Spontaneous fertility after expectant or surgical management of rectovaginal endometriosis in women with or without ovarian endometrioma: a retrospective analysis

Umberto Leone Roberti Maggiore, M.D.,[a,b] Carolina Scala, M.D.,[a,b] Emanuela Tafi, M.D.,[a,b] Annalisa Racca, M.D.,[a,b] Ennio Biscaldi, M.D.,[c] Valerio Gaetano Vellone, Ph.D.,[d] Pier Luigi Venturini, M.D.,[a,b] and Simone Ferrero, Ph.D.[a,b]

[a] Academic Unit of Obstetrics and Gynecology, IRCCS AOU San Martino—IST; [b] Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, and Maternal and Child Health, University of Genoa; [c] Department of Radiology, Galliera Hospital; [d] Department of Surgical and Diagnostic Sciences, IRCCS San Martino Hospital and National Institute for Cancer Research, University of Genoa, Genoa, Italy

Objective: To investigate spontaneous pregnancy rate (SPRs) of women with rectovaginal endometriosis (RV) with/without ovarian endometrioma (OMA) and treated with the use of expectant or surgical management.
Design: Retrospective study.
Setting: University hospital.
Patient(s): The study included patients with RV with or without OMA who tried to conceive spontaneously for 1 year either without undergoing surgery (group E; n = 284) or after surgery (group S; n = 221). The study population was further divided into four subgroups: women with RV without OMA who directly tried to conceive (group eRV; n = 121) or tried to conceive after surgery (group sRV; n = 96), and women with RV with OMA who directly tried to conceive (group eOMA; n = 163) or tried to conceive after surgery (group sOMA; n = 125).
Interventions(s): Expectant or surgical management.
Main Outcome Measure(s): Crude and cumulative SPRs.
Result(s): At 1 year, crude and cumulative SPRs were lower in group E (17.3% and 23.8%, respectively) than in group S (35.7% and 39.5%). Similarly, crude and cumulative SPRs were lower in group eRV (24.8% and 30.6%) than in group sRV (42.7% and 45.7%, respectively) and in group eOMA (11.7% and 18.0%) than group sOMA (30.4% and 34.5%). At 1 year, crude and cumulative SPRs were higher in group eRV (24.8% and 30.6%) than in group eOMA (11.7% and 18.0%), and in group sRV (42.7% and 45.7%) than in group sOMA (30.4% and 34.5%).
Conclusion(s): Crude and cumulative SPRs are lower in women treated with the use of expectant rather than surgical management. The presence of OMAs decreases SPRs independently from the treatment modality adopted. (Fertil Steril® 2017;107:969–76. ©2017 by American Society for Reproductive Medicine.)
Key Words: Endometrioma, endometriosis, fertility, pregnancy rate, surgery

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Reprint requests: Simone Ferrero, Ph.D., Academic Unit of Obstetrics and Gynecology, IRCCS AOU San Martino—IST, Largo R. Benzi 10, Genoa 16132, Italy (E-mail: simone.ferrero@unige.it).

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Endometriosis is a benign estrogen-dependent condition of reproductive-age women associated with pain symptoms and infertility. It can be categorized into three different forms: superficial endometriosis, deep infiltrating endometriosis (lesions penetrating ≥5 mm under the peritoneal surface), and ovarian endometriosis. Rectovaginal endometriosis (RV) is a severe form of deep infiltrating endometriosis that can partially or completely obliterate the pouch of Douglas. It is well established that RV causes bothersome pain symptoms and deterioration of quality of life and sexual function (1–4). However, the impact of RV on fertility is uncertain, because the burial of endometriosis beneath rectouterine adhesions with exclusion of the deepest part of the pouch of Douglas may not hamper fertilization processes (5). The majority of research has focused on the impact of medical/surgical management on pain relief (6–12), whereas scattered and scant evidence is available on the reproductive performance of patients with RV (5, 13–15). Furthermore, to the best of our knowledge, no previous study has compared the impact of expectant versus surgical management on the reproductive outcome of women with RV without a history of infertility. Therefore, the present retrospective study aimed to investigate the spontaneous pregnancy rates (SPRs) of women with RV treated with the use of expectant or surgical management.

MATERIALS AND METHODS

Study Design

This study was based on a retrospective analysis of a database prospectively collected from January 2009 to December 2015. All of the women signed written informed consents to record their data for scientific purposes, and the Regional Ethics Committee approved the study.

Outcomes of the Study

The primary end point of the study was to compare the crude and the cumulative SPRs at 1-year follow-up in women with RV treated with the use of expectant or surgical management. Crude pregnancy rate was calculated according to intention-to-treat analysis at 12-month follow-up, and cumulative pregnancy rate was calculated with the use of a Kaplan-Meier analysis. The secondary end point was to evaluate the influence of endometriomas (OMAs) on crude and cumulative SPRs in women with RV treated with the use of either expectant or surgical management. The tertiary end point was to assess crude and cumulative SPRs according to the age of the study population (<35 years and ≥35 years). Other end points of the study were to compare time to pregnancy, pregnancy outcomes, and reasons for stopping trying to conceive among the study groups. Pregnancy was defined as visualization of a gestational sac with demonstration of embryonic cardiac activity.

Study Population

The study included patients with RV wishing to conceive spontaneously who underwent either expectant or surgical management with 1 year of follow-up since the first attempt to become pregnant. Patients with RV were informed about the available evidence, expected benefits, risks, and contraindications of expectant and surgical management. In particular, they were told that scientific literature on the efficacy of conservative surgery as a fertility-enhancing procedure in women with RV was scant, and that the complete excision of this type of lesions might be technically challenging and associated with intraoperative or postoperative complications. It was explained that only one study investigated the reproductive prognosis in untreated women with RV, showing that, at 24 month-follow-up, the cumulative pregnancy rate was similar between expectant management (46.8%) and surgery (44.9%) although the latter increased pain-free survival time (5).

In all of the patients (also for those with a longer follow-up), we arbitrarily decided to present the outcomes only of the 1st year of follow-up. In fact, after ≥12 months of regular unprotected sexual intercourses without achieving a conception, a couple should be considered to be infertile and, especially in patients with endometriosis, they should be counseled about the possibility of undergoing assisted reproductive techniques. The following additional inclusion criteria were used for the study: regular menstrual cycle (24–35 days); and male partner with normal semen analysis (accordingly to World Health Organization [WHO] criteria). The exclusion criteria were: age ≥40 years; previous live births; diminished ovarian reserve as shown by low antral follicle count (AFC; five or fewer) and increased basal FSH (>12 IU/L); previous surgery for endometriosis; previous adnexal surgery (not related to endometriosis); history/diagnosis of hydrosalpinx or history of pelvic inflammatory disease; and uterine malformations. In case of preconceptional use of hormonal therapy, patients were advised to try to conceive after at least one menstruation after the interruption of the medical treatment.

The analysis of the primary outcome was performed considering the whole study population. SPRs were compared between patients who directly tried to conceive (group E) and those who tried to conceive after surgery (group S). In addition, for secondary outcomes, a further division into four subgroups was performed to assess the secondary outcome of the study, the influence of OMAs on SPRs. Therefore, the study population was divided into patients with RV without OMA who directly tried to conceive (group eRV) or tried to conceive after surgery (group sRV), and patients with RV with OMA who directly tried to conceive (group eOMA) or tried to conceive after surgery (group sOMA). In addition, for tertiary outcomes, the main groups and the subgroups were further distinguished according to the age of the patients (<35 years and ≥35 years). Other outcomes were time to pregnancy, pregnancy outcomes, and reasons for stopping trying to conceive between the study groups. Definitions of pregnancy and of pregnancy outcomes were classified according to the International Committee for Monitoring Assisted Reproductive Technology and the WHO revised glossary of ART terminology (16).

Study Protocol

The diagnosis of RV and OMAs was based on transvaginal ultrasonography (TVS), which was performed by two expert gynecologists (S.F. and U.L.R.M.) using a Voluson E6 ultrasound

machine (General Electric Medical Systems). RV was diagnosed when a hypoechoic nodule was seen on TVS in the rectovaginal space below the line passing along the lower border of the posterior lip of the cervix (under the peritoneum) (17). OMA cysts were diagnosed when a round-shaped cystic mass with thick walls, regular margins, and homogeneous low echogenic fluid content with scattered internal echoes without papillary projections was observed (18). The presence and severity of ovarian adhesions was assessed by means of a combination of gentle pressure with the vaginal probe and abdominal pressure with the examiner's free hand. The presence of ovarian adhesions was diagnosed when ovarian mobility was restricted and the ovary could not be separated from the peritoneum of the lateral pelvic wall and/or pouch of Douglas. We defined mild adhesions when some of the surrounding structures could not be separated from the ovary with gentle pressure but the ovary could be mobilized from part of the surrounding structures. We defined severe adhesions in the presence of fixed ovaries which could not be mobilized at all with pressure or separated from any of the surrounding structures (19). Rectal water-contrast TVS was performed when the presence of bowel infiltration was suspected (20). Patients were requested to contact our center in case of conception. However, all the patients were contacted by telephone or e-mail after 6 and 12 months of unprotected intercourses.

At baseline, the severity of pain symptoms (dysmenorrhea, nonmenstrual pelvic pain, and deep dyspareunia) was evaluated with the use of a 100-mm visual analog scale, with the left extreme of the scale indicating the absence of pain and the right indicating pain as bad as it could be. A score of 1–50 was considered to be mild pain, 51–80 moderate pain, and 81–100 severe pain. Patients were requested to rate the intensity of the pain experienced in the past month.

At baseline, AFC was assessed on the 2nd and 5th days of the menstrual cycle by counting the number of follicles with average diameters of 2–9 mm in both ovaries. Venous blood samples were drawn on day 3 of the menstrual cycle at baseline assessment. Ovarian reserve was estimated by measuring the levels of FSH. FSH levels were analyzed with the use of the Immulite 2000 XPi immunoassay system (Siemens Healthcare Diagnostics).

Surgical Treatment

All surgical procedures were performed laparoscopically and under general anesthesia. During surgery all visible endometriotic lesions (apart from those located on the diaphragm) were excised. RV was excised from the posterior vagina, rectum, posterior cervix, and uterosacral ligaments. Careful dissection of the endometriotic nodule from the anterior rectal wall was performed until the loose tissue of the rectovaginal spaces was reached. When RV infiltrated at least the muscularis propria of the rectosigmoid, segmental bowel resection was performed as previously described (21). The goal of the operation was to remove the disease en bloc; no attempt was made to dissect the endometriotic nodule from the rectosigmoid. A nerve-sparing technique was used to avoid postoperative functional complications. After adhesiolysis and bowel preparation, the rectosigmoid was transected caudal to the endometriotic lesions with the use of an Endopath ETS-Flex stapler (Ethicon Endo-Surgery). The cephalic portion of the rectosigmoid was extracted from the abdominal cavity through a small suprapubic incision (4–5 cm) and transected after inspection and palpation. A purse was created for the anvil before placing the colon in the pelvic cavity and closing the suprapubic abdominal incision. An end-to-end anastomosis was performed intra-abdominally with the use of a Curved Intraluminal Stapler (ILS 29; Ethicon Endo-Surgery). OMAs were treated according to a standardized laparoscopic stripping technique as previously described (22). Adhesiolysis from the surrounding structures was performed to allow proper mobilization of the ovaries. In case the cyst remained intact despite manipulation, it was punctured to drain the chocolate content. A sharp cortical incision was performed to detect a cleavage plane. Traction and countertraction were used to strip the cyst from the healthy surrounding ovary; as described by Canis et al., when the stripping became difficult, the red fibrotic tissue on the surface of the cyst was coagulated with the use of bipolar forceps (20–30 W current) and cut (23). After removal of the cyst, hemostasis was achieved by means of selective bipolar coagulation; when significant bleeding occurred, intraovarian suture was applied.

Statistical Analysis

The normal distribution of continuous-variable data was evaluated with the use of the Kolmogorov-Smirnov test. Categoric variables were compared by means of the chi-square test and the Fisher exact test according to sample size. Continuous variables were compared with the use of *t* test or Mann-Whitney test according to data distribution. Crude SPR was calculated according to intention-to-treat analysis considering as failures all women who had not conceived at 1 year and those who stopped trying to conceive before 1 year. Kaplan-Meier analysis was used to estimate cumulative SPR as a function of follow-up, and comparisons were performed with the use of the log-rank test.

RESULTS

A total of 284 and 221 patients were identified for inclusion in the study in group E and group S, respectively (Supplemental Fig. 1). No statistical significant difference between group E and group S was reported in the main demographic and clinical information, as reported in Table 1. Supplemental Tables 1 and 2 present the comparisons of demographic and clinical characteristics among the subgroups.

Spontaneous Pregnancy Rates

Crude and cumulative SPRs between group E and group S and for all subanalysis are reported in Table 2 and represented in Figures 1 and 2. Crude and cumulative SPRs were significantly higher in patients who underwent surgery versus those who were treated with expectant management (group E vs. group S, group eRV vs. group sRV, and group eOMA vs. group sOMA). Furthermore, the presence of OMA decreased crude and cumulative SPRs independently from

TABLE 1

Main demographic and clinical characteristics of the study population.

Variable	Group E (n = 284)	Group S (n = 221)	*P* value
Age (y)	33.1 ± 4.5	33.3 ± 3.8	.780
BMI (kg/m^2)	22.7 ± 2.5	22.6 ± 2.3	.416
Smokers	96 (33.8)	74 (33.5)	.984
Educational level			
Primary	19 (6.7)	11 (5.0)	.629
Secondary	186 (65.5)	152 (68.8)	
University	79 (27.8)	58 (26.2)	
Previous live births	0 (0)	0 (0)	1
Previous hormonal treatment			
None	14 (4.9)	9 (4.1)	.808
Any type	270 (95.1)	212 (95.9)	
Presence of OMA			
Unilateral	133 (81.6)	101 (80.8)	.923
Bilateral	30 (18.4)	24 (19.2)	
Number of OMA			
1	171 (88.6)	127 (85.2)	.225
2	20 (10.4)	22 (14.8)	
3	2 (1.0)	0 (0)	
OMA main diameter, cm			
<3	67 (34.7)	56 (37.6)	.792
3–4	53 (27.5)	39 (26.2)	
4–5	34 (17.6)	24 (16.1)	
5–6	22 (11.4)	21 (14.1)	
≥6	17 (8.8)	9 (6.0)	
Total	193 (100)	149 (100)	
Infiltration of at least the muscularis propria of the rectosigmoid	39 (13.7)	35 (15.8)	.591
Depth of infiltration of the bowel wall			
Muscularis propria	29 (74.4)	27 (77.1)	.770
Submucosa	6 (15.4)	6 (17.1)	
Mucosa	4 (10.2)	2 (5.2)	
Location of rectosigmoid nodule			
Lower rectum	6 (15.4)	2 (5.8)	.395
Upper rectum	13 (33.3)	11 (31.4)	
Rectosigmoid	20 (51.3)	22 (62.8)	
Sonographic length of the rectosigmoid nodule (mm)	24.1 ± 10.1	23.8 ± 8.4	.144
Adenomyosis			
Focal	19 (6.7)	17 (7.7)	.372
Diffuse	48 (16.9)	42 (19.0)	
Uterine myomas	81 (28.5)	59 (26.7)	.362
Dysmenorrhea			
Absent	41 (14.4)	30 (13.6)	.883
Mild	13 (4.6)	14 (6.3)	
Moderate	102 (35.9)	67 (30.3)	
Severe	128 (45.1)	110 (49.8)	
Severity of dysmenorrhea (mm, VAS)	76.2 ± 18.1	79.2 ± 18.2	.294
Dyspareunia			
Absent	71 (25.0)	50 (22.6)	.606
Mild	79 (27.8)	69 (31.2)	
Moderate	116 (40.9)	81 (36.7)	
Severe	18 (6.3)	21 (9.5)	
Severity of dyspareunia (mm, VAS)	55.8 ± 19.4	57.2 ± 20.2	.278
Noncyclic pelvic pain			
Absent	143 (50.4)	105 (47.5)	.587
Mild	23 (8.1)	12 (5.4)	
Moderate	104 (36.6)	83 (37.6)	
Severe	14 (4.9)	21 (9.5)	
Severity of noncyclic pelvic pain (mm, VAS)	62.8 ± 16.8	65.9 ± 16.1	.089
Dyschezia			
Absent	166 (58.5)	119 (53.8)	.345
Mild	10 (3.5)	11 (5.0)	
Moderate	102 (35.9)	82 (37.2)	
Severe	6 (2.1)	9 (4.0)	
Severity of dyschezia (mm, VAS)	59.3 ± 14.1	61.8 ± 15.6	.435

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TABLE 1

Continued.

Note: Results are presented as mean ± SD or n (%). BMI = body mass index; NA = not applicable; OMA = ovarian endometrioma; VAS = visual analog scale (0–100 mm).

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expectant or surgical management (group eRV vs. group eOMA and group sRV vs. group sOMA).

Spontaneous Pregnancy Rates according to Age < 35 Years

Crude and cumulative SPRs between group E and group S and for all subanalyses are reported in Supplemental Table 4 and represented in Supplemental Figures 2 and 3. Crude and cumulative SPRs were significantly higher in patients who underwent surgery versus those who were treated with expectant management (group E vs. group S and group eOMA vs. group sOMA) but not in those with only RV (group eRV vs. group sRV). Furthermore, the presence of OMA decreased crude and cumulative SPRs in patients treated by means of expectant management (group eRV vs. group eOMA) but not in those receiving surgical management (group sRV vs. group sOMA).

Spontaneous Pregnancy Rates according to Age ≥35 Years

Crude and cumulative SPRs between group E and group S and for all subanalysis are reported in Supplemental Table 5 and represented in Supplemental Figures 4 and 5. Crude and cumulative SPRs were significantly higher in patients who underwent surgery versus those who were treated with expectant management (group E vs. group S and group eRV vs. group sRV), whereas in those with OMA only crude SPRs were significantly higher (group eOMA vs. group sOMA). Furthermore, the presence of OMA decreased crude and cumulative SPRs in patients treated by means of expectant management (group sRV vs. group sOMA) but not in those receiving surgical management (group eRV vs. group eOMA).

Time to Pregnancy and Pregnancy and Delivery Outcomes

Data on time to pregnancy and the description of pregnancy and delivery outcomes are reported in Supplemental Tables 6, 7, and 8. Times to pregnancy were similar between group E and group S, with no statistical difference (Supplemental Table 6). No significant differences in time to pregnancy and pregnancy and delivery outcomes were observed between the subgroups Supplemental Tables 7 and 8.

Characteristics of Other Patients

A total of 185 (65.1%) in group E and 57 (25.8%) in group S stopped trying to conceive before 1 year. Patients in group

TABLE 2

Cumulative spontaneous pregnancy rates (SPRs) in the whole study population and subanalysis.

Group comparison	Number of pregnancies and crude SPR	Cumulative SPR
Group E (n = 284)	49 (17.3%)	23.8%
Group S (n = 221)	79 (35.7%)	39.5%
Chi-square test	$P<.001$	NA
Log-rank test	NA	$\chi^2 = 9.3$; $P=.002$
Group eRV (n = 121)	30 (24.8%)	30.6%
Group sRV (n = 96)	41 (42.7%)	45.7%
Chi-square test	$P=.004$	NA
Log-rank test	NA	$\chi^2 = 4.3$; $P=.039$
Group eOMA (n = 163)	19 (11.7%)	18.0%
Group sOMA (n = 125)	38 (30.4%)	34.5%
Chi-square test	$P<.001$	NA
Log-rank test	NA	$\chi^2 = 5.5$; $P=.019$
Group eRV (n = 121)	30 (24.8%)	30.6%
Group eOMA (n = 163)	19 (11.7%)	18.0%
Chi-square test	$P=.003$	NA
Log-rank test	NA	$\chi^2 = 6.0$; $P=.014$
Group sRV (n = 96)	41 (42.7%)	45.7%
Group sOMA (n = 125)	38 (30.4%)	34.5%
Chi-square test	$P=.040$	NA
Log-rank test	NA	$\chi^2 = 4.7$; $P=.031$

Note: E = expectant management; OMA = rectovaginal endometriosis with ovarian endometrioma; RV = rectovaginal endometriosis without ovarian endometrioma; S = surgical management.

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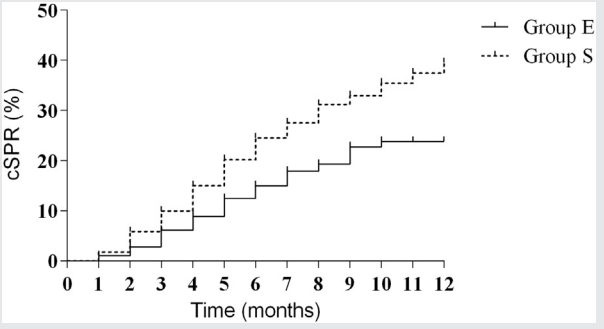
E stopped trying to conceive earlier than those in group S. The main causes for withdrawal are listed in Supplemental Table 9. Request for surgery because of pain symptoms was the main reason that induced patients of group E to stop trying to conceive spontaneously, and request for assisted reproductive technologies was the main cause that induced patients of group S to abandon the attempt to conceive spontaneously. Supplemental Tables 10 and 11 present the characteristics of patients who did not conceive in the subgroups. Patients in group eOMA stopped trying to conceive earlier than those of group sOMA. Significantly larger numbers of patients in group eRV (82.6%) and in group eOMA (82.2%) stopped trying to conceive before 1 year compared with group sRV (60.8%) and group sOMA (55.2%), respectively. The main causes for withdrawal are listed in Supplemental Table 10. Similar numbers of patients in group eOMA (82.2%) and group eRV (82.4%) stopped trying to conceive before 1 year, and no significant differences in time to stop trying to conceive and in the causes of withdrawal were reported between groups eRV versus eOMA or between groups sRV versus sOMA (Supplemental Table 11).

DISCUSSION

Robust evidence shows an association between endometriosis and infertility, but the exact mechanisms of this relationship are largely unknown (24). For these reasons, patients affected by endometriosis are significantly worried about their reproductive outcome and the most appropriate treatment options to increase the chance to conceive. The use of several medical and surgical techniques to improve pain symptoms and fertility outcomes has been widely investigated (6–11, 25, 26), but very little attention has been paid to study the reproductive performance of women who underwent expectant or surgical management (5, 27, 28). The choice of any form of treatment for endometriosis should be based on the patient's needs and expectations, and especially on reliable evidence. Furthermore, there is currently a pronounced trend toward delayed childbearing across industrialized nations. Therefore, the decision of the most appropriate strategy is often influenced by patient's needs to avoid any waste of time and to achieve pregnancy in a shorter time frame. Ideally, therefore, the physician should be able to counsel the woman by describing a reproductive prognosis and underlying an estimate of the potential benefits and limits of any interventional option.

The present retrospective study was designed to estimate the reproductive outcome of patients with RV and without a history of infertility who directly tried to conceive compared with those who underwent conservative surgery and subsequently tried to conceive. This research showed that both crude and cumulative SPRs were superior in patients who underwent surgery than in those who were treated by means of expectant management. The association between RV and decreased fertility is controversial (29). An explanation for this may be that RV is frequently related to other forms of endometriosis that may affect spontaneous conception (30, 31). Superficial endometriotic implants may cause a local inflammatory reaction, and the release of inflammatory cytokines in the peritoneal fluid may damage the quality of the released oocyte and its fertilization (32). Furthermore, adhesions are common in patients with RV, and their presence may cause anatomic distortion that deteriorates tubal function (33). Therefore, it is possible that the laparoscopic excision of superficial lesions and adhesiolysis

FIGURE 1



Cumulative 12-month spontaneous pregnancy rate (cSPR) according to the treatment modality adopted in the whole study population (log-rank test: $\chi^2 = 9.3$; $P=.002$). E = expectant management; S = surgical management.

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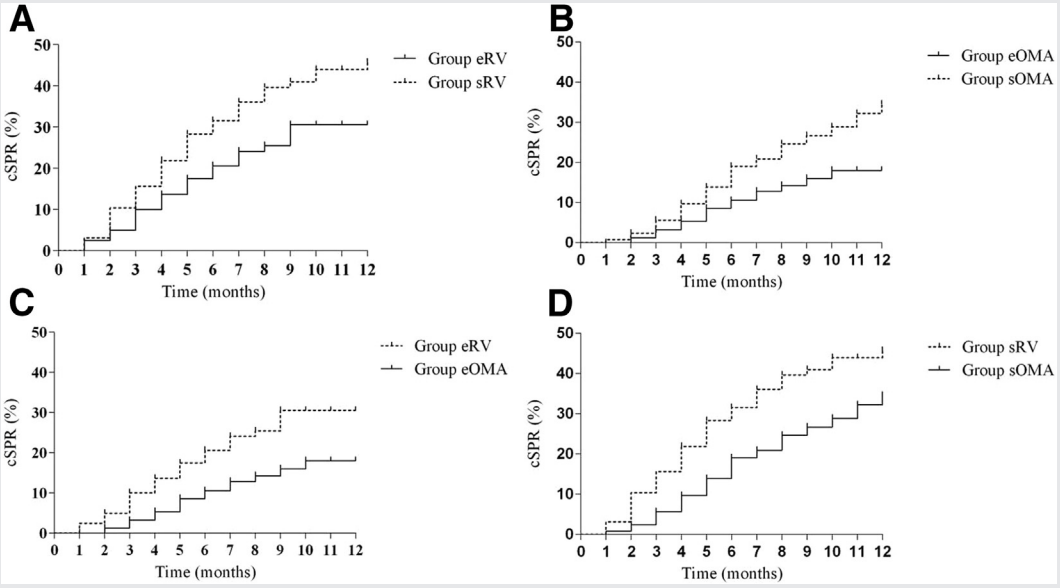
FIGURE 2



12-month cSPR in the subgroups: (**A**) according to the treatment modality adopted in women with rectovaginal endometriosis (RV) without ovarian endometrioma (OMA; log-rank test: $\chi^2 = 4.3$; P=.039); (**B**) according to the treatment modality adopted in women with RV with OMA (log-rank test: $\chi^2 = 5.5$; P=.019); (**C**) in women on expectant management with RV without OMA versus with OMA (log-rank test: $\chi^2 = 6.0$; P=.014); (**D**) in surgically treated women with RV without OMA with OMA (log-rank test: $\chi^2 = 4.7$; P=.031). Abbreviations as in Figure 1.

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improved the SPRs of patients who underwent surgical treatment compared with those who underwent expectant management.

Another possible explanation for the lower crude and cumulative SPRs observed in patients in group E is the presence of pain symptoms. Although the intensity of these symptoms was similar between the two study groups at baseline, it significantly decreased after surgical treatment in group S (data not presented). Therefore, pain and especially dyspareunia may have interfered with regular intercourse, consequently affecting the likelihood of a spontaneous conception.

To the best of our knowledge, only one prospective study compared the incidence of pregnancy in women with RV undergoing conservative surgery compared with those undergoing expectant management (5). In that study by Vercellini et al., all of the patients were infertile and those who were surgically treated were operated on by means of laparotomy. In contrast, our study population included only women without a history of infertility, and laparoscopy was always performed in patients who underwent surgery. In the research by Vercellini et al., cumulative pregnancy rates at 12-month follow-up were 20.5% in patients who underwent surgery and 34.7% in those on expectant management. Opposite findings were observed in the present study. However, in Vercellini et al.'s research, the percentage of patients who withdrew from the study was lower (19.5%–19.7%) compared with the percentage reported in our study (25.8%–65.1%); this certainly influenced the cumulative SPRs of our study. Furthermore, it may be speculated that both the prospective design of the earlier study and the presence of infertile patients may have influenced the rate of patients who were motivated to complete the study until 1 year. Finally, in the Vercellini et al.'s study, additional infertility treatments, such as clomiphene citrate alone, clomiphene citrate with timed intrauterine insemination, and controlled ovarian hyperstimulation with intramuscular gonadotropins and timed intrauterine insemination, were allowed and may have further improved the reproductive performance.

A second interesting finding of the present study was that the presence of OMAs reduced crude and cumulative SPRs compared with patients without OMAs, in patients treated with the use of either expectant or surgical management. Several studies tried to elucidate whether the presence of OMA per se may deteriorate ovarian physiology. The detrimental effect induced by OMAs is supported by the demonstration of a plethora of morphologic and functional features (34). In particular, the altered biologic mechanisms related to the presence of OMAs per se support a detrimental effect on the ovarian cortex surrounding the endometriotic cyst (35) and an impairment of the normal ovarian physiology (36). However, the clinical impact of these biologic modifications seems limited. Recently, our group demonstrated that spontaneous ovulation in the affected ovary is not influenced by the presence of unilateral OMAs, independently from its size and the number and laterality of the endometriotic cysts. Furthermore, that study showed clinically relevant crude SPRs of 43.0% and 41.0% in the general study population and in the subgroup of women with concomitant deep infiltrating endometriosis, respectively (37).

In addition, current evidence does not support a detrimental effect on ovarian reserve owing to the presence of OMAs per se (38, 39). Despite these considerations, we deem that, in the present study, the lower crude and cumulative SPRs in patients with OMAs undergoing expectant management compared with those undergoing expectant management without OMAs may be justified by the high severity of the stage of the disease and the consequent severity of anatomic distortion. Instead, in patients with OMAs who underwent laparoscopy, it should be considered that the surgical excision of OMAs may cause a decrease in ovarian reserve (40, 41) and this may explain the lower crude and cumulative SPRs despite adhesiolysis and restoration of anatomy.

A third intriguing issue of this study is the very high rate (~65%) of patients on expectant management who decided to stop trying to conceive before 1 year. In fact, both crude and cumulative SPRs in patients on expectant management were strongly influenced by the fact that about two-thirds of those women gave up any attempt to conceive spontaneously before 1 year. The majority of them decided to undergo surgery owing to the severity of pain symptoms. Therefore, women with RV wishing to conceive spontaneously should be informed that they have ~30% probability of changing their plans to undergo surgery in the 1st year. This is particularly relevant for older patients, because it may postpone spontaneous conception or the access to an IVF path.

A fourth relevant point of the present research is the stratification of the results according to age. Patients aged <35 years with only RV (group eRV vs. group sRV) and those receiving surgical management (group sRV vs. group sOMA) showed no difference in both crude and cumulative SPRs. Patients aged ≥35 years with OMA (group eOMA vs. group sOMA) demonstrated no difference in cumulative SPRs, and those receiving expectant management (group eRV vs. group eOMA) demonstrated no difference in both crude and cumulative SPRs. However, we deem that these results should be interpreted with caution because this subanalysis was performed between small sample sizes of patients and any speculation may be hazardous.

A fifth point that deserves to be considered when counseling a patient with RV is the history of previous live births. The present study included only nulliparous women, and therefore our findings can not be generalized to all patients with RV. In fact, a previous live birth decreases the risk of infertility, particularly if it occurred within a few years and with the same partner; such women might be informed that the chances to conceive with expectant management are higher than those observed in this study.

This is the first study comparing SPRs of women with RV and without a history of infertility treated by means of expectant or surgical management. The main strength of this study is the large sample size and the consequent possibility to stratify patients and to assess the influence of OMAs on reproductive performance. Another strength of this study is that it offers a complete overview on the rate of patients who actually tried to conceive for ≥1 year. We deem that this information, together with the knowledge on SPRs, may significantly influence clinical practice, allowing the physician to improve counseling of the patient with RV with or without OMAs.

The main limitation of this study is the retrospective study design and the lack of randomization between surgical and expectant management. However, the demographic and clinical characteristics of the study groups and subgroups did not significantly differ, thus limiting any possible bias on the final findings of this research. Another important limitation of this study is that the population included was highly selected, and therefore its findings can not be extrapolated to the general population of women with endometriosis but only to patients with RV, no history of infertility, and with partners with normal semen analysis.

CONCLUSION

This study describes for the first time SPRs in patients with RV and without history of infertility who underwent expectant or surgical management. Furthermore, this study confirms that the presence of OMAs decreases SPRs independently from the treatment modality adopted.

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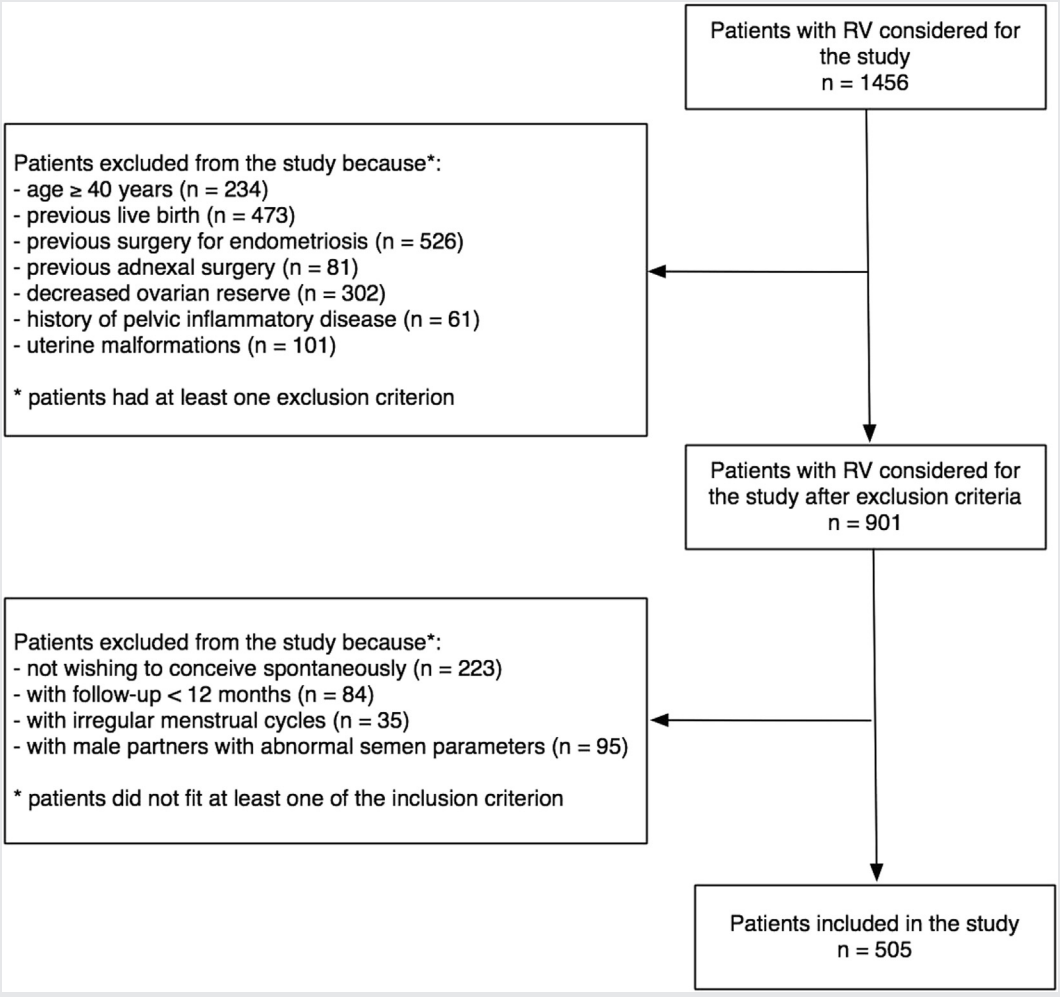
SUPPLEMENTAL FIGURE 1



Flow chart showing patients' selection through the study. RV = rectovaginal endometriosis.

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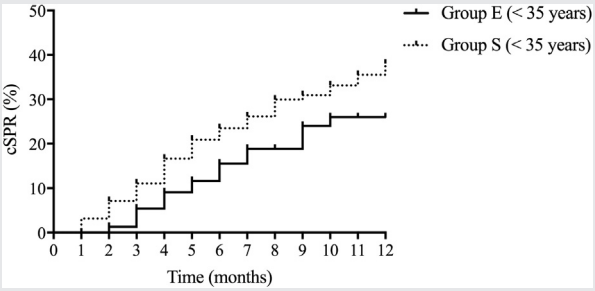
SUPPLEMENTAL FIGURE 2



Cumulative 12-month spontaneous pregnancy rate (cSPR) according to the treatment modality adopted in the study population aged <35 years (log-rank test: $\chi^2 = 3.9$; P=.049). E = expectant management; S = surgical management.

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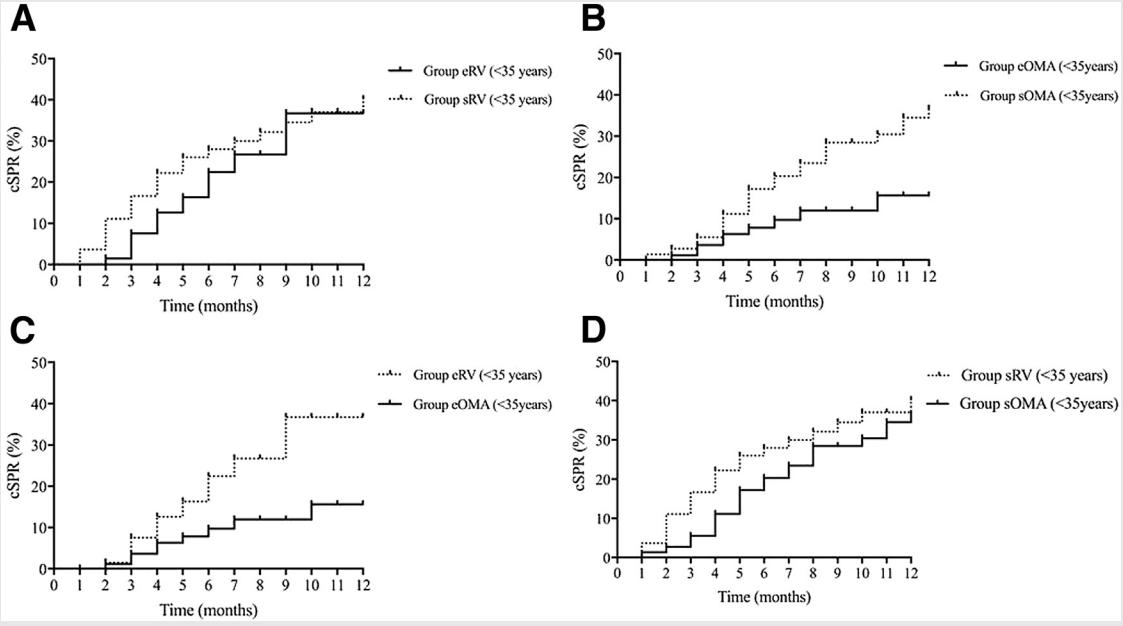
SUPPLEMENTAL FIGURE 3



12-month cSPR in the subgroups of women aged <35 years: (**A**) according to the treatment modality adopted in women with without ovarian endometrioma (OMA; log-rank test: $\chi^2 = 0.4$; P=.052); (**B**) according to the treatment modality adopted in women with RV with OMA (log-rank test: $\chi^2 = 5.2$; P=.022); (**C**) in women on expectant management with RV without endometriomas versus with endometriomas (log-rank test: $\chi^2 = 5.5$; P=.019); (**D**) in surgically treated women with RV without OMA versus with endometriomas (log-rank test: $\chi^2 = 0.6$; P=.456). Abbreviations as in Supplemental Figures 1 and 2.

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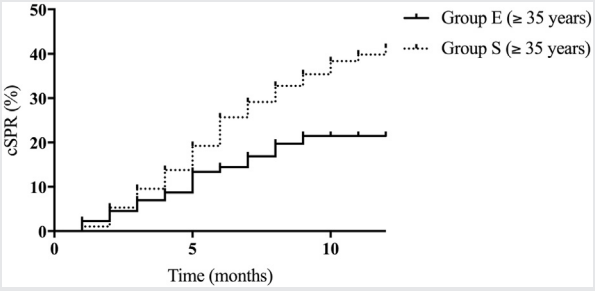
SUPPLEMENTAL FIGURE 4



12-month cSPR according to the treatment modality adopted in the study population aged ≥35 years (log-rank test: $\chi^2 = 5.9$; P=.015). Abbreviations as in Supplemental Figure 2.

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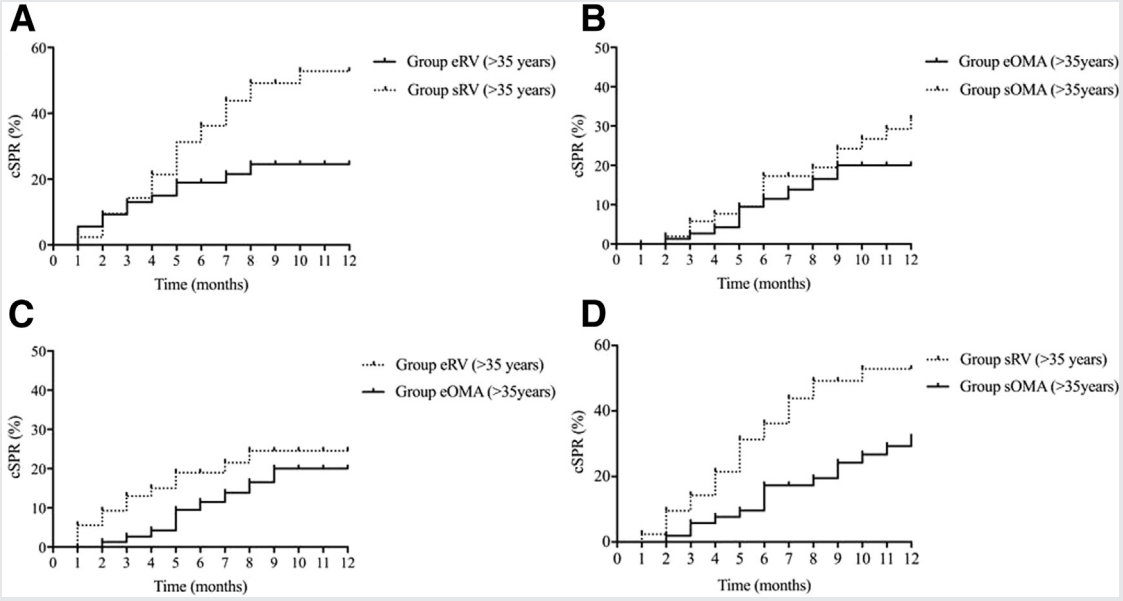
SUPPLEMENTAL FIGURE 5



12-month cSPR in the subgroups of women aged ≥35 years: (**A**) according to the treatment modality adopted in women with RVs without OMA (log-rank test: $\chi^2 = 5.4$; P=.020); (**B**) according to the treatment modality adopted in women with RV with OMA (log-rank test: $\chi^2 = 0.8$; P=.357); (**C**) in women on expectant management with RV without OMA versus with OMA (log-rank test: $\chi^2 = 1.3$; P=.259); (**D**) in surgically treated women with RV without OMA versus with OMA (log-rank test: $\chi^2 = 6.0$; P=.014). Abbreviations as in Supplemental Figures 1 and 2.

Leone Roberti Maggiore. Fertility in women with endometriosis. Fertil Steril 2017.