

Evaluation of the Laparoscopic Cystectomy for Endometrioma in Women of the Reproductive Age

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Abstract: Aim of the study is to evaluate the pregnancy outcome and recurrence of the disease in patients with endometrioma. All patients who underwent laparoscopic surgery for endometrioma between January 2017- 2020 in Etlik Zubeyde Hanım Women Health Training and Research Hospital, had a stage 3-4 disease, and met the inclusion criteria were evaluated. The exclusion criteria were; being menopausal, having laparotomy for endometrioma surgery, or presence of concomitant leiomyoma. The post-operative reproductive outcome and the recurrence rate were evaluated. Out of the 97 patients recruited, 57 (58.8%) were followed up for infertility, while the remaining forty had no desire for future pregnancy. Sixty-seven patients had elective surgery, and 30 (30.9%) underwent emergency surgery. Pregnancy was achieved in 18 (31.5%) within 3-18 months (8.94 ± 4.54) after surgery, of which seven (38.8%) were spontaneous pregnancies while 11 had pregnancy through assisted reproductive techniques. The live birth rate was 88.8%, thirteen term delivery. Out of 97 patients, only four (4,1%) had recurrent endometrioma. The total pregnancy rate was high in the secondary infertile group (44.8%-17.8%), and the IVF pregnancy rate (60%) was high in the primary infertile group. Endometrioma surgery can be recommended for selected patients while preserving ovarian tissue.

Keywords: Infertility; endometriosis; reproductive outcome; recurrent endometrioma

INTRODUCTION

Endometriosis is a hormone-dependent gynecologic disorder defined as the presence of endometrial-like tissue outside the uterine cavity. It is a chronic inflammatory disease that may be progressive in many cases^{1,2}. Endometriosis predominantly affects women of reproductive age (10%)³. The prevalence of endometriosis is estimated at around 20-50% in the infertile patient group^{4,5}. Almost 17 to 44 % of patients with endometriosis will have endometrioma in the future^{6,7}. Endometriosis is associated with pain symptoms (dysmenorrhea, chronic pelvic pain, deep dyspareunia, dyschezia, and dysuria) and may accompany infertility; however, some cases may be asymptomatic regardless of the severity of the disease⁸. Moreover, endometriosis harms the psychological and social aspects of women's lives and thus deteriorates their quality of life⁹.

The choice of treatment for patients with endometriosis is one of the most controversial issues. Medical treatments can be used to treat endometriosis in women

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who do not desire pregnancy, as these medications suppress ovarian function. Medical treatments aim to suppress estrogen-dependent ectopic endometrial tissue without extirpating the endometriotic lesions. Endometriosis surgery aims to ablate or extract all the endometriotic tissue and cysts¹⁰. On the other hand, surgery for endometriomas might deteriorate the ovarian reserve due to the extraction of normal ovarian tissue and ovarian follicles neighbouring endometrioma during the extraction of the ovarian cyst from the ovarian tissue. The presence of endometrioma also harms ovarian function and ovarian reserve through various mechanisms¹¹. The age of the patient, severity of the symptoms, desire for fertility, and women's preferences are the factors that should be considered while choosing a treatment modality¹². However, medical treatment after surgery is recommended to prevent disease recurrence, but the choice of medical treatment depends on the fertility expectancy of the women.

A surgical approach might be required for definitive histopathological diagnosis, especially in women with large ovarian masses. Surgery for endometrioma can be performed via laparotomy or laparoscopy, while laparoscopy is usually the first-line surgical approach in patients who require surgery. Studies in the literature demonstrate higher clinical pregnancy, live birth, or ongoing pregnancy rates in infertile patients after operative laparoscopy compared to diagnostic laparoscopy¹³. When the surgical technique was evaluated, clinical pregnancy rates were higher, and recurrence of the disease was lower after excision of the endometrioma than drainage or ablation of the endometriotic cyst¹⁴. Expectant management was not found to be superior to operative laparoscopy in terms of achieving pregnancy¹⁵.

In the presented study, we aimed to evaluate the disease's pregnancy outcomes, ovarian reserve, and post-operative recurrence rates in patients who underwent laparoscopic surgery for endometrioma in an experienced centre.

MATERIALS AND METHODS

Patients

Overall ninety-seven patients who underwent laparoscopic surgery for endometrioma at the Infertility Clinic of Health Sciences University Ankara Etilik Zubeyde Hanim Training and Research Hospital between January 2017- and January 2020 were recruited for this retrospective study. Women between the ages of 18 to 40 having symptomatic endometrioma with a cyst size greater than 5 cm or who had an emergency laparoscopy for ruptured endometrioma were recruited for the study. The exclusion criteria were; being menopausal, having laparotomy for endometrioma surgery or presence of concomitant leiomyoma, and having male infertility that required ICSI or TESE. The study protocol was approved by the Institutional Review Board of Health Sciences University, Etilik Zubeyde Hanim Women's Health Research and Training Hospital (Date:19.11.2021, No:13). As a hospital policy, before each procedure, written informed consent was obtained from each patient that permitted to use the medical data anonymously for future studies. Informed consent was obtained from all the study participants.

Medical and gynecological histories of the study subjects were taken from the electronic records. Sociodemographic and medical characteristics of the patients (age, gravida, parity, infertility type, duration, of infertility) were recorded from the patient's data. All patients were operated on laparoscopically by the same surgical team, and post-

operative reproductive outcome and recurrence of the disease were evaluated. The stage of the cases was evaluated and recorded during laparoscopy using the "revised American Society for Reproductive Medicine (r-ASRM) classification"¹⁶. Serum AMH levels were measured by the immune assay method (Beckman Coulter UniCel DxI 800 Access Immunoassay System USA) before and within one month after the operation.

Surgery

Laparoscopic surgery was carried out under general anesthesia during the early follicular phase of the cycle. No pre-surgical medical suppressive treatment was given to the patients (GnRH Agonist, GnRH Antagonist, Aromatase inhibitors, Combined Hormonal Contraceptives, or Progestagens). After exploration of the abdominal cavity, peritoneal washing was taken and sent for cytological evaluation. Cystectomy was carried out through an incision performed to the antimesenteric side of the ovarian cyst capsule. The cyst capsule was separated from the ovarian tissue by hydro-dissection, and in the case of smaller cysts, the cyst was removed intact, whereas, in larger cysts, the cyst content was drained. Cystectomy was performed by using the traction-counter traction technique. Hydro dissection and gentle stripping removed the cyst capsule from the ovarian tissue. At the same time, extensive electrosurgical energy use was avoided, and bipolar cauterization was performed using a power of fewer than 40 Watts for achieving hemostasis only when required. The cyst capsule was removed from the abdominal cavity within an Endobag (Medtronic Co., Davis & Geck Caribe Limited, Dublin, Ireland). Adhesiolysis accompanied the procedure when necessary. In infertile patients, tubal patency was evaluated with the dye test using methylene blue. All the procedures were completed via laparoscopy without a concomitant laparotomy. All surgeries were performed by the same surgical team, using the same surgical technique. The peritoneal cavity was washed using Ringer Lactate's solution after ovarian surgery. All the patients were followed up two years post-operatively to evaluate the pregnancy outcome, and endometrioma recurrence was recorded in infertile patients.

Statistical Analyses

Statistical analysis was performed using IBM SPSS 26.0 software (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). An Independent T-test was used for parametric parameters, and a Paired T-test was used for preoperative-postoperative AMH levels and 95% confidence intervals for means and standard deviation. The reproductive outcome and frequencies were given as a percentage. A p-value <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The mean age of the 97 patients recruited for the study was $30,05 \pm 5.21$ years (Range=19-44). Fifty-seven patients (58.8%) were followed up due to infertility, while forty patients (41.2%) had no desire for future pregnancy. Twenty-eight (49.1%) of the 57 infertile patients were primary infertile, while the remaining 29 (50.9%) infertile patients had secondary infertility (Figure 1). Demographic characteristics all of the patients were as follows: gravida $0,45 \pm 0.81$ (R=0-4), parity $0.24 \pm 0,45$ (R=0-2), number of spontaneous abortion $0,17 \pm 0,54$ (R=1-4), number of living children $0,24 \pm 0.45$ (R=0-2). The mean duration of infertility was $16,9 \pm 12,8$ (R=5-72) months.

As expected, the most common symptoms of the patients were pain, mainly dysmenorrhea (n:45, 46.4%) and chronic pelvic pain (n:33, 34%). While 30 (30.9%) of the

patients who applied with signs of acute abdomen underwent emergency surgery due to ruptured endometrioma, elective surgery was performed in 67 (69,1%) symptomatic patients. Thirty-one (32%) of the patients had bilateral endometrioma. Twenty-five (25.7%) patients had endometriotic cysts ≥ 10 cm (Figure1).

Out of 97 patients, 44 (45,4%) had an r-ASRM score of 3, and 53 (54,6%) had an r-ASRM score of 4. In the infertile group, r-ASRM Stage 3 was seen in 30 patients (52.6%), and Stage 4 was seen in 27 patients (47.4%). Unilateral tubal obstruction was diagnosed during laparoscopic cystectomy in 11 of the patients with infertility (11/57; 19.29%), while one infertile patient had bilateral tubal occlusion (1/57;1.75%, Figure 1). Pre and post-operative AMH levels were compared in unilateral and bilateral endometrioma and endometriomas with a diameter of 5-9 cm and ≥ 10 cm. Post-operative AMH levels were statistically significantly lower than the pre-operative values in bilateral endometriomas and endometriomas with a diameter ≥ 10 cm (Table 1).

Demographic characteristics of the patients of the pregnancy and non-pregnancy groups were the same and are detailed in Table 2. Pregnancy was achieved in 18 (31.5%) of 57 infertile patients, of which 13 were (72.2%) in the secondary infertile group. The average time between pregnancy and laparoscopic surgery was 8.94 ± 4.54 months (R=3-18). The live birth rate was seen in 16 (88.8%) patients. Of the 18 pregnancies obtained, seven (38.8%) were spontaneous, eight (44.4%) were IVF-ET, and the remaining three achieved pregnancy after ovarian stimulation and intrauterine insemination. Thirteen (81.2%) of 16 live births were term delivery.

Out of 20 infertile patients with bilateral endometrioma, pregnancy was achieved in five (5/20, 25%) after the operation. Five of the 12 patients (5/12, 41,6%) with accompanying tubal obstruction had a live birth after IVF-ET. Although r-ASRM stage 3 and Stage 4 were seen in similar numbers (52.6%, 47.4%, respectively) in the infertile group, the pregnancy rate in the stage 3 group (61.1%) was higher than that of stage 4 (38.9%), as expected (Figure 1).

Table 1. The Changes in Pre-operative and-Post-operative AMH Levels According To The Characteristics of The Cyst

	Pre-op AMH Std.D (ng/ml)	Post-op AMH Std.D (ng/ml)	p-value
Unilateral Endometrioma (N:66)	3,39 \pm 2,53	2,70 \pm 3,12	0,075
Bilateral Endometrioma (N:31)	2,91 \pm 2,69	1,90 \pm 1,64	0,004*
p-value	0,4	0,191	
Cyst diameter 5-9 cm (N:72)	3,26 \pm 2,48	2,60 \pm 3,03	0,066
Cyst diameter ≥ 10 cm (N:25)	3,15 \pm 2,88	1,99 \pm 1,67	0,003*
p-value	0,856	0,34	

Independent T-Test and Paired T-test were applied, *p<0.05 was significant.

Std.D: Standart Deviation

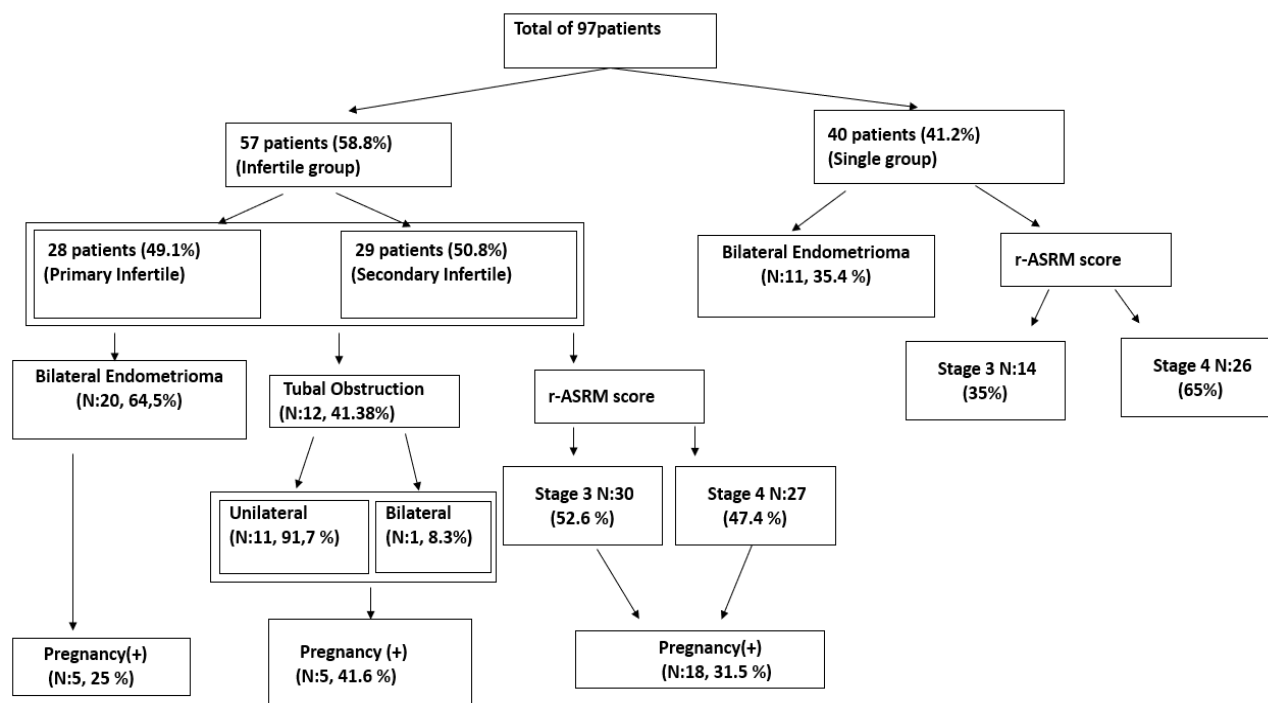


Figure 1. Distribution of Patients According To Reproductive Results and Stage of Disease

Table 2. Comparison of the Characteristics of Pregnant and Non-Pregnant Infertile Patients

	Pregnant Mean± Std.D (N=18)	Non-Pregnant Mean± Std.D (N=39)	P value
Age	30.22±3.91	31.58±4.63	.28
Gravidaty	0.88± .67	0.69±1.02	.46
Parity	0.55±0.51	0.33±0.52	.14
Number of the Spontaneous Abortus	0.22±0.42	0.30±0.76	.66
Number of the Living Children	0.55±0.51	0.33±0.52	.14
Duration of Infertility (months)	19.5±15.4	15.7±11.4	.30
Cyst Size (mm)	6.8±1.99	7.07±2.78	.79
Bilaterality	0.27±0.46	0.38±0.49	.44
Stage of Endometriomas	3.33±0.48	3.5±0.50	.15
Pre-op AMH ng/ml	4.03±2.83	3.21±2.74	.32
Postop AMH ng/ml	3.24±4.89	2.25±2.62	.44
Pre-op Ca125 IU/mL	65.2±58.6	75.7±42.5	.51
Post-op Ca125 IU/mL	22.7±17.2	31.1±22.8	.14

An Independent T-test was applied p< .05 was significant.

Std.D: Standart Deviation

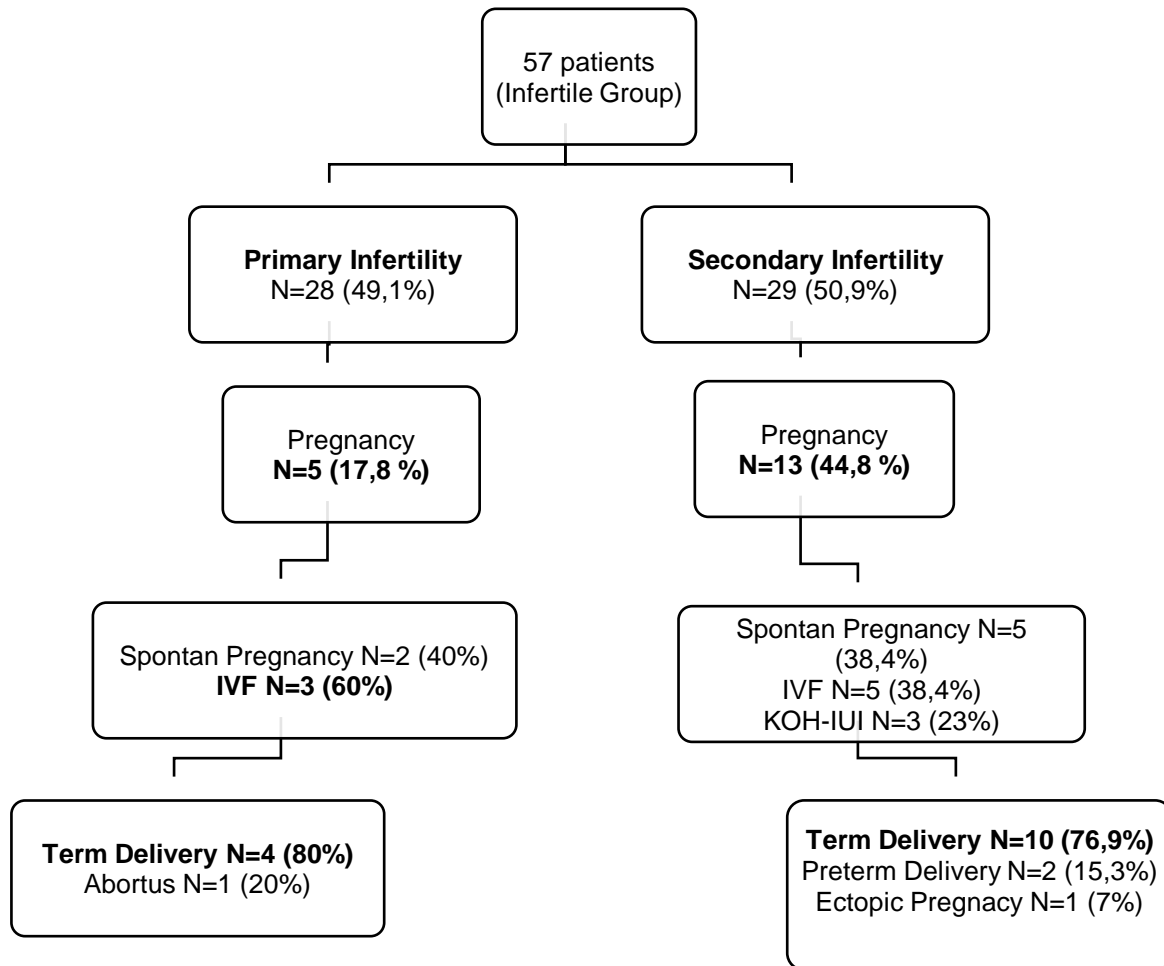


Figure 2. Distribution of Infertile Patients According To The Reproductive Outcome

The distribution of patients in infertile groups is detailed in Table 3. Although the distribution of patients in the infertile group (49.1%, 50.1%, respectively) and the term pregnancy rate (80%, 76.9%, respectively) were similar, the total pregnancy rate was high in the secondary infertile group (44.8%-17.8%). In comparison, IVF pregnancy rates (60%) were high in the primary infertile group (Figure 2). In addition, there was no difference between primary and secondary infertile groups for cyst size and cyst stage, bilaterality, recurrence, tubal patency, and duration of infertility.

After the diagnosis of endometrioma was histopathologically confirmed, Dienogest (Visanne, 2mg/day, continuous use, Bayer Turkish Chemical Industry Trade Ltd. Comp.) was prescribed for patients who do not want to plan pregnancy. Four patients (4/97, 4,1%) had a recurrence, two with unilateral endometrioma and the remaining two with bilateral endometriomas (1 year, 2.5 years, five years, and six years after the operation). Three of these four patients were infertile and achieved pregnancy and live birth after IVF-ET without performing a second operation.

There was no difference between the patients who achieved pregnancy and who failed to get pregnant during the follow-up period in terms of duration of infertility, cyst size, pre-operative and post-operative AMH- Ca125 levels, and demographic characteristics.

The study aimed to evaluate surgery results for endometrioma, which is widely discussed in the literature. Laparoscopy is the gold standard for identifying endometriotic lesions, and the definitive diagnosis is based on the histopathological confirmation of the excised lesions. However, surgery is generally avoided due to the possible damage to the ovarian tissue and, thus, ovarian reserve. Studies that favour surgery support the hypothesis that endometrioma ruptures, and thus the risk of abscess formation is prevented, and early diagnosis of malignancies is assured¹⁷. Some of the studies in the literature demonstrate the improvement of IVF results after endometrioma surgery^{18,19}. In our study, IVF pregnancy rates were high in the primary infertile group (Figure.1).

Currently, surgery for endometrioma is reserved for symptomatic patients (mainly pain symptoms), especially if the symptoms fail to improve with medical treatment and infertile patients who need surgery for accompanying tubal occlusion and hydrosalpinx. Large masses are also more prone to a surgical approach to rule out malignancy. The decision for surgery was made on individual bases in our patient's group after evaluation of the signs and symptoms and the results of the laboratory test and imaging techniques. The indications for surgery in our patient's group coincided with those cited in the literature²⁰. When the surgical techniques for endometrioma are compared, capsule excision rather than fenestration, drainage, or coagulation is more successful in recurrence and pregnancy rates^{15,22,23}.

The Current European Society of Human Reproduction and Embryology (ESHRE) Guideline strongly recommends cystectomy instead of drainage and coagulation of the cyst wall while showing extreme caution to avoid ovarian damage²¹. American Society of Reproductive Medicine (ASRM) also advocates developing a management plan for women with endometriosis according to the patient's age, the severity of symptoms, duration of fertility, and stage of endometriosis, and also recommends resection or ablation after drainage of the endometrioma rather than drainage alone²⁴. The nice guideline also recommends using excision with special care to the women's ovarian reserve and fertility preservation instead of ablation in the surgical treatment of endometriomas, as the recurrence rate is low²⁵. In our study, cyst capsule excision was performed in all patients. Similar to the published studies²⁶, bilaterality and increased size of the endometrioma had a more profound negative effect on the ovarian reserve with AMH (Table 1).

Symptoms might recur after surgical treatment of endometrioma, while endometriotic cysts might signify recurrence. The incidence of return of clinical symptoms might be higher than ultrasonographic or surgical findings that prove the recurrence of the disease²⁷. The incidence of recurrence depends on the stage of the disease and the duration of the follow-up. Parazzini et al. reported a recurrence rate of 14.4% in Stage III-IV²⁸. Tandoi et al. followed up 57 women aged ≤ 21 for five years and reported a recurrence rate of 56%, while 34% recurrence was confirmed via second-look laparoscopy and stated that the recurrence rate increased with increasing time to surgery²⁹. In our study, the shortest duration of follow-up was one year, and recurrence was seen in only four patients (4,1%). Three patients with a recurrence were infertile and had a live birth after IVF without needing a re-operation (Figure 2).

Table 3. Distribution of Patient Characteristics in the Infertile Groups

	Groups	N	Mean	Std.D.	p-value
r-ASRM Stage	1	28	3.57	0.504	.152
	2	29	3.38	0.49	
Cyst Size	1	28	6.92	2.80	.798
	2	29	7.10	2.32	
Bilaterality	1	28	0.39	0.50	.523
	2	29	0.31	0.47	
Recurrence	1	1	1.00		1
	2	2	1.00	0.00	
Tubal Patency	1	5	1.80	0.45	.513
	2	7	2.14	.21	
Duration of the Infertility period (Months)	1	28	14.36	8.45	.134
	2	29	19.45	15.74	

Independent T-Test applied

Group1: Primary infertility, **Group 2:** Secondary infertility, **Std.D:**Standart Deviation

The impact of laparoscopic surgery for endometrioma on fertility and reproductive outcome of assisted reproductive technologies is controversial. A study from Korea gave a spontaneous fertility rate of 53.3% and 20.0% for stage III and IV disease, respectively, and out of 22 patients with endometrioma, 10 (45.5%) were pregnant after surgery, and overall 41.9% of the women who were followed up for one year successfully conceived without ART³⁰. Hui et al. followed up with 258 patients for three years and reported that age of <35 years, duration of infertility less than five years, having secondary infertility, having a high EFI score, and receiving post-operative ART had a positive effect on pregnancy rates³¹. In the presented study, the pregnancy rate in women with AFS scores 3 and 4 was 26% and 11.2%, respectively. However, we did not find any statistically significant difference between the patients who achieved pregnancy and who failed to get pregnant during the follow-up period in terms of duration of infertility, cyst size, pre-operative and post-operative AMH- Ca125 levels (Table 2). The total pregnancy rate was significantly higher in the secondary infertile group (44.8 %) compared with the women with primary infertility (17.8%). However, after surgery, the symptomatic primer infertile group's pregnancy rate was high in the ART patients (Table 3). Natural conception rates are reportedly high in the early post-operative period³⁰. In the presented study, we found high spontaneous pregnancy rates in the secondary infertility group (Table3).

In studies conducted for assisted reproductive techniques (ART), it has been shown that surgery is not routinely recommended before ART, and it may cause cycle cancellation during ART due to diminished ovarian reserve and inadequate oocyte retrieval. In our study, pregnancy rates were high 3 to 12 months after surgery. There is no increase in the live pregnancy rate^{32,33}. All patients who underwent cyst excision in the presented series were symptomatic patients with chronic pelvic pain resistant to medical treatment or patients who underwent emergency surgery due to ruptured endometrioma. None of the patients underwent laparoscopic surgery for endometrioma as preparation for ART.

The limitations of our study are its retrospective nature and the lack of a control group who did not have an operation and were followed up for future fertility during a similar period. However, the patients in our group had histopathologically confirmed endometriosis and laparoscopic staging that would not have been available if we had chosen a control group without any intervention. Future studies with a more significant number of recruited patients with a more extended follow-up period are required for definitive results to analyze the impact of laparoscopic surgery on endometrioma in patients with infertility and to measure the recurrence rate.

CONCLUSION

As a result, endometriotic cyst excision can be preserved in a defined group of symptomatic patients or have an emergency operation for ruptured endometrioma. While the total pregnancy rate was high in the secondary infertile group (44.8%-17.8%), the IVF pregnancy rate (60%) was high in the primary infertile group. Although the term pregnancy rate in the post-operative period was similar in the primary and secondary groups (80%, 76.9%, respectively), it was found promising for total pregnancy in the secondary infertile group and pregnancy rates after ART in the primary infertile group. Considering the ovarian reserve, laparoscopic cyst capsule excision should be performed with care by experienced clinicians and in a selected group of patients.

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CONFLICT OF INTEREST

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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