Laparoscopic treatment of endometriosis in patients with failed in vitro fertilization cycles

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Endometriosis is one of the most common gynecologic disorders and is significantly more prevalent in the setting of infertility. The prevalence of endometriosis in infertile women ranges from 25% to 50% compared to 5% in fertile women. Successful laparoscopic management of all stages of endometriosis was reported as early as 1986. This has revolutionized the management of endometriosis. The benefits of surgical therapy for infertility associated with endometriosis have been well documented.

Objective:
To report our experience in patients with previous IVF failures who conceived after laparoscopic treatment of endometriosis.

Design:
Retrospective case series.

Setting:
Tertiary center IVF and endoscopy programs.

Patient(s):
Infertility patients with history of prior IVF failures.

Intervention(s):
Laparoscopic evaluation and treatment of endometriosis by the same surgeon.

Main Outcome Measure(s):
Occurrence of conception after laparoscopic treatment of endometriosis.

Result(s):
Of 29 patients with prior IVF failures, 22 conceived after laparoscopic treatment of endometriosis, including 15 non-IVF pregnancies and 7 IVF pregnancies.

Conclusion(s):
In the absence of tubal occlusion or severe male factor infertility, laparoscopy may still be considered for the treatment of endometriosis even after multiple IVF failures.


Key Words: Laparoscopy, endometriosis, infertility, IVF
failed IVF cycles. Patients with severe male factor infertility requiring intracytoplasmic sperm injection (ICSI) or tubal factor infertility with bilateral tubal obstruction were not included.

Surgical treatment consisted of thorough CO2 laser ablation or excision of all peritoneal and nonperitoneal endometriotic lesions, lysis of adhesions, and appropriate management of ovarian endometriomas. The surgical approach was based on intraoperative assessment of the pathophysiology or the type of endometrioma, which is found to be quite varied. For example, reassurance was made that type I endometriomas are totally removed. In type II endometriomas, only the endometriotic plaque, not the luteal cyst wall is removed. No medical treatment of endometriosis was administered after surgery. All surgeries were performed by the senior surgeon (CN).

Statistical calculations were performed using Student's t test and \( \chi^2 \) test as appropriate, and statistical significance was defined as \( P < .01 \). Institutional review board approval was obtained before chart review.

**Results**

Twenty-nine patients with multiple IVF failures underwent laparoscopic treatment. Eighteen of these patients were nulliparous. Three patients had a known history of endometriosis before IVF treatment, whereas the remaining 26 had no previous laparoscopy. At least one IVF cycle had failed in all patients, with an average of 2.2 (±0.7) failed cycles. Twenty-two of 29 (76%) of the patients who had laparoscopic treatment of endometriosis conceived. The mean age of this group was 34.3 ± 3.6 years with a range of 28–40 years. The characteristics of these patients are shown in Table 1. Of the patients in the study who were diagnosed with stage I disease, 4/4 (100%) conceived. Five of 6 (83%) of patients with stage II disease conceived. Five of 6 (83%) of patients with stage III disease conceived and 8/13 (62%) of those with stage IV disease conceived.

Twelve patients conceived spontaneously and two patients conceived with clomid/IUI. Time to conception, in these 14 patients, ranged from 1 to 8 months after surgery. Seven patients conceived with additional IVF treatment after surgery. An additional patient conceived by IVF and also had a subsequent spontaneous conception. Twenty-four percent of the patients in the laparoscopy group did not conceive (7/29). The mean age of these patients was 36.4 ± 5.7 years, with a range of 31–40 years. The majority of these patients had stage IV endometriosis (5/7). For further analysis, the outcome of patients who decided not to undergo laparoscopy was compared with those of patients who elected laparoscopic evaluation. The mean age of this group was 35.1 years and the average number of cycles was 2.4, which was not significantly different from the laparoscopy group. In this nonlaparoscopy group 13 of 35 conceived. Of those who conceived, two of the pregnancies were spontaneous and the rest were from repeat IVF cycles.

The group who underwent laparoscopy after failed IVF cycles is compared to the control group in Table 2. There was no significant difference in the mean age or FSH level in either of the patient groups. A significantly higher pregnancy rate (PR) was demonstrated in the laparoscopy group vs. the nonlaparoscopy group. Also, the number of patients who were able to conceive spontaneously was significantly higher in the group that had undergone laparoscopic treatment of endometriosis. Statistical significance was defined as \( P < .01 \).

**Discussion**

Fecundity rates in women with endometriosis tend to be lower than normal in both natural and ART cycles, and despite extensive research, no agreement has been reached concerning the mechanism of infertility. A reduction in PR may be due to decreased fertilization secondary to the effect of endometriosis on oocyte quality, decreased embryo quality, and a decrease in implantation. Several studies have examined the association of endometriosis and implantation failure on a molecular level. These basic science studies suggest that endometriosis may be involved in the deregulation of select genes that play critical roles in the process of implantation. Therefore, in addition to decreasing inflammation in the pelvis and associated toxicity to embryos and gametes, surgical treatment of disease may result in enhanced uterine receptivity.

In our study, 22 of 29 patients (76%) achieved pregnancy after laparoscopic treatment for
endometriosis. Other studies have quoted a range of 20%–65% PR after laparoscopic treatment. We believe that the remarkably high PR achieved in the patients who underwent laparoscopic evaluation is a reflection of the thorough surgical technique. A recent study by Alborzi et al. concurred with this theory. This suggests that, even in the setting of multiple IVF failures, laparoscopic management of endometriosis remains a viable option. A large number of patients, especially when age is a factor, opt to proceed with IVF, without undergoing surgical evaluation and treatment of endometriosis. It is likely that in many of these women, IVF can still be successful despite the presence of untreated endometriosis. However, bypassing the pelvic factor may not always be sufficient to achieve optimal success. A meta-analysis conducted by Barnhart et al., including 22 published studies pertaining to the effect of endometriosis on IVF success rates, concluded that patients with endometriosis-associated infertility undergoing IVF respond with significantly decreased levels of all markers of reproductive outcome and have 50% of the chance of achieving pregnancy compared with tubal factor controls. It is our stance that complete and thorough microsurgical eradication of endometriosis allows many patients to conceive without further IVF therapy and may help optimize success for those who require subsequent IVF cycles. Our findings are in concordance with several published studies on the effect of ablation of endometriosis lesions on fertility in patients with minimal-to-mild endometriosis, although there are some contradictory reports present in the literature. The fact that almost 50% of the patients in our study (14/29) conceived without further IVF therapy is very encouraging. Several studies have assessed the impact of the stage of endometriosis on ART outcomes. Those investigators found that patients with stage III–IV endometriosis had significantly reduced fertilization rates as compared with patients with milder endometriosis. Thus, it may be that increasing stages of endometriosis correlate inversely with fertilization potential. Although there is still a lack of randomized controlled trials that evaluate the effectiveness of laparoscopic surgery for severe endometriosis-associated infertility, many observational studies suggest that in women with stage III–IV endometriosis, without other identifiable infertility factors, conservative surgical treatment with laparoscopy may increase fertility. Parallel to these findings, in our study, 13 of 19 patients (68.4%) with stage III–IV endometriosis conceived spontaneously or with the aid of IVF. Although there are concerns that surgical treatment may result in diminished ovarian reserve, in experienced hands, laparoscopic resection or ablation of endometriosis may enhance fecundity in infertile women, regardless of the severity of the disease. In fact, it has been our personal experience that more than 90% of the infertile couples with unexplained infertility have endometriosis or other pelvic pathology, like adhesions, at the time of laparoscopy. Several studies have concluded that laparoscopic removal of endometriomas before IVF does not improve fertility outcomes. For example, a study by Garcia-Velasco et al. was recently published on this issue. However, the design of this study may confound interpretation of its results. For example, diagnosis of endometriomas in the control group was solely based on ultrasound observation, which has only an 85% positive predictive value. It is difficult to distinguish by ultrasound the presence of a hemorrhagic corpus luteum vs. endometrioma. Studies addressing the impact of endometriosis on IVF outcome often fail to take into account the intrinsic diagnostic limitations of ultrasound. Recently, Moore et al. reviewed 38 articles related to diagnosis of endometriosis by ultrasound scan. Although transvaginal ultrasonography was found to be a useful test to detect or exclude the presence of an ovarian endometrioma, the mean size of the endometriomas included in these studies was 40 mm. This suggest that the resolution obtained with current ultrasound techniques is inadequate to detect smaller endometriomas, and most smaller endometriomas are “true” endometriomas and require complete excision, not partial treatment by coagulation, if we are expecting the best results. Ultrasound can be used by the clinician to help establish a presumptive diagnosis of ovarian involvement with endometriosis, but laparoscopy is necessary to confirm the diagnosis.
In addition, Garcia-Velasco et al. stated that they were unable to surgically remove the entire endometrioma cyst wall in some cases. This inability to thoroughly treat the endometriosis might have also been a contributing factor to the results of that study. As previously reported we classify endometriomas into two types. Type I endometriomas are smaller and 100% consist of endometrial glands and stroma. These endometriomas usually result from invagination of endometriotic plaques into the stroma. They are usually smaller than 5 cm and are more difficult to remove. One often has to piecemeal these cyst walls carefully. Most often surgeons end up coagulating these endometriomas, which leads to inadequate treatment. Type II endometriomas are invasion of functional cysts like corpus luteum in varying degrees by endometriosis plaques. Furthermore, in our experience, almost all of the patients with endometriomas have peritoneal endometriosis, and this should be thoroughly treated in patients who desire pregnancy. In the article by Garcia-Velasco et al. no mention was made in that regard, except for treating the endometriomas. The contrast in findings may also be explained by the presence of varying etiologies or types of endometriosis and endometriomas, as well as differing approaches and philosophies of treating endometrial lesions, adhesions, and endometriosis. It has been proposed that peritoneal endometriosis, ovarian endometriosis, and adenomyotic nodules of the rectovaginal septum are three different entities. It has also been suggested that if indeed this is the case, then different treatment modalities may be applicable to certain types of endometriosis. It is our belief that the subset of patients with failed multiple cycles of IVF may harbor a certain type of endometriosis that allows them to benefit from thorough surgical therapy. Further studies examining these issues are needed to provide additional clarification.

It is not unusual for patients and healthcare providers to perceive IVF as the final treatment for infertility. When this definitive therapy fails repeatedly, clinicians and patients may be inclined to pursue oocyte donation or elect to forego further treatment altogether. This is especially true in women of advanced age and in patients with borderline embryo quality. Presently, as a result of our clinical observation in patients with failed IVF, before egg donation or adoption, we offer the option to have meticulous laparoscopic evaluation and treatment by a skilled surgeon. Furthermore, we would not classify an infertility condition as unexplained without confirming the absence of endometriosis by a thorough laparoscopy. In our experience, patients under 35 years old with unexplained infertility who are found to have endometriosis at the time of laparoscopy have an excellent chance of pregnancy following surgical treatment without ART. However, we acknowledge the best way to evaluate this issue would be to conduct a multicenter randomized clinical trial.

Table 1: Characteristics of patients who underwent laparoscopic treatment of endometriosis.

<table>
<thead>
<tr>
<th>Age</th>
<th>Parity</th>
<th>Prior Cycles</th>
<th>Date of Surgery</th>
<th>Stage of Endometriosis</th>
<th>Method of Conception</th>
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<tr>
<td>38</td>
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<td>2</td>
<td>7/99, 1/02</td>
<td>II</td>
<td>IV (endometriomas)</td>
</tr>
<tr>
<td>33</td>
<td>G0</td>
<td>2</td>
<td>8/99</td>
<td>I</td>
<td>IVF</td>
</tr>
<tr>
<td>28</td>
<td>G0</td>
<td>2</td>
<td>6/00</td>
<td>IV</td>
<td>IVF</td>
</tr>
<tr>
<td>34</td>
<td>G2P20</td>
<td>1</td>
<td>8/00</td>
<td>II</td>
<td>IVF</td>
</tr>
<tr>
<td>32</td>
<td>G0</td>
<td>1</td>
<td>8/01</td>
<td>IV</td>
<td>Spontaneous</td>
</tr>
</tbody>
</table>
### Table 2

<table>
<thead>
<tr>
<th>Case</th>
<th>G3P30</th>
<th>12/01</th>
<th>2/02</th>
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<th>Spontaneous</th>
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<tbody>
<tr>
<td>32</td>
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<td>2</td>
<td>3/02</td>
<td>I</td>
<td>Spontaneous</td>
</tr>
<tr>
<td>34</td>
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<td>1 IVF 1 FET</td>
<td>5/02</td>
<td>IV</td>
<td>IVF</td>
</tr>
<tr>
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<td>G0</td>
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<td>5/02</td>
<td>IV</td>
<td>IVF</td>
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<td>FET</td>
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<td>12/02</td>
<td>III</td>
<td>Spontaneous</td>
</tr>
<tr>
<td>31</td>
<td>G0</td>
<td>3 IVF</td>
<td>1/03</td>
<td>IV</td>
<td>Spontaneous</td>
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<tr>
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<td>I</td>
<td>Spontaneous</td>
</tr>
<tr>
<td>34</td>
<td>G0</td>
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<td>4/03</td>
<td>II</td>
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</tr>
<tr>
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<td>G1P00</td>
<td>20</td>
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<td>7/03</td>
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<tr>
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<td>10/01</td>
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<tr>
<td>38</td>
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<td>IV (endometriosis)</td>
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<td>12/02</td>
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<tr>
<td>31</td>
<td>G0</td>
<td>1 IVF</td>
<td>12/02</td>
<td>IV (endometriosis)</td>
<td>No pregnancy</td>
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<tr>
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<td>G1P10</td>
<td>01</td>
<td>5 IVF</td>
<td>4/03</td>
<td>IV (endometriosis)</td>
</tr>
</tbody>
</table>

NOTE: FET = frozen embryo transfer, N/A = data not available
Littman Laparoscopy after failed IVF, Fertil Steril 2005

### References:

Laparoscopic treatment of endometriosis in patients with failed in vitro fertilization cycles
Published on Physicians Practice (http://www.physicianspractice.com)

Table 2
References
Laparoscopic treatment of endometriosis in patients with failed in vitro fertilization cycles


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