part with appearance of placenta previa or retained placenta after delivery, both known to cause excessive bleeding. To date, however, we found no studies with histopathologic evidence of the extent of defective placentation in women with endometriosis. Moreover, the amount of bleeding is very difficult to measure exactly and has rarely been reported in other

studies. Therefore, the impact of endometriosis on postpartum hemorrhage needs further research.

The cesarean delivery rate approached 50% in both our treatment groups. This is a high figure compared to the Finnish national cesarean delivery rate of 16% to 17% in recent years (www.thl.fi). The finding is in line with a Danish cohort study (21) and with two systematic reviews (23, 32) on all types of endometriosis. In studies concerning RVE, Vercellini et al. (24) found the cesarean delivery rate to be highest (42.9%) in women with RVE compared with other types of endometriosis; by contrast, Nirgianakis et al. (30) suggested similar rates of successful vaginal delivery in women with history of laparoscopically treated DE compared with women without endometriosis.

In Finland, most common indications for elective cesarean delivery are breech presentation (19.2%) and fear of childbirth (9.2%) (33). In our study, placenta previa was over-represented as an indication for elective cesarean delivery, as to be expected. However, in the emergency cesarean deliveries, the most common indications—fetal distress and failure

of labor progress—were similar compared with the general population (37.5% and 37.6%) (33).

Moreover, the high rate of complicated cesarean deliveries cannot be overlooked. Our results are in line with a recent systematic review and meta-analysis in which DE and severe endometriosis were found to be associated with increased risk of surgical complications (for example, bladder injury and peripartum hysterectomy) during cesarean delivery (34). Our results are also comparable to a recent retrospective cohort study evaluating maternal and neonatal outcomes in women with resected or in situ colorectal endometriosis (26). In that study, half of the women underwent cesarean delivery and had a high incidence of postoperative complications (39%) irrespective of prior surgery. Similarly, the rate of complicated cesarean deliveries in a study by Exacoustos et al. (25) was comparable with our study among women with and without persisting RVE nodule after surgical treatment of DE.

The strengths of our study include the large number of patients and a long follow-up time. Our hospital is a tertiary referral center for both severe endometriosis and MAR. In Finland, access to health care is available to all citizens, regardless of socioeconomic status, and MAR and surgery are both available at low cost. Also, the codes for diagnoses are primarily used for clinical purposes, meaning that information retrieved from patient records is reliable. Electronic medical records used in public health care are comprehensive, providing medical data from all hospitals in the university hospital district area, including all deliveries and demanding operative care.

There are also some limitations to our study. The retrospective nature of the study leads to the possibility of missing data, memory, and selection biases. Data collection by two researchers can lead to a possibility of interperson variation. However, the effect of these biases was partly diminished by electronic patient files. Further, some important factors could not be assessed nor adjusted for. Adenomyosis was not been systematically evaluated by ultrasound or magnetic resonance imaging in our clinic during the study period, and it may not be equally distributed between the groups. Moreover, we may have missed some MARs performed in the private clinics outside our hospital, as only-half of the women in the CONS group and two-thirds in the OPER group answered the follow-up questionnaires. Even though our goal was to accomplish a study including a diverse spectrum of women with rectovaginal endometriosis, it represents only women who were referred to our tertiary health care center and excludes those asymptomatic women with RVE who conceived spontaneously. Therefore, the results cannot be generalized.

In addition, there are further limitations related to infertility treatments. The low-cost infertility treatments offered by the society are restricted to women <40 years-old. Also, during the study period, treatment with ovum donation was possible only in private clinics. We were not able to analyze other factors possibly contributing to infertility (i.e., male factor) or the indication for IVF: reasons related to endometriosis (i.e., severe adhesion formation) compared with other reasons (i.e., tubal defect). In addition, we were not able to assess whether MAR was sufficiently offered or was refused for in-

dividual reasons in some cases. Moreover, fertility might be affected also by the improving surgical and infertility treatments. Although the strategy toward surgical management was stable in our department during the study period, it is possible that the increasing surgical experience might have affected the results.

CONCLUSION

When counseling women with RVE, all the aspects of the disease, including fertility issues, must be considered. According to our study, the decisions between conservative and operative treatment of RVE can be made individually according to the symptoms and patient's preferences without sacrificing reproductive health. Close collaboration between both high-quality MAR and surgery is a prerequisite for successful outcomes of both conservative and operative treatment of RVE.

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Resultados en la gestación y en el parto en mujeres con endometriosis rectovaginal tratadas tanto de manera conservadora o quirúrgicamente.

Objetivo: Estudiar los resultados reproductivos y las complicaciones durante el embarazo y el parto después del tratamiento conservador o quirúrgico de la endometriosis rectovaginal durante el seguimiento a largo plazo.

Diseño: Estudio retrospectivo de cohortes.

Entorno: Hospital universitario.

Paciente (s): Mujeres con endometriosis rectovaginal derivadas al hospital debido a cualquier indicación entre 2004 y 2013 (N = 543) que fueron tratadas inicialmente de manera conservadora (grupo CONS, n = 183) o quirúrgicamente (OPER, n = 360) ya sea con resección de nódulo rectovaginal (RVR, n = 192) o con resección intestinal concomitante (BR, n = 132).

Intervención (es): Manejo conservador o quirúrgico.

Principales medidas de resultado: Tasa de embarazo clínico, tasa de nacidos vivos y evaluación de las complicaciones durante el embarazo y el parto.

Resultados: Entre las mujeres del grupo CONS o del grupo OPER, no se encontraron diferencias ni en la tasa de embarazo clínico (56%, n = 102 vs. 50%, n = 181) ni en la tasa de nacidos vivos (48%, n=87 vs.42%, n=153). De los embarazos, el 64% (n = 65) y el 49% (n = 89), respectivamente, tuvieron lugar tras tratamientos de reproducción asistida. No se encontraron diferencias en el subanálisis de mujeres <40 años que deseaban concebir. La complicación más común del embarazo fue el parto prematuro: 15% (n = 13) en el grupo CONS y 20% (n = 30) en el grupo OPER. La tasa de partos por cesárea también fue alta (46%, n = 40 vs. a 49%, n = 76). Surgieron complicaciones en el 21% (n = 10) versus el 29% (n = 23) de los partos vaginales y el 45% (n = 18) versus el 53% (n = 40) de los partos por cesárea. La complicación más común del parto fue sangrado excesivo. El período de seguimiento fue de 4,9 años en el grupo CONS y de 5,6 años en el grupo OPER.

Conclusiones: Las mujeres con endometriosis rectovaginal tienen resultados comparables y buen pronóstico reproductivo independientemente del método de tratamiento.