ORIGINAL ARTICLE: REPRODUCTIVE SURGERY

Fertility outcome of laparoscopic treatment in patients with severe endometriosis and repeated in vitro fertilization failures

David Soriano, M.D.,[a,b,e] Iris Adler, M.D.,[e] Jerome Bouaziz, M.D.,[a,b,e] Matti Zolti, M.D.,[a,b,e] Vered H. Eisenberg, M.D.,[a,b,e] Mordechai Goldenberg, M.D.,[a,e] Daniel S. Seidman, M.D.,[a,c,d,e] and Shai E. Elizur, M.D.[a,c,d,e]

[a] Department of Obstetrics and Gynecology, [b] Endometriosis Center, and [c] IVF Unit, Sheba Medical Center Tel Hashomer, Ramat Gan; [d] IVF Unit, Assuta Medical Center; and [e] Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Objective: To evaluate fertility outcomes in infertile women with severe endometriosis (The revised American Fertility Society classification [AFS] 3–4) and repeated IVF failures, who underwent surgery due to exacerbation of endometriosis-related symptoms.
Design: Retrospective cohort study.
Setting: University hospital.
Patient(s): All women who failed IVF treatment before surgery and who underwent laparoscopic surgery for severe endometriosis between January 2006 and December 2014.
Intervention(s): All patients were operated by highly skilled surgeons specializing in laparoscopic surgery for advanced endometriosis. Only patients with evidence of endometriosis in the pathology specimens were included in this study.
Main Outcome Measure(s): Delivery rate after surgery.
Result(s): Seventy-eight women were included in the present study. All women were diagnosed with severe endometriosis during surgery (AFS 3–4) and all women had experienced failed IVF treatments before surgery. All women were symptomatic before their surgery. After surgical treatment 33 women (42.3%) delivered. Three women (9%) conceived spontaneously and all other women conceived after IVF treatment. Women who delivered were younger (32.5 [±4.1] years vs. 35.5 [±3.8] years), were less often diagnosed with diminished ovarian reserve before surgery (6% vs. 28.8%), and were more often diagnosed with normal uterine anatomy (by preoperative transvaginal ultrasound and during operation). In addition, performing salpingectomy during surgery was associated with a trend of improvement in delivery rates after surgery (70% in women who delivered vs. 51% in women who failed to deliver).
Conclusion(s): Symptomatic women with severe endometriosis and repeated IVF implantation failures may benefit from extensive laparoscopic surgery when performed by an experienced multidisciplinary surgical team to improve IVF outcome. (Fertil Steril® 2016;■:■–■. ©2016 by American Society for Reproductive Medicine.)
Key Words: Endometriosis, radical surgery, fertility, IVF failure

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Endometriosis is the presence of endometrial glands or stroma in sites other than the uterine cavity such as the ovaries, pelvic peritoneum, and the rectovaginal septum. It affects 5%–15% of women of reproductive age and is associated with dysmenorrhea, dyspareunia, chronic pelvic pain, irregular uterine bleeding, and infertility (1). The prevalence of endometriosis among women experiencing pain, infertility, or both is 35%–50% (2), but its diagnosis is often delayed several years from the onset of symptoms (3).

Endometriosis causes infertility through some changes that are known (e.g., pelvic adhesions, anatomical pelvic distortion, inflammatory changes in the peritoneal fluid [PF] that affect sperm motility, and endometriomas that lead to diminished ovarian reserve) (4–8) and probably by some other unknown changes. The severity of endometrial symptoms cannot be

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D.S., and I.A. should be considered similar in author order.
Reprint requests: David Soriano, M.D., Endometriosis Center, Department of Obstetrics and Gynecology, Sheba Medical Center and Tel-Aviv University-Saklar Medical School, Ramat Gan, Israel (E-mail: didisoriano@gmail.com).

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correlated with the location and spread of endometrial lesions, and noninvasive diagnostic tests and serum markers for endometriosis do not exist. Although transvaginal ultrasound (TVS) has recently emerged as a first-line imaging modality for the noninvasive diagnosis of endometriosis (9), the gold standard for diagnosis and staging remains surgery, with lesser consideration given to symptoms, physical examination, and imaging.

The role of surgery in improving fertility outcome in women with endometriosis is a matter of debate. Therefore, current guidelines of the European Society of Human Reproduction and Embryology (ESHRE) remain inconclusive (10). Some studies (11) have shown that surgical ablation for mild endometriosis (The American Fertility Society [AFS] stage 1–2) improves pregnancy rates (PRs) compared with diagnostic laparoscopy, even in women undergoing IVF treatments (12). Other studies (13) do not concur. Barri et al. (14) reported that women with large endometriomas (mean, 5.6 cm) have a higher PR when treated with surgery followed by IVF compared with that of surgery or IVF alone. However, it should be noted that Barri et al. (14) reported the cumulative PR after surgery alone as 54.2% (with conception occurring within a mean interval of 11.2 months; range, 1–66 months), whereas the PR after IVF was reported as 32.2% per retrieval. Because the recurrence rate after surgery was 22% (14) and the cumulative PR after IVF was not noted, the comparisons made by Barri et al. (14) may have been inappropriate.

Patients with deep infiltrating endometriosis may represent a separate subset. Bianchi et al. (15) reported on a cohort of patients who underwent extensive deep infiltrating endometriosis resection before IVF. In their study, patients who underwent resection had fewer oocytes retrieved and required higher gonadotropin doses, yet they achieved significantly higher PRs than those who did not undergo resection. However, Bianchi et al. (15) did not specify associated ovarian factors (e.g., diminished ovarian reserve) for the women who underwent IVF treatment without resection, thus possibly biasing the results. We have to note that in the present study fewer oocytes were retrieved in only women who had associated endometriomas cystectomy suggesting also that deleterious effects are related to ovarian surgery rather than to deep endometriosis surgery. Bianchi et al. (15) did not report spontaneous pregnancies recorded during the follow-up. But as mentioned in the review of Roman (16), there were 2.5-fold more spontaneous conceptions in the surgical arm than in the IVF arm.

Littman et al. (17) reported a 76% PR after endometrial surgery in women who failed IVF treatments. However, it was a small study based on 29 patients, and most of the women who conceived had mild endometriosis (AFS 1–2) and underwent only one or two IVF cycles before surgery. The aim of our study was to evaluate fertility outcomes in infertile women with severe endometriosis (AFS 3–4) and repeated IVF failures who underwent surgery for exacerbation of endometriosis-related symptoms.

MATERIALS AND METHODS

This is a retrospective cohort study of all women with endometriosis who underwent laparoscopic surgery at the Sheba Medical Center, Tel Hashomer, between January 2006 and December 2014. Institutional review board approval was obtained. All patients were operated by highly skilled surgeons specializing in laparoscopic surgery for advanced endometriosis (D.S., M.Z., M.G.).

Only patients who met the following criteria were included: [1] patients with pathological evidence of endometriosis; and [2] patients with infertility who underwent IVF treatment before surgery and who wished to conceive after surgery. Data regarding IVF treatments were obtained from patients' files at the Sheba Medical Center and at the IVF unit at Assuta Medical Center, Tel Aviv, Israel. The patients' medical records and operative reports were reviewed, and characteristics such as age, duration of infertility, additional infertility problems, previous assisted reproductive technology (ART) treatments, prior surgeries, and preoperative symptom profile were recorded. In addition, all surgical findings and procedures were documented, and any missing information was obtained by phone. Telephone interviews were conducted for long-term follow-up of fertility outcomes.

The data were analyzed using a computer-based software (SSPS). Continuous data were assessed for distribution with the D'Agostino-Pearson normality test. Parametric and nonparametric data were analyzed using the *t* test and Mann-Whitney test, and categorical data were analyzed using Fisher's exact test of a contingency table. Statistical significance was defined as $P<.05$.

RESULTS

Seven hundred ten women with endometriosis underwent laparoscopic surgery between 2006 and 2014 at the Sheba Medical Center. One hundred ten of those patients suffered from infertility and failed IVF treatments before surgery, but 32 of them were excluded from the study for the following reasons: 9 women (7 of whom had a hysterectomy) were offered surrogacy after surgery, 6 women did not wish to conceive after their operation, 4 women who underwent IVF treatment before their surgery were offered oocyte donation before surgery, 8 women were lost to follow-up, and 4 women had no histologic evidence of endometriosis during surgery.

A total of 78 women were included in this study. Their characteristics are presented in Table 1. The mean age was 34.3 ± 4.2 years. Most were nulliparous (71.8%), had experienced an average duration of 52.9 ± 36.1 months of infertility, and had undergone an average of 6.6 ± 4.9 unsuccessful IVF cycles before surgery. Sixty women (75.9%) had had at least one prior surgery for endometriosis. All women were diagnosed with severe endometriosis (AFS 3–4) and failed IVF treatments before surgery. All of them were also symptomatic before surgery. The most common preoperative symptoms were dysmenorrhea (87%), gastrointestinal symptoms (e.g., constipation, diarrhea, dyschezia, tenesmus, rectal bleeding; 47%), and dyspareunia (41%). Fifteen patients (19%) had urinary symptoms such as dysuria, frequency, urgency, or hematuria. After surgical treatment, 33 women (42.3%) delivered. Three women (9%) conceived spontaneously and all other women conceived after IVF treatment. The median interval between surgery and pregnancy was 6 months, and the median