https://doi.org/10.2298/VSP160408363D

UDC: 618.1-089

ORIGINAL ARTICLES



Ovarian reserve in patients who have undergone endometriosis surgery

Ovarijalna rezerva kod bolesnica operisanih od endometrioze

Olivera Džatić Smiljković, Mladenko Vasiljević, Ivana Rudić, Jelena Vugdelić, Aleksandar Ristić, Rada Vugdelić

University of Belgrade, Faculty of Medicine, University Clinic of Gynecology and Obstetrics "Narodni Front", Belgrade, Serbia

Abstract

Background/Aim. Endometriosis is a gynaecological disorder characterized by the presence of endometrial tissue outside the uterine cavity. The aim of this paper was to determine the effect of laparoscopic cystotomy and cystectomy on ovarian function, as well as to compare these two methods in terms of qualitative and quantitative damage to the ovaries, achieved pregnancies and recurrence. Methods. The prospective study, conducted in "Narodni Front" Obstetrics and Gynaecology Clinic in Belgrade at the Endoscopic Infertility Treatment Ward, included a total of 150 patients. The study group was represented by 100 patients who underwent a surgical treatment of endometrial ovarian cysts. The patients in the study group were divided into 2 subgroups: Subgroup I consisted of 50 patients who underwent a laparoscopic cystotomy (incision of the cyst and thermal coagulation) and subgroup II which included 50 women who underwent a laparoscopic cystectomy. The control group consised of patients who underwent a surgery due to tubal factor infertility. The following parameters of the ovarian function were tested: the ovarian vol-

Apstrakt

Uvod/Cilj. Endometrioza je ginekološko oboljenje koje karakteriše prisustvo endometrijalnog tkiva van materične šupljine. Cilj ovog rada bio je da se utvrdi uticaj laparoskopske cistotomije i cistektomije na funkciju jajnika, kao i da se uporede ove dve metode, po pitanju kvalitativnog i kvantitativnog oštećenja jajnika, ostvarenih trudnoća i recidiva. Metode. Sprovedena je prospektivna studija u Ginekološko-akušerskoj klinici (GAK) "Narodni Front" u Beogradu, u Odeljenju za endoskopsko lečenje infertiliteta. Studijom je bilo obuhvaćeno ukupno 150 bolesnica. Ispitivanu grupu je sačinjavalo 100 bolesnica koje su operisane zbog postojanja endometriotičnih cista na jajniku. Bolesnice ispitivane grupe su podeljene u dve podgrupe: podgrupu I sačinjavalo je 50 operisanih bolesnica ume, the antral follicle count, the presence of the preovulatory follicle on the operated ovary, the serum levels of anti-Müllerian hormone (AMH), follicle-stimulating hormone (FSH), ovarian tumor marker (Ca 125), inhibin B, as well as the rate of achieved pregnancies one year after the surgery. Results. The ovarian volume and the antral follicle count as well as the FSH values were significantly higher in the control group in comparison with the patients in the study group. There were no significant differences in the ovarian volume, the antral follicle count, the AMH values and inhibin B values in the study group between the patients with cystectomy and those with the incision and coagulation of the cyst. Conclusion. Both surgical techniques diminished the ovarian reserve: cystectomy was more aggressive method in terms of the damage inflicted on the ovarian tissue, and incision with coagulation carried a higher risk of recurrence.

Key words:

endometriosis; infertility; laparoscopy; cystectomy; cystotomy; treatment outcome.

kod kojih je urađena laparoskopska incizija ciste sa termokoagulacijom (cistotomija), dok je podgrupa II obuhvatila 50 operisanih bolesnica kod kojih je urađena laparoskopska cistektomija. Kontrolnu grupu su činile bolesnice operisane zbog tubarnog faktora infertiliteta. Ispitivani su parametri ovarijalne funkcije: volumen jajnika, broj antralnih folikula, prisustvo preovulatornog folikula na operisanom jajniku, serumski nivoi anti-milerovog hormona (AMH), folikulostimulirajućeg hormona (FSH), inhibina B, tumorskog markera jajnika (CA 125), kao i stopa ostvarenih trudnoća nakon operacije. Rezultati. Volumen jajnika i broj antralnih folikula kao i vrednosti FSH su bili značajno veći u kontrolnoj grupi u odnosu na ispitivanu grupu bolesnica. Nije nađena značajna razlika u volumenu jajnika, broju antralnih folikula, vrednostima AMH i Inhibina B u ispitivanoj grupi bolesnica između onih sa

Correspondence to: Olivera Džatić Smiljković, Kozjačka 10, 11 000 Belgrade, Serbia; E-mail: lola.dzatic.smiljkovic@gmail.com

cistektomijom i onih sa incizijom i koagulacijom ciste. Zaključak. Obe operativne tehnike smanjuju ovarijalnu rezervu: cistektomija je agresivnija metoda u smislu oštećenja tkiva jajnika, a incizija nosi veći rizik od recidiva.

Ključne reči: endometrioza; neplodnost; laparoskopija; cistektomija; cistotomija; lečenje, ishod.

Introduction

Endometriosis is a benign estrogen-dependent gynaecological disorder characterized by the presence of endometrial tissue outside the uterine cavity. It is associated with pelvic pain, dysmenorrhoea and infertility¹. Pelvic organs and peritoneum are the most commonly affected areas. It ranges from minimal lesions to massive ovarian cysts and adhesions which disturb the tubo-ovarian anatomy. The prevalence in the female population is around 5%-10%, although in particular groups of women with severe gynaecological disorders as well as in women who underwent a laparoscopic sterilisation, the frequency of around 20% was recorded². A very high prevalence, ranging from 20% to 50%, is present in women with pelvic pain and decreased fertility ³. The etiology of endometriosis has still not been fully explained. It is evident that the process of etiopathogenesis of endometriosis includes, besides retrograde menstruation, numerous mechanisms such as an altered immune response, genetic predisposition as well as environmental factors. There are two types of endometrial cysts, depending on the origin, the clinical course, the histopathological findings and the response to treatment: TYPE I or primary endometriomas and TYPE II, the so-called secondary endometriomas⁴. The mechanisms that are related to decreased fertility are numerous: ovular dysfunction, luteal phase defect, luteinised unruptured follicle syndrome, multiple abortions, altered immune response, intraperitoneal inflammation, implantation dysfunction ⁵. Laparoscopy is a 'golden standard' in the treatment of endometriosis. A complete excision of the capsule is an acceptable method in terms of complete removal of endometriosis and prevention of the recurrence of the disease. Various parameters can be used to estimate the ovarian reserve. The use of a colour Doppler ultrasound makes it possible to estimate the ovarian volume, the antral follicle count, to analyse the stromal blood flows and to assess the vascular network in the ovary. The determination of the basal serum concentrations of the follicle stimulating hormone (FSH), luteinsing hormone (LH), estradiol, inhibin B and anti-Müllerian hormone (AMH) is of great significance in the estimation of the ovarian reserve ⁶.

The aims of this paper were the following: to estimate the ovarian reserve in patients who have undergone a surgical treatment due to ovarian endometriomas (endometriotic ovarian cysts); to estimate which of the two applied laparoscopic techniques, the laparoscopic cystotomy or the laparoscopic incision (cystectomy), causes greater damage to the ovarian function, i.e. diminishes the ovarian reserve; to estimate the percentage of recurrence of endometriosis during the first year after the surgery, depending on the surgical technique used, i.e. cystotomy and cystectomy; to determine the percentage of achieved pregnancies in the first year after the surgery and to estimate whether that rate depends on the type of the laparoscopic surgery that was performed.

Methods

A prospective study was conducted in Obstetrics and Gynaecology Clinic "Narodni Front" in Belgrade at the Endoscopic Infertility Treatment Ward. A total of 150 patients were included in the study. The study group was represented by 100 patients who underwent a surgical treatment of endometrial ovarian cysts. The patients in the study group were divided into 2 subgroups: Subgroup I consisted of 50 patients who underwent a laparoscopic cystotomy and subgroup II which included 50 women who underwent a laparoscopic cystectomy. The decision to perform a surgical procedure was made when endometrial cyst was suspected based on the case history, clinical findings, ultrasound findings and the findings of the colour Doppler as well as the serum concentrations of ovarian tumor marker (CA-125). A definitive diagnosis was made using diagnostic laparoscopy and as soon as the diagnosis was made, the laparoscopic surgical procedure was continued. The ultrasound exams were performed using a 5-7 MHz transvaginal probe. The control group consisted of 50 patients who underwent a surgical treatment due to tubal factor infertility. Patients up to 35 years of age who previously had not had an ovarian surgery participated in the study. Patients who were given medical treatment prior to surgery, that is, gonodotropin-releasing hormone (GnRh) analogues as well as those who had a history of polycystic ovaries were excluded from the study. All the patients were selected randomly. A type of the surgical technique, cystectomy or cystotomy, was selected at the discretion of the surgeon and based on the intraoperative findings. The surgical procedures performed on all the patients were laparoscopic, monitored on a TV screen. Cystotomy was performed by opening the capsule of the cyst on the antimesenteric side of the ovary and emptying the contents of the cyst using an aspirator. The inside of the cyst was flushed with saline solution and then laparoscopic camera was inserted into the cyst and the interior wall of the cyst was inspected. If pockets of endometriosis were found on the capsule, they were cut out with scissors and sent to the histopathological (HP) analysis. After that, the place where the pocket was found was coagulated using the bipolar. Cystectomy was performed by making an incision on the wall of the cyst on the antimesenteric side of the ovary using the large general cutting scissors (LCS) (ultrasonic laparoscopic coagulation shears), after which the contents of the cyst was aspirated. The inside of the cyst was flushed. The capsule of the cyst was, in part sharply and in part bluntly, separated from the ovary, making sure that ovarian tissue was preserved to the maximum extent. Haemostasis using a bipolar was performed where there was bleeding. The removed

Džatić Smiljković O, et al. Vojnosanit Pregl 2018; 75 (7): 644-650.

tissue was sent to a HP analysis. Based on the stage of the disease according to the Revised American Fertility Society (r-AFS), the patients in the study group were divided into those who were in stage II (mild), III (moderate) and IV (severe). The patients with minimal endometriosis (stage I) were not included in the study group. Ovarian reserve was estimated before and after the surgery in all patients in both the study and control groups. The estimation of the ovarian reserve was based on the following: a) ovarian volume and the antral follicle count, b) hormonal status was determined radioimmunoassay (RIA) by on the second or the third day of a menstrual cycle: FSH, LH, estradiol, inhibin B, AMH. The analyses were performed before the surgery and 1 month after the surgical treatment if no postoperative therapy was introduced (GnRh analogues, oral contraceptives, progestogens). If postoperative therapy was applied, the analyses were performed after the patient got her first regular menstruation. The RIA of the hormonal status was performed on the second or the third day of a menstrual cycle. The ultrasound examinations were performed as follows: for the ovarian volume in the early follicular phase of the cycle and the volume of the operated ovary was compared to the volume of the ovary on the same side in the control group, while the ultrasound exam of the preovulatory follicle was performed between the 10th and the 14th day of the menstrual cycle. In order to determine the antral follicle count, the measurement was performed in one cross-section. The serum concentration of the CA-125 tumour marker was determined before and after the surgical procedure. The percentage of the recurrence of the endometrioma as well as the percentage of spontaneous pregnancies during the first year after surgery were analysed in all patients in the study group. The results obtained during this study were compared within the study group between the patients who had undergone laparoscopic cystotomy and those who had undergone laparoscopic cystectomy. Each of these two subgroups of the patients from the study group was compared with the patients from the control group. All the obtained data was statistically processed using the χ^2 -test, Fisher's test, the Kruskal-Wallis single-factor analysis of variance, the Kolmogorov-Smirnov test and the obtained results were compared with the results of the domestic and foreign researchers. Certain conclusions were made based on the obtained results.

Results

On the basis of the statistical data analysis shown in Figure 1, the study group and the control group showed extremely high statistically significant difference in the ovarian volume after the surgical procedure (p < 0.001). No statistically significant difference was determined between the two subgroups of the patients who had undergone surgical treatment (p > 0.05). Statistically highly significant difference was recorded between the control group and the cystotomy subgroup (p < 0.001) as well as between the cystectomy subgroup and the control group (p < 0.001).



Fig. 1. - Ovarian volume after surgical procedures.

Table 1 shows the presence of a preovulatory follicle on the operated ovary in the patients from the study group in comparison with the ovary on the same side in the patients from the control group. In the study group, 72% of the patients did not have a preovulatory follicle on the operated ovary. There was no preovulatory follicle in 68% of the patients in the cystotomy subgroup nor in 76% of the patients in the cystectomy subgroup. A preovulatory follicle was not present on the ovary on the same side in 56% of the patients in the control group. The study group and the control group were statistically significantly different (p < 0.05), as well as the control group and the subgroup of the cystectomy patients (p < 0.05).

As for the antral follicles, the majority of patients in the control group (62%) had 3–5 on the operated ovary while the majority in the study group, 66%, had 2 or fewer follicles: 62% of the cystotomy patients and 70% of the cystectomy patients. No statistically significant difference was determined between the two subgroups of the patients who had undergone surgical treatment, cystotomy or cystectomy (p > 0.05). Statistically highly significant difference was recorded between the control group and the cystotomy subgroup (p < 0.001) as well as between the cystectomy subgroup and the control group (p < 0.001).

	Presence of a preovulatory follicle			1 able	
Preovulatory follicle	Study group			- Control group	
	Cystotomy n (%)	Cystectomy n (%)	Total n (%)	n (%)	
Yes	16 (32)	12 (24)	28 (28)	22 (44)	
No	34 (68)	38 (76)	72 (72)	28 (56)	
Total	50 (100)	50 (100)	50 (100)	50 (100)	

Džatić Smiljković O, et al. Vojnosanit Pregl 2018; 75 (7): 644-650.

A Figure 2 shows AMH values in the study group before and after the surgery, depending on the stage of the endometriosis as well as in the control group. Before the surgery, the highest AMH values were recorded in the patients with stage II endometriosis $(5.7 \pm 1.9 \text{ ng/mL})$, while the lowest value was recorded in patients with stage IV endometriosis $(3.53 \pm 1.6 \text{ ng/mL})$. In the cystotomy subgroup, the highest AMH value after the surgery was recorded in the patients with stage II endometriosis $(5.2 \pm 2.4 \text{ ng/mL})$; the highest AMH value was also recorded in the same stage of endometriosis in the cystectomy subgroup $(5.0 \pm 2.2 \text{ ng/mL})$. The highest AMH value was recorded in the control group $(6.9 \pm 2.8 \text{ ng/mL})$. The lowest AMH value after the surgery was recorded in the patients with stage IV endometriosis who had undergone cystectomy and cystotomy. Although the mean AMH value in the control group was higher than the values in both subgroups of the study group, no statistically significant difference was determined between the study and the control groups (p > 0.05).



Fig. 2 – Anti-Müllerian hormone (AMH) average values in presenting groups.

The highest FSH value after the surgery in the cystotomy subgroup was recorded in patients with stage IV endometriosis ($8.5 \pm 1.9 \text{ mIU/L}$). This was also the case in the cystectomy subgroup where the highest FSH value was recorded in stage IV endometriosis ($8.7 \pm 1.5 \text{ mIU/L}$) (Figure 3).



Fig. 3 – Follicle-stimulating hormone (FSH) average values in presenting groups.

Džatić Smiljković O, et al. Vojnosanit Pregl 2018; 75 (7): 644-650.

The FSH values after the surgery showed statistically highly significant difference (p < 0.001) in relation to the control group, regardless of the type of the surgical technique and the stage of the disease.

The highest preoperative inhibin B values were recorded in the patients with stage II endometriosis (97.4 \pm 25.1 pg/mL) while the lowest value was recorded in patients with stage IV endometriosis (42.6 \pm 18.4 pg/mL). After the surgery, the highest inhibin B values were recorded in the patients in stage II of the disease. The lowest mean inhibin B values were recorded in patients with stage IV endometriosis, both in the cystectomy and the cystotomy subgroups. The mean inhibin B value in the patients from the control group was higher than the value in the patients in both subgroups of the study group (Figure 4). No statistically significant difference (p > 0.05) was determined between the two subgroups of the study group nor in relation to the control group.



Fig. 4 – Inhibin B average values in presenting groups.

The mean values of the CA-125 tumour marker before the surgical procedure showed statistically highly significant difference (p < 0.001) in relation to the values of the CA-125 tumour marker after the surgical procedure in all stages of endometriosis, both in the subgroup of the patients who had undergone cystotomy and the patients who had undergone cystectomy. The mean CA-125 values between the subgroups of cystotomy and cystectomy patients were statistically significantly different only in the patients with stage II endometriosis (Figure 5).



Fig. 5 – Ovarian tumor marker (CA-125) average values in presenting groups.

The mean values of the CA-125 tumour marker before the surgical procedure showed extremely high statistically significant difference (p < 0.001) in relation to the values of the CA-125 tumour marker after the surgical procedure in all stages of endometriosis both in the subgroup of the patients who had undergone cystotomy and the patients who had undergone cystectomy.

Figure 6 shows the distribution of achieved pregnancies one year after the surgery in the patients in both the study group and the control group. Pregnancy was achieved in 19% of the patients from the study group, more precisely, in 16% of cystotomy patients and 22% of cystectomy patients. There was no statistically significant difference between the study group and the control group (p > 0.05).



Fig. 6 – Achieved pregnancies.

The recurrence of endometriosis was diagnosed in 46% of the patients who had undergone cystotomy, whereas in patients who had undergone cystectomy the percentage of recurrence was 36%. The cystotomy and cystectomy subgroups did not show statistically significant difference in the rate of recurrence of endometriosis after the surgical procedure (p > 0.05).

Discussion

Various parameters can be used to estimate the ovarian reserve. The use of an ultrasound makes it possible to estimate the ovarian volume and the antral follicle count. The change in the ovarian volume and the direct correlation with the hormonal status was first noticed by Goswamy et al.⁶. Many studies conducted later indicated that a decrease in the ovarian volume together with a decrease in the antral follicle count represented a possible indicator of a weaker response to a controlled ovarian stimulation ⁷. Diminished ovarian reserve was directly confirmed by the decreased ovarian volume and lower antral follicle count and the ultrasound parameters were in direct correlation with the decrease in estradiol values, increase in FSH values, decreased number of aspirated oocytes and lower pregnancy rate ⁸. There was data in literature that showed that the antral follicle count was bet-

ter indicator of a poor ovarian response than the basal level of FSH⁹. Serum levels of FSH, estradiol and inhibin B in the early follicular stage of the menstrual cycle are used for the estimation of the ovarian reserve. All these hormones are a part of the pituitary-ovarian feedback loop, hence their values are mutually dependent and the levels show significant variability during the cycle. AMH is the only serum marker not controlled by gonadotropin and it is very useful in determining ovarian aging. The excision of the fibrous capsule of the endometrium as well as thermal cauterisation for the purpose of achieving haemostasis, reduces the healthy ovarian tissue and in cystotomy, after the incision and drainage of the cyst, the endometrial pockets, which can take up large areas of the cyst capsule, are thermally cauterised. This surgical technique may cause thermal damage to the ovary ¹⁰. The retraction of the scar tissue after the surgery can also lead to the decreased ovarian volume. Electrosurgical instruments achieve high-frequency electric current and thus cause the tissue to heat up, so that haemostasis of smaller blood vessels is achieved in addition to the dissection. Cutting, coagulation or cauterisation can be performed by adjusting the power. When using these instruments, the depth of the thermal action must be taken into consideration. Candiani et al.¹¹ determined by ultrasound examinations a significant decrease in ovarian volume after the excision of the endometrial cyst in comparison with the contralateral ovary. The mean recorded decrease in the volume of the operated ovary was 33%, which was not linked to the damaged vascularisation of the ovary because the stromal blood flows did not change significantly. Other papers also indicated that there was a significant decrease in the basal volume of the operated ovary as well as in the number of the preovulatory follicles in the process of the controlled ovarian stimulation ¹². Based on the ultrasound measurements of the antral follicle (AF) count on the operated ovary, it was concluded that the largest percent (2/3) of the operated patients in the study group had up to 2 antral follicles (measured in one cross-section) in comparison with the control group in which the largest percentage of women (62%) had 3-5 AFs. There were differences between the study subgroups (the cystotomy patients had a larger number of antral follicles), but they were not statistically significant. In a paper written by Chinese authors, a significant reduction in the antral follicle count was recorded both in the ovarian suture and in the haemostasis by electrocoagulation, with the decrease in antral follicle count being more progressive in the second group ¹³. There was a difference in the reduction of the ovulation rate of the operated ovary in a non-stimulated cycle in relation to the control group. The largest number of the patients in the study group did not have a preovulatory follicle on the operated ovary, 68% in the cystotomy patients and 76% in cystectomy patients, to be precise. In the control group, the monitoring of the ovulation on the ovary on the same side showed that 56% of the patients did not have a preovulatory follicle. There was a statistically significant difference between the subgroup of patients who underwent cystectomy in relation to the control group (p < 0.001), while the same did not apply to the cystotomy subgroup in relation to the control group (p

> 0.05). That suggests that cystotomy is a less invasive procedure than cystectomy. In their study, Beretta et al.¹⁴ stated a statistically significant difference (p < 0.05) in the 24month cumulative pregnancy rate in the cystectomy group (66.7%) in comparison with the cystotomy group (23.5%). Ragni et al.¹⁵ evaluated the reduced ovarian response to hyperstimulation in women who underwent unilateral endometriosis surgery. Comparing the operated ovary with the contralateral one in the same patient, the rate of dominant follicles, the number of oocytes, embryos and high quality embryos, they reached a conclusion that a laparoscopic excision of the endometrium was associated with quantitative (but not qualitative) damage to the ovarian reserve. The comparison of the results in the patient groups depending on whether they underwent excision of the cyst capsule or cystotomy showed similar hormonal levels, and in relation to the control group the FSH level is significantly higher. Different results of studies can be found in literature: from those that corresponded with the results obtained in this study where significantly higher FSH levels after the surgery spoke in favour of diminished ovarian reserve ¹⁶ to those in which no significant differences were recorded in the FSH levels, indicating that the endometrial cyst surgery did not compromise ovarian function¹⁷. A significant increase in FSH levels after endometrial surgery was also recorded by other authors. A larger extent in electrocoagulation than in ovarian suture was applied for the purpose of achieving haemostasis ¹⁷. The values of serum AMH levels in all patients who underwent endometriosis surgery showed the inverse correlation with the stage of the disease and with a mild decrease in the values after the surgery. Furthermore, these values were lower than those in the control group. However, due to the numerical factor, these differences were not statistically significant. The highest values before the surgery were present in the patients with stage II endometriosis $(5.7 \pm 1.9 \text{ ng/mL})$, and the lowest in the patients with stage IV of the disease (3.53 ± 1.6 ng/mL). The highest value among the operated patients in the cystotomy subgroup was in the patients in stage II (5.2 ± 2.4 ng/mL) and in the cystectomy subgroup the highest value was also in stage II (5.0 \pm 2.2 ng/mL). The lowest values were recorded in stage IV (cystotomy: 2.9 ± 1.2 ng/mL; cystectomy: 2.9 ± 1.9 ng/mL). The obtained results corresponded to those of other studies ¹⁸. They suggested that the damage to the ovarian tissue was similar in both surgical techniques: the cystotomy with a coagulation of endometrial pockets and the excision of the endometrioma capsule. Normal inhibin pg/mL values were > than 45 pg/mL. The highest values before the surgery were recorded in the patients with stage II endometriosis (97.4 \pm 25.1 pg/mL), and the lowest in the patients with stage IV of the disease (42.6 \pm 18.4. pg/mL). After the surgery, the highest mean inhibin B value was in the patients in stage II of the disease who underwent cystotomy ($85.8 \pm 32.5 \text{ pg/mL}$) and the lowest in the patients with stage IV endometriosis who underwent cystectomy (40.7 \pm 19.4 pg/mL). The mean inhibin B value in the patients belonging to the control group was 123.8 ± 36.8 pg/mL. It can be noted that inhibin B level in the patients with endometriosis was lower even before the surgical pro-

cedure and that it depended on the extensiveness of the disease, which means that the very presence of the endometrial process had a negative impact on the ovarian reserve. The mean inhibin B values in the control group were higher than the values in the patients from both subgroups of the study group, which means that they had better ovarian fertility potential. A mild decrease in the level of this hormone after the surgery, regardless of the surgical technique applied, indicated that the surgery made further damage to the healthy ovarian tissue, whether by coagulation or by excision of the endometrioma capsule. The clinical significance of the determination of inhibin B level in the serum was reflected in the estimation of ovarian reserve, as well as the number and quality of the follicles. The serum values of this hormone can be used as the basis for estimating the ability of the ovary to activate a larger number of follicles during stimulation of ovulation by medication. No statistically significant difference was determined between the inhibin B values in both subgroups of the study group (p > 0.05) and the same applies to AMH values, due to the small amount of available data. The highest CA-125 values before the surgery were recorded in the stage IV patients in the study group, 69.5 ± 9.3 , and the lowest in stage II of the disease, 28.5 ± 8.2 IV/L. After the surgery, the mean CA-125 values in all stages of the disease in both subgroups of the study group were statistically significantly lower in comparison with the preoperative values. The CA-125 values were in direct correlation with the stage of the disease, which can be seen from the results of the study. Cheng et al.¹⁹ stated that the values higher than 65 IU/L were associated with later stages of endometriosis, the pouch of Douglas obliteration and endometriosis that spreaded into the bladder. The serum levels were significantly higher in women with ovarian endometriosis as well as in cases of deep endometriosis, but not in mild forms of the disease. It was assumed that endometrial lesions contained higher amounts of CA-125 than normal endometrium. When these lesions were damaged due to constantly present inflammation, CA-125 was released ²⁰. No significant difference was found in the number of

achieved pregnancies between the subgroups of the study group one year after the surgery. The percentage of achieved pregnancies in the study group was 19%, with 22% in cystotomy patients and, 16% in cystectomy subgroup, but this difference was not statistically significant. The reconstruction of normal pelvic anatomy is achieved surgically. The success rate in decreased fertility cases depends on the severity of endometriosis. The treatment of moderately severe disease resulted in approximately 60% pregnancy rate, while in severe endometriosis the rate was 35%^{21, 22}. Recurrence was diagnosed in 41% of the patients in the study group, with the cystotomy subgroup having a higher recurrence rate (46%) while in the cystectomy subgroup that rate was lower (36%). However, this difference was not statistically significant. There are studies in which similar conclusions were reached. Hemmings et al.²³ published in a paper that the recurrence rate 36 months after the laparoscopic surgery was similar, regardless of whether the laparoscopic technique applied was cystectomy or cystotomy. The reoperation rate after 18 months was 6.1% in the cystectomy group, in comparison with the 21.9% in the cystotomy group. The reoperation rate after 48 months was 23.6% after cystectomy and 57.8% after cystotomy. Alborzi et al. ²⁴ stated that the reoperation rate was statistically significantly lower after cystectomy than after cystotomy.

Conclusion

Laparoscopic surgery represents a golden standard in the treatment of ovarian endometriosis. The excision technique gives better results than the drainage of endometrial cysts in terms of recurrence, pain and spontaneous pregnancies in women who suffer from decreased fertility. However, the excision and the ablation of the capsule may cause damage to the normal cortex of the ovary. When performing the excision of the capsule, healthy ovarian tissue is often also removed, resulting in follicular loss. The ablation of the capsule may result in thermal damage to the ovarian tissue under the cyst capsule. Considering the fact that endometriosis is a disorder affecting young women, surgical treatment should be performed with utmost caution in order to preserve the reproductive function. Due to the proximity of the fibrous pseudocapsule of the endometrial cyst and the ovarian tissue, it must be taken into account that any surgical technique may cause damage of the ovaries and consequently decrease the ovarian reserve.

REFERENCES

- 1. Ulukus M, Cakmak H, Arici A. The role of endometrium in endometriosis. J Soc Gynecol Investig 2006; 13(7): 467–76.
- Waller KG, Lindsay P, Curtis P, Shaw RW. The prevalence of endometriosis in women with infertile partners. Eur J Obstet Gynecol Reprod Biol 1993; 48(2): 135–9.
- Haney AF. Endometriosis: Pathogenesis and pathophysiology. In: Wilson EA, editor. Endometriosis. New York: AR Liss; 1987. p. 23-51.
- Nezhat F, Nezhat C, Allan CJ, Metzger DA, Sears DL. Clinical and histologic classification of endometriomas. Implications for a mechanism of pathogenesis. J Reprod Med 1992; 37(9): 771–6. PubMed PMID: 1453396
- 5. *Cahill DJ, Hull MG*. Pituitary-ovarian dysfunction and endometriosis. Hum Reprod Update 2000; 6(1): 56–66.
- 6. Goswamy RK, Campbell S, Royston JP, Bhan V, Battersby RH, Hall VJ, et al. Ovarian size in postmenopausal women. Br J Obstet Gynecol 1988; 95(8): 795-801.
- Ng EH, Yeung WS, Fong DY, Ho PC. Effects of age on hormonal and ultrasound markers of ovarian reserve in Chinese women with proven fertility. Hum Reprod 2003; 18(10): 2169–74.
- 8. *Marton U.* Significance of three-dimensional ultrasound and three-dimensional colod Doppler in evaluation of in vitro fertilisation outcome [dissertation]. Zagreb: Facultz of Medicine; 2005. (Croatian)
- Hendriks DJ, Mol BW, Bansci LF, te Velde ER, Broekmans FJ. Antral follicle count in the prediction of poor ovarian response and pregnancy after in vitro fertilization: A metaanalysis after comparison with basal FSH level. Fertil Steril 2005; 83(2): 291-301.
- Salihoğlu KN, Dilbaz B, Cırık DA, Ozelci R, Ozkaya E, Mollamahmutoğlu L. Short-Term Impact of Laparoscopic Cystectomy on Ovarian Reserve Tests in Bilateral and Unilateral Endometriotic and Nonendometriotic Cysts. J Minim Invasive Gynecol 2016; 23(5): 719–25.
- Candiani M, Barbieri M, Bottani B, Bertulessi C, Vignali M, Agnoli B, et al. Ovarian recovery after laparoscopic enucleation of ovarian cysts: Insights from echographic shortterm postsurgical follow-up. J Min Invasive Gynecol 2005; 12(5): 409–14.
- 12. Somigliana E, Ragni G, Benedetti F, Borroni R, Vegetti W, Crosignani PG. Does laparoscopic exision of ovarian cysts significantly affect ovarian reserve? Insights from IVF. Hum Reprod 2003; 18(11): 2450-3.
- Zhang CH, Wu L, Li PQ. Clinical study of the impact on ovarian reserve by different hemostasis methods in laparoscopic cystectomy for ovarian endometrioma. Taiwan J Obstet Gynecol 2016; 55(4): 507–11.

- Beretta P, Franchi M, Ghezzi F, Busacca M, Zupi E, Bolis P. Randomised clinical trial of two laparoscopic treatments of endometriomas: Cystectomy versus drainage and coagulation. Fertil Steril 1998; 70(6): 1176–80.
- 15. Ragni G, Somigliana E, Benedetti F, Paffoni A, Vegetti W, Resteli L, et al. Demage to ovarian reserve associated with laparoscopic excision of endometriomas: A quantitative rather than a qualitative injury. Am J Obstet Gynecol 2005; 193(6): 1908-14.
- Hock DL, Sharafi K, Dagostino L, Kemmann E, Seifer DB. Contribution of diminished ovarian reserve to hypofertility associated with endometriosis. J Reprod Med 2001; 46(1): 7–10.
- Frankurt S, Nunes AL, Reis AD, Crostofolini DM, Bianco B, Barbosa CP. Evaluation of basal FSH, serum levels in infertile patients with deep ovarian endometriosis who underwent surgery. Rev Bras Ginecol Obstet 2009; 31(7): 349-52. (Portuguesse)
- Lemos NA, Arbo E, Scalco R, Weiler E, Rosa V, Cunha-Filho JS. Decreased anti-Mullerian hormone and altered ovarian follicular cohort in infertile patients mild/minimal endometriosis. Fertil Steril 2008; 89(5): 1064–8.
- Cheng YM, Wang ST, Chou CY. Serum CA-125 in preoperative patients at high risk for endometriosis. Obstet Gynecol 2002; 99(3): 375–80.
- Ruan YQ, Liang WG, Huang SH. Analysis of laparoscopy on endometriosis patients with high expression of CA125. Eur Rev Med Pharmacol Sci 2015; 19(8): 1334–7.
- Sutton CJG, Nair S, Ewen SP, Haines P. A comparison between the CO2 and KTP lasers in the treatment of large ovarian endometriomas. Gynecol Endoscopy 1993; 2: 113–6.
- Muzii L, Luciano A, Zupi E, Panici PB. Effect of Surgery for Endometrioma on Ovarian Function: A Different Point of View. J Minim Invasive Gynecol 2016; 21(4): 531–3.
- Hemmings R, Bissonnette F, Bouzayen R. Results of laparoscopic treatments of ovarian endometriomas: Laparoscopic ovarian fenestration and coagulation. Fertil Steril 1998; 70(3): 527-9.
- 24. Alborzi S, Momtahan M, Parsanezhad ME, Dehbashi S, Zolshardi J, Alborzi S. A prospective, randomized study comparing laparoscopic ovarian cystectomy versus fenestration and coagulation in patients with endometriomas. Fertil Steril 2004; 82(6): 1633–7.

Received on April 08, 2016. Revised on September 14, 2016. Accepted on October 03, 2016. Online First December, 2016.

Džatić Smiljković O, et al. Vojnosanit Pregl 2018; 75 (7): 644-650.