

Reproductive Outcome After Surgical Treatment of Endometriosis – Retrospective Analytical Study

Retrospektywna analiza oceniająca płodność kobiet po operacyjnym leczeniu endometriozy

Teksin Cirpan, Levent Akman, Mehmet Sait Yucebilgin, Mustafa Cosan Terek, Mert Kazandi,

Ege University Medical School, Department of Obstetrics and Gynecology, Izmir, Turkey

Abstract

Objective: The aim of the study was to investigate the reproductive outcomes of patients after surgical treatment of endometriosis.

Material and Methods: The study included 100 infertile women, aged 21 to 41 years, who underwent surgical treatment of endometriosis. From January 2007 to January 2012, excision of endometriosis was performed by operative laparoscopy or laparotomy. Demographic, clinical, surgical and reproductive outcomes of 52 patients were retrospectively analyzed.

Result: Twenty-three pregnancies (44%) were obtained in 52 patients, resulting in 16 term pregnancies, 4 spontaneous abortions under 16 weeks gestation, 2 spontaneous abortions at 20 gestational weeks and 1 ectopic pregnancy. Twenty nine patients did not achieve pregnancy and 68.9% (20/29) of them were treated with IVF-ICSI. Spontaneous pregnancies were obtained within 7 months after the surgery, whereas IVF-ICSI pregnancies were obtained within the period of 11 months. Seven patients were stage I, 14 patients stage II, 19 patients stage III, and 12 patients stage IV according to the American Fertility Society (AFS) Classification of Endometriosis. The pregnancy rate was 57% in stages I-II, 47% in stage III, 16% in stage IV endometriosis; and the rate of term pregnancies was 83%, 66%, and 0%, respectively. Seven pregnancies (7/14) were obtained in patients with bilateral endometriosis and 5 of them resulted in term pregnancy. Sixteen pregnancies (16/38) were obtained in patients with unilateral endometriosis and 11 of them resulted in term pregnancy.

Conclusion: After surgical treatment of endometriosis, the pregnancy and live birth rates seem to be improved. Reproductive outcome is closely associated with the AFS score. Bilaterality of endometriosis does not affect pregnancy outcome.

Key words: **endometriosis / fertility / reproductive outcome / laparoscopy /**

Corresponding author:

Levent Akman
Ege University Medical School
Department of Obstetrics and Gynecology
35100, Bornova, Izmir, Turkey
Phone Number: +90-232-3901700
Fax: +90-232-3901741
E-mail: leventakman@gmail.com

Otrzymano: 05.10.2012
Zaakceptowano do druku: 20.07.2013

Streszczenie

Cel pracy: Celem pracy była ocena płodności kobiet po operacyjnym leczeniu endometriozy.

Materiał i metody: Do badania włączono 100 nieplodnych kobiet, w wieku 21 do 41 lat, które przeszły leczenie operacyjne z powodu endometriozy. W okresie od stycznia 2007 do stycznia 2012 wykonano zabieg usunięcia endometriozy na drodze laparoskopii bądź laparotomii. Przeprowadzono retrospektywną analizę demograficzną, kliniczną, operacyjną i rozrodczości u 52 pacjentek.

Wyniki: Dwadzieścia trzy (44%) ciąży uzyskano u 52 pacjentek, z których 16 zakończyło się porodem o czasie, 4 poronieniem samoistnym poniżej 16 tyg., 2 poronieniem samoistnymi w 20 tyg. i 1 ciążą ektopową. Dwadzieścia dziewięć pacjentek nie zaszło w ciążę a 68,9% (20/29) z nich leczono przy pomocy IVF-ICSI. Samoistne ciążę wystąpiły w ciągu 7 miesięcy po leczeniu operacyjnym, podczas gdy ciążę po IVF-ICSI uzyskano w ciągu 11 miesięcy. Siedem pacjentek było w stopniu I, 14 w II, 19 w III a 12 w IV stopniu zaawansowania endometriozy według American Fertility Society (AFS). Wskaźnik ciąż w stopniu I-II wynosił 57%, 47% w stopniu III, 16% w stopniu IV; wskaźnik porodów w terminie wynosił odpowiednio 83%, 66% i 0%. Siedem ciąż (7/14) wystąpiło u pacjentek z obustronną endometriozą a 5 z nich zakończyło się o czasie. Szesnaście ciąż (16/38) było związanych z jednostronną endometriozą a 11 z nich zakończyło się porodem o czasie.

Wnioski: Po leczeniu operacyjnym endometriozy odsetek ciąż i żywych urodzeń wydaje się zwiększać. Płodność kobiet jest ściśle związana z klasyfikacją AFS. Obustronne występowanie endometriozy nie wpływa na wyniki położnicze.

Słowa kluczowe: **endometrioza / płodność / wyniki rozrodu / laparoscopia /**

Introduction

Endometriosis is frequently encountered in patients with fertility problems. Moderate and severe endometriosis are known to cause infertility; however the association between minimal or mild endometriosis and infertility remains controversial [1, 2]. Cramer et al., [3] in a multicenter study, diagnosed endometriosis in 17% of women with primary infertility.

The exact cause and effect relationship between endometriosis and infertility in the absence of a distortion in pelvic anatomy is unknown [4]. Surgery offers a better prognosis for pregnancy than endocrine therapy in many cases of advanced disease. Therapeutic planning depends on the age of the patient, the extent of the disease and previous treatments [5].

In the present study, we investigated the reproductive outcomes of patients after surgical treatment of endometriosis.

Material and Methods

The study included 100 infertile women, aged 21 to 41 years, who underwent surgical treatment of endometriosis. From January 2007 to January 2012, excision of endometriosis was performed by operative laparoscopy or laparotomy. Due to the retrospective nature of the study, the approval of our institutional review board was not required. Medical records of 52 patients were available for the analysis.

All women had not become pregnant before the operation, despite having regular sexual intercourse, without any contraception, for the duration of one year. In addition, couples with infertility did not have the male factor contributing to their infertility. Standard laparoscopic procedures were performed by two authors (T.C., M.S.Y.). Laparoscopic ovarian cystectomy was performed after fenestration of the cyst. The cut edges of the ovarian cortex and cyst wall were held and teased apart. Hemostasis was accomplished with light application of bipolar

forceps. Large defects were closed with laparoscopic suturing. Small defects were left to heal by second intention. At the completion of procedure, the peritoneal cavity was irrigated liberally until it was devoid of carbon material and debris. Excision of ovarian endometrioma by laparotomy was done by the excision of the ovarian cortex. The incision was made along the longitudinal axis of the ovary. The endometrioma was peeled out by blunt dissection. The ovarian defect was closed with two layers of 2-0 absorbable suture material.

The mean age of the patients was 31 (21-41) years, the mean CA125 level was 71 (23-196) U/mL, and the mean endometrioma diameter was 5.4 (3-10) cm.

Results

Twenty-three pregnancies (44%) were obtained in 52 patients, resulting in 16 term pregnancies (13 spontaneous gestations, and 3 assisted reproductive techniques), 4 spontaneous abortions under 16 weeks of gestation, 2 spontaneous abortions at 20 weeks of gestation and 1 ectopic pregnancy. Twenty nine patients did not achieve pregnancy and 68.9% (20/29) of them were treated with IVF-ICSI.

Spontaneous pregnancies were obtained within a 7-month post-operative period, whereas IVF-ICSI pregnancies were obtained within 11 months. American Fertility Society stages, number of pregnancies obtained and pregnancy outcomes were summarized in Table 1.

Seven patients were stage I, 14 patients stage II, 19 patients stage III, and 12 patients stage IV according to the American Fertility Society Classification of Endometriosis. The pregnancy outcomes and methylene blue test results were summarized in Table 2.

Bilateral endometriosis was present in 14 (26.9%) patients. Seven pregnancies were obtained in patients with bilateral

Table I. American Fertility Society (AFS) stages, number of pregnancies obtained and pregnancy outcomes of 52 infertile surgically-treated endometriosis patients.

AFS stages	I – II (n=21)	III (n=19)	IV (n=12)
Number of pregnancies (%)	12 (57)	9 (47)	2 (16)
Number of term pregnancies (%)	10 (83)	6 (66)	0 (0)

Table II. Pregnancy outcomes and methylene blue test results of 52 infertile surgically-treated endometriosis patients.

Methylene blue test	Both tubes are patent	One of the tubes in patent	Both tubes are occluded
Number	16	20	16
Number of pregnancies obtained (%)	11 (68)	8 (40)	4 (25)
Live births (%)	8 (72)	6 (75)	2 (50)

endometriosis and 5 of them resulted in term pregnancy. Unilateral endometriosis was present in 38 (73.1%) patients. Sixteen pregnancies were obtained in patients with unilateral endometriosis and 11 of them resulted in term pregnancy.

Discussion

Endometriosis is a common problem in patients with infertility. The issue whether surgery improves fertility results remains controversial. Tulandi et al., compared pregnancy rates of infertile women with mild endometriosis treated laparoscopically by surgical excision and by electrocoagulation [6]. The total pregnancy rates were 57.1% and 53.5%, respectively. Of the total 24 pregnancies in the electrocoagulation group, there were 3 spontaneous abortions (12.5%), and 1 ectopic pregnancy (4.2%), whereas in the surgical excision group the abortion rate was 17.4% (4 of 23), and the ectopic pregnancy rate was 8.7% (2 of 23). These authors found no difference in the pregnancy rates of infertile women with mild endometriosis treated laparoscopically by surgical excision or by electrocoagulation. In our study endometriosis was treated by surgical excision in all patients.

Somigliana et al., assessed IVF-ICSI outcome in women operated on for bilateral endometriomas [7]. Women selected for IVF-ICSI cycles, who previously underwent bilateral endometriomas cystectomy, were matched (1:2) for age and study period with patients who did not undergo prior ovarian surgery. Sixty-eight cases and 136 controls were recruited. Women operated on for bilateral endometriotic ovarian cysts had a higher withdrawal rate for poor response. In these patients despite the use of higher doses of gonadotropins, the number of follicles, oocytes retrieved and embryos obtained was significantly lower. The clinical pregnancy rate per started cycle in cases and controls was 7% and 19% and the delivery rate per started cycle was 4% and 17%, respectively. IVF outcome is found to be significantly impaired in women operated on for bilateral ovarian endometriomas. In our study, significant differences between bilateral and unilateral endometriomas with respect to pregnancy and live birth rates, both for spontaneous and IVF pregnancies, were observed.

Esinler et al., evaluated ICSI outcome in a small group of 23 cases, using patients with tubal factor infertility as a control group [8]. They reported a lower antral follicle count, a higher dosage of administered gonadotropins and a lower number of retrieved oocytes. Surgery may directly affect ovarian reserve. During cystectomy a consistent amount of ovarian tissue may be removed accidentally. Ovarian reserve may also be reduced by the damage inflicted on the ovarian stroma and vascularization by both surgery-related local inflammation and electrosurgical coagulation during hemostasis [7,9].

Yu et al., assessed whether the experience of the surgeon can affect ovarian reserve and pregnancy outcome in IVF-ICSI patients who previously underwent laparoscopic conservative treatment for ovarian endometriomas [10]. They compared 76 cycles with an inexperienced surgeon and 73 cycles with an experienced surgeon. The number of the antral follicle count and live-born rate per cycle was significantly lower in the inexperienced group.

Maruyama et al., examined how preexisting tubal adhesions and endometriosis affect pregnancy outcome after laparoscopic treatment in infertile women [11]. Pregnancy outcomes in 186 infertile women for the follow-up period of 18 months after laparoscopy were analyzed. Patients were classified in three groups: with no tubal adhesions (Group A), unilateral tubal adhesions (group B), and bilateral adhesions with at least one tube patent (group C). The cumulative pregnancy rate of group C (13.2%) was lower than in groups A (41.8%) and B (45.7%) 18 months after laparoscopy. In group A, pregnancy rates were essentially the same between minimal/mild endometriosis and moderate/severe endometriosis. Regarding group B, women with minimal/mild endometriosis exhibited significantly higher pregnancy rates than those with moderate/severe endometriosis.

Fuchs et al., evaluated fertility outcome after laparoscopic management of endometriosis in a infertile population [12]. Thirty four patients, presenting with infertility associated with minimal to severe endometriotic lesions, were treated using laparoscopic surgery to allow for the removal of the entire lesion. The pregnancy rate was 65% (n=22) within an 8.5-month post-surgical period of

time, and 86.5% pregnancies resulted in a delivery. Sixty percent of the pregnancies were spontaneous within a 5-month period and the median post-surgical time to pregnancy was 12 months in IVF-ICSI cases. Among women with stages I-II endometriosis, the median post-surgical time to pregnancy was 2 months when spontaneous and 20.5 months when induced. In the case of stages III-IV endometriosis, pregnancy delay was 8 and 12 months, respectively. Among the 21% of women who had had an induced pregnancy failure before surgery, 71% became pregnant and 80% of them spontaneously. Eighteen patients (53%) had an ovarian endometrioma and 50% of them became pregnant. Among the 4 patients who had colorectal endometriosis requiring colorectal resection, 1 pregnancy was obtained. Complete operative laparoscopic treatment enabled 65% of the patients to be pregnant within an 8.5-month post-surgical median time to pregnancy and spontaneously in 60% of patients with infertility related to endometriosis.

Kucera et al., operated 70 infertile women with an endometrioma [13]. The cumulative delivery rate after surgery was 55.7% (n=39). Porpora et al., evaluated 47 infertile women undergoing laparoscopic treatment of endometriosis [14]. rAFS stage was: 11% stage I, 11% stage II; 53.3% stage III, and 24.4% stage IV. The mean duration of follow-up was 48.5+18.4 months. The overall pregnancy rate was 64.4%. Eighteen out of 26 women (69%) became pregnant within six months after the laparoscopy, 23% in the course of 12 months, 11% within 24 months, and 11% after 2 years. Adnexal adhesions and tubal status significantly affected the pregnancy rate.

In our study, the highest pregnancy rate (57%) and live birth rate (83%) were found in patients with stage I-II endometriosis. In patients with stage III endometriosis, these rates were close to stage I-II endometriosis (47% and 66%, respectively). The lowest pregnancy rate was found in stage IV endometriosis (16%), also there were no live births in that group. Live birth rates were similar between patients with both patent tubes and one patent tube (72% vs. 75%, respectively). However, the pregnancy rate was higher in patients who had both patent tubes. Advanced stage might contribute to these results.

Conclusion

After surgical treatment of endometriosis, the pregnancy and live birth rates seem to be improved. Reproductive outcome is closely associated with the AFS score. Bilaterality of endometriosis does not affect pregnancy outcome.

Authors' Contribution:

1. Teksin Cirpan – concept, study design, analysis and interpretation of data, revised article critically.
2. Levent Akman – analysis and interpretation of data, article draft, corresponding author, revised article critically.
3. Mehmet Sait Yucebilgin – study design, concept, revised article critically.
4. Mustafa Cosan Terek - study design, acquisition of data, revised article critically.
5. Mert Kazandi – study design, acquisition of data, analysis and interpretation of data.

Authors' statement:

- This is to certify, that the publication will not violate the copyrights of a third party, as understood according to the Act in the matter of copyright and related rights of 14 February 1994, Official Journal 2006, No. 90, Clause 63, with respect to the text, data, tables and illustrations (graphs, figures, photographs);
- there is no 'conflict of interests' which occurs when the author remains in a financial or personal relationship which unjustly affects his/her actions associated with the publication of the manuscript;
- any possible relationship(s) of the author(s) with the party/parties interested in the publication of the manuscript are revealed in the text of the article;
- the manuscript has not been published in or submitted to any other journal.

Source of financing:

None.

References

1. Tulandi T, Mouchawar M. Treatment-dependent and treatment-independent pregnancy in women with minimal and mild endometriosis. *Fertil Steril.* 1991, 56, 790-791.
2. Hughes EG, Fedorkow DM, Collins JA. A quantitative overview of controlled trials in endometriosis-associated infertility. *Fertil Steril.* 1993, 59, 963-970.
3. Cramer DW, Missmer SA. The epidemiology of endometriosis. *Ann NY Acad Sci.* 2002, 955, :11-22, discussion 34-36, 396-406.
4. Mahmood TA, Templeton A. Pathophysiology of mild endometriosis: review of literature. *Hum Reprod.* 1990, 5, 765-784.
5. Rock JA. Endometriosis. In: TeLinde's operative Gynecology. 10th. Ed. Rock JA, Jones HW. *Lippincott Williams&Wilkins.* 2008, 438-477.
6. Tulandi T, al-Took S. Reproductive outcome after treatment of mild endometriosis with laparoscopic excision and electrocoagulation. *Fertil Steril.* 1998, 69, 229-231.
7. Somigiana E, Arnoldi M, Benaglia L, [et al.]. IVF-ICSI outcome in women operated on for bilateral endometriomas. *Hum Reprod.* 2008, 23, :1526-1530.
8. Esinler I, Bozdog G, Aybar F, [et al.]. Outcome of in vitro fertilization/intracytoplasmic sperm injection after laparoscopic cystectomy for endometriomas. *Fertil Steril.* 2006, 85, 1730-1735.
9. Muzii L, Bianchi A, Crocè C, [et al.]. Laparoscopic excision of ovarian cysts: is the stripping technique a tissue-sparing procedure? *Fertil Steril.* 2002, 77, 609-614.
10. Yu HT, Huang HY, Soong YK, [et al.]. Laparoscopic ovarian cystectomy of endometriomas: surgeons' experience may affect ovarian reserve and live-born rate in infertile patients with in vitro fertilization-intracytoplasmic sperm injection. *Eur J Obstet Gynecol Reprod Biol.* 2010, 152, 172-175.
11. Maruyama M, Osuga Y, Momoeda M, [et al.]. Pregnancy rates after laparoscopic treatment. Differences related to tubal status and presence of endometriosis. *J Reprod Med.* 2000, 45, 89-93.
12. Fuchs F, Raynal P, Salama S, [et al.]. Reproductive outcome after laparoscopic treatment of endometriosis in an infertile population. *J Gynecol Obstet Biol Reprod (Paris).* 2007, 36, 354-359.
13. Kucera E, Herman H. Reproductive outcome in women with ovarian endometriosis--retrospective analytical study. *Ceska Gynekol.* 2005, 70 (6),431-435.
14. Porpora MG, Pultrone DC, Bellavia M, [et al.]. Reproductive outcome after laparoscopic treatment of endometriosis. *Clin Exp Obstet Gynecol.* 2002, 29, 271-273.