

# Recurrence rate of ovarian endometriosis in patients treated with laparoscopic surgery and postoperative suppressive therapy

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## Summary

**Introduction:** The testing represented a prospective study that was performed at the Gynaecology and Obstetrics Clinic "Narodni Front" in Belgrade during a two-year period. The study encompassed female patients with ovarian endometrioma operated with laparoscopic surgery. The research objective was to determine the percentage of occurrence of relapses in patients operated for endometriosis of the ovary in relation to the stage of the disease and the type of performed operation, and which were receiving suppressive therapy with gonadotropin-releasing hormone (GnRH) analogues after the surgery compared to those who were not receiving suppressive therapy after the operation. **Materials and Methods:** The recurrence of endometriosis on the ovary of the test and control groups was monitored during the first year after surgery. In all patients ultrasound checks were done every month during the first six months after surgery, and then every three months for the next six months. In all patients in whom the recurrence, i.e. endometrioma on the ovary larger than three cm was revealed postoperatively by ultrasound, the laparoscopic removal of the endometrioma was performed again as well as the histopathological examination of the material. **Results and Conclusion:** There was no statistically significant difference in the distribution of recurrence of endometriosis between the groups formed according to the type of surgical technique (cystectomy or cystotomy). The recurrence of endometriosis occurred later in the group of patients in which the treatment GnRH analogues was applied after the surgical treatment. The recurrence of endometriosis in more severe stages (Stage III and IV) occurs later in the group of patients in which the treatment GnRH analogues is applied after the surgical treatment.

**Key words:** GnRH analogues; Ovarian endometrioma; Cystectomy; Cystotomy; Laparoscopy.

## Introduction

Endometriosis is one of the common diseases in the reproductive age of women. It affects 5-10% of the total female population and is revealed in 40% of infertile women and 60% of women with chronic pelvic pain [1, 2]. The treatment of endometriosis can be surgical and with medication. In the last ten years gonadotropin-releasing hormone (GnRH) analogues have been used in therapy [3, 4]. The use of GnRH analogues substantially reduces the symptoms of endometriosis [5]. Despite great progress in surgical techniques and due to the nature of the disease, endometriosis often relapses. The research objective was to determine the percentage of occurrence of relapses in patients operated on for endometriosis of the ovary in relation to the stage of the disease and the type of performed operation, and which were receiving suppressive therapy with GnRH analogues after the surgery, compared to those who were not receiving suppressive therapy after the operation.

## Materials and Methods

The testing represented a prospective study that was performed at the Gynaecology and Obstetrics Clinic "Narodni Front" in Belgrade during a two-year period.

The study encompassed 200 female patients with ovarian endometrioma operated on with laparoscopic surgery. The patients were from 20-45 years of age. The indications for the surgery were set based on the anamnesis, the pelvic ultrasound examination, and the serum concentrations of cancer antigen 125 (CA 125). The operated patients were divided into two groups, the test and control groups. The test group consists of 100 patients operated with laparoscopy due to endometrial cysts of ovary and in which suppressive therapy with GnRH analogues was applied after surgery. Out of the GnRH analogues, triptorelin was administered in the form of acetate, i.e. dipherelin 3.75 mg intramuscularly once a month, or goserelin in the form of acetate, i.e. zoladex 3.6 mg subcutaneously into the anterior abdominal wall, once per month. GnRH analogues were administered over the course of four to six months depending on the severity of the endometriosis. Depending on the type of surgery, all tested patients were divided into two subgroups. The first subgroup consists of patients who had undergone laparoscopic cystectomy, while the other subgroup consists of patients who had undergone laparoscopic cystotomy and coagulation of the cyst capsule. The decision regarding which type of surgery was performed in patients was made by the surgeon, based on the surgical report.

The degree of severity of endometriosis was assessed according to the classification of the American Society for Fertility and Sterility (AFS classification). In relation to the degree of progress of endometriosis, all patients in the test group were divided into three subgroups as follows: patients with II, III and IV stage of endometriosis.

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The control group consisted of 100 patients with endometrial cysts of ovary, which were operated with laparoscopic method and who did not receive suppressive therapy with GnRH analogues after the operation. All patients in the control group were divided into two subgroups according to the type of performed surgery. The first subgroup consists of patients who had undergone laparoscopic cystectomy and the other subgroup consists of patients who had undergone laparoscopic cystotomy. In relation to the degree of severity of the disease all patients of the control group were divided into three subgroups as follows: patients with the II, III and IV stage of endometriosis.

The recurrence of endometriosis on the ovary of the test and control groups was monitored during the first year after surgery. In all patients ultrasound checks were done every month during the first six months after surgery, and then every three months for the next six months. The ultrasound examinations were performed on a device with a transvaginal probe with the power of five MHz in the sagittal and coronal section.

In all patients in whom the recurrence, i.e. endometrioma on the ovary larger than three cm revealed postoperatively by ultrasound, the laparoscopic removal of the endometrioma was performed again as well as the histopathological examination of the material.

In all patients diagnosed with ovarian endometriosis the following were analyzed: type of surgery, stage of endometriosis, length of application of the suppressive therapy, recurrence of endometriosis, and finding of the new laparoscopy in patients in whom the ultrasound examination revealed the recurrence of endometriosis on the ovary. The frequency of recurrence was analyzed in relation to the type of laparoscopic surgery (cystectomy or cystotomy), as well as in relation to the severity of the disease.

The obtained data were statistically analyzed by using descriptive and analytical statistical methods. As to descriptive statistical methods, measures of central tendency and measures of variability were used, and from the analytical methods the chi-square test, Kruskal-Wallis, and the t-test.

## Results

The study encompassed 200 patients. Laparoscopic cystectomy was performed in 112 (56%) patients and laparoscopic cystotomy in 88 (44%) patients. Out of the total of 200 patients, 100 of them received GnRH analogues postoperatively and the other 100 patients received no suppressive therapy with GnRH analogues postoperatively. Out of the total of 200 patients, GnRH analogues were administered in 44 (22%) patients after a laparoscopic cystectomy and in 56 (28%) patients after a laparoscopic cystotomy. Sixty-eight (34%) patients after laparoscopic cystectomy and 32 (16%) patients after laparoscopic cystotomy did not receive GnRH analogues.

Table 1 shows the distribution of patients by stage of endometriosis according to the type of operation and application of suppressive therapy. The differences were not statistically significant in terms of the type of operation and stage of endometriosis between these two groups of patients ( $p < 0.05$ ).

The stage of endometriosis shows a statistically significant correlation with the type of applied laparoscopic operation. In stage II of endometriosis, significantly more frequently laparoscopic cystectomy was applied and in the III and IV stage laparoscopic cystotomy ( $p < 0.01$ ).

Table 1. — *Distribution of female patients according to the stage of endometriosis, type of operation, and application of suppressive therapy.*

Group		Stage of endometriosis			Total
		II	III	IV	
CC/GnRH+	N	38	6	0	44
	%	86.4	13.6	0	100
CC/GnRH-	N	64	4	0	68
	%	94.1	5.9	0	100
CT/GnRH+	N	46	5	5	56
	%	82.1	8.9	8.9	100
CT/GnRH-	N	21	6	5	32
	%	65.6	18.8	15.6	100
All patients	N	169	21	10	200
	%	84.5	10.5	5	100

CC: cystectomy; CT: cystotomy

Table 2. — *Distribution of patients according to the recurrence of endometriosis in relation to the type of operation and application of suppressive therapy.*

Group		Recurrence (months)			Total
		1-3	4-6	7-12	
CC/GnRH+	N	6	15	23	44
	%	13.6	34.1	52.3	100
CC/GnRH-	N	26	33	9	68
	%	38.2	48.5	13.2	100
CT/GnRH+	N	8	20	28	56
	%	14.3	35.7	50	100
CT/GnRH-	N	13	13	6	32
	%	40.6	40.6	18.8	100
All patients	N	53	81	66	200
	%	26.5	40.5	33.0	100

Table 2 shows the distribution of patients according to the recurrence of endometriosis in the studied groups. The statistical analysis did not show any significant difference as to the distribution of recurrence of endometriosis between groups formed according to the type of applied surgical technique (cystectomy or cystotomy) ( $p > 0.05$ ). By comparing the group of patients that received suppressive therapy after surgery and the group of patients that did not receive the therapy, a statistically significant difference was found between the recurrence of endometriosis ( $p < 0.01$ ). The groups of patients formed according to the type of surgical technique and depending on the application of GnRH analogues showed a statistically significant difference in the relapse of endometriosis ( $p < 0.01$ ). This suggests that the recurrence of endometriosis emerged later in the group of patients that received GnRH analogues after surgical treatment.

Table 3 shows the distribution of patients according to the recurrence of the disease in more severe stages of endometriosis (stages III and IV). When we look at all patients with stage III and IV of endometriosis, it is seen that the recurrence of endometriosis usually occurred four

Table 3. — *Distribution of patients according to the occurrence of recurrence in more severe stages of endometriosis.*

Stage of endometriosis		Recurrence (months)			Total
		1-3	4-6	7-12	
III	N	6	6	9	21
	%	28.6	28.6	42.9	100
IV	N	1	6	3	10
	%	10	60	30	100
All patients	N	7	12	12	31
	%	22.6	38.7	38.7	100

months after the first therapy session. The statistical analysis showed no significant difference in the distribution of recurrence of endometriosis among groups of patients in stage III and IV of endometriosis ( $p > 0.05$ ). In the entire group of patients with more severe stages of endometriosis (stages III and IV), the distribution of the period in which endometriosis occurred, does not show a statistically significant difference ( $p > 0.05$ ).

## Discussion

The study encompassed 200 patients that were operated for endometriosis of the ovary with a laparoscopic technique. Forty-four (22%) patients were treated with GnRH analogues after laparoscopic cystectomy, whereas 68 (34%) patients were not given GnRH analogues after it; 56 (28%) patients received GnRH analogues after laparoscopic cystotomy, whereas 32 (16%) patients did not receive GnRH analogues after it. In 66.7% of the patients that were receiving GnRH analogues after a laparoscopic cystectomy, recurrence was diagnosed seven to 12 months after the first therapeutic treatment, while the percentage amounted to 60% in patients in which treatment with GnRH analogues was applied after laparoscopic cystotomy. In the group of patients in which therapy with GnRH analogues was not applied after a laparoscopic cystectomy, 48.5% had a recurrence of endometriosis four to six months after the first therapeutic treatment. The study in Korea that examined the effect of GnRH analogues after laparoscopic surgery of ovarian endometriosis showed that this therapy has a positive effect on the prevention of recurrence after six months of treatment [6, 7].

Patients that did not receive the suppressive therapy with GnRH analogues after a laparoscopic cystotomy had a recurrence of endometriosis in the period of one to three months after the first therapy in 45.5% of the cases. The postoperative use of GnRH analogues after a laparoscopic cystectomy of the endometrial cyst in the ovary reduces the relapse rate and this rate for 18 months after surgery was 6% [8] and 9.6% [9], while in patients who did not use this therapy, it amounted to 16.6% [8]. Other authors suggest that the excision of ovarian endometrioma may reduce the

reserve of the ovary, resulting in a lesser percentage of pregnancy by means of in vitro fertilization in these patients [10]. The overall recurrence rate two years after the excision of the ovarian endometrioma is about 30.4% [11]. Other authors suggest that the overall recurrence rate of endometrioma 12 months after the laparoscopic operation of ovarian endometrioma is 16.5%, and the postoperative use of GnRH analogues significantly reduces the rate of recurrence of the disease. They stated that if GnRH analogues are used for three months after the operation, the rate of recurrence 12 months after the surgery is 17.9%, 24 months after surgery is 12.5%, and 36 months after surgery is 25%. If GnRH analogues are administered during the first six months after surgery, the recurrence rate is significantly lower and was 4.3% 12 months after surgery, 5.3% 24 months after surgery, and 5.3% 36 months after surgery [5]. If laparoscopic cystectomy is performed on the endometrioma of the ovary and subsequently also with laser vaporization of the wall surface of the endometrium toward the hilus of the ovary, the recurrence rate was 2% [12]. The rate of recurrence after a laparoscopic excision of the endometrioma was significantly lower in patients who used oral contraception after surgery with 18.6%, and among those who did not use this therapy, it amounted to 33.1% [13]. The rate of recurrence after laparoscopic cystotomy, i.e. cyst fenestration, drainage of the contents, and coagulation of the capsule of the cyst is about 22.9%, after laparoscopic cystectomy, 5.8%, which are significant differences [14]. When the present authors analyzed the representation of stages of endometriosis in patients from the group that received GnRH analogues after laparoscopic cystectomy and those who did not receive GnRH analogues, they found that in both groups the most common was stage II of endometriosis. Patients who did not receive GnRH analogues after the laparoscopic cystotomy had more often stages III and IV of endometriosis than those who received GnRH analogues after it. The differences were statistically significant ( $p < 0.05$ ).

The present data show a statistically significant difference in the distribution of patients according to the stage of endometriosis between groups formed according to the type of surgical technique (cystectomy or cystotomy). This indicates that in the II stage of endometriosis, laparoscopic cystectomy was more often applied and in stage III and IV laparoscopic cystotomy. In 28.6% of the patients treated with laparoscopic cystectomy, there was a relapse of the endometriosis between the first and third month after the first therapy treatment. In the group of patients who underwent laparoscopic cystotomy, 23.9% of them had a relapse of endometriosis between one to three months after the first therapy treatment. The differences are not statistically significant ( $p > 0.03$ ). In 14% of patients in the group that received GnRH analogues after surgery, recurrences occurred after one to three months after the first therapy, and in 51% after seven to 12 months

after the first therapeutic treatment. In the group of patients that were not receiving GnRH analogues after the surgical procedure, in 39% there was a recurrence of endometriosis one to three months after the first therapeutic treatment, and in 46% four to six months after the first therapeutic treatment. In the group of patients where no therapy with GnRH analogues was applied after the laparoscopic cystectomy, 38.2% of patients had a recurrence of endometriosis one to three months after the initial therapeutic treatment. In 40.6% of the patients who did not receive suppressive therapy after the laparoscopic cystotomy, had a recurrence of endometriosis one to three months after the first therapeutic treatment. Through the statistical analysis of the data no significant differences in the distribution of recurrence of endometriosis between the groups formed according to the type of surgical technique (cystectomy or cystotomy) were found.

There was a statistically significant difference in the recurrence of endometriosis between groups of patients based on the applied therapy. The application of GnRH analogues shows a statistically significant correlation with the recurrence of endometriosis. This suggests that the recurrence of endometriosis emerged later in the group of patients in which the treatment with GnRH analogues was applied after surgical treatment. The postoperative use of GnRH analogues after the laparoscopic cystectomy of the endometrial ovarian cyst reduces the relapse rate and that rate for 18 months after surgery was 6% (30) or 9.6% (31), and in patients who did not use this therapy it was 16.6% (30). Other authors suggest that the rate of recurrence of ovarian endometrioma 12 months after laparoscopic surgery is 16.5% and that the postoperative use of GnRH analogues significantly reduces the rate of recurrence of the disease. They state that if GnRH analogues are used during the first three months postoperatively, the rate of recurrence 12 months after the surgery is 17.9%; 24 months after the surgery is 12.5% and 36 months after the surgery is 25%. If GnRH analogues are administered during the first six months after the surgery the recurrence rate is significantly lower; 12 months after surgery is 4.3%, 24 months after surgery is 5.3%, and 36 months after surgery is 5.3%. [15]. A study in Italy followed the recurrence in patients in which laparoscopic treatment of endometriosis was performed. One group was treated with GnRH analogues and the other group received a placebo therapy. Comparing the results, they have come to the conclusion that there was no significant effect of suppressive therapy and that recurrence depended on the type of surgical techniques [16].

When we look at all patients with stage III and IV of endometriosis, regardless of the applied therapeutic modalities, the highest percentage of relapse occurred four months after the application of the first therapeutic treatment. The study in Korea analyzed the effect of GnRH treatment on recurrence in patients with stage III and IV of

endometriosis after laparoscopic surgery. The results showed a lower incidence of relapse in patients who were treated with GnRH analogues for six months as compared to those who were treated for only three months. The difference was not statistically significant. The therapy with GnRH analogues in the duration of six months after the laparoscopic surgery had a favourable impact on the recurrence of endometriosis [17].

## Conclusion

There was no statistically significant difference in the distribution of recurrence of endometriosis between the groups formed according to the type of surgical technique (cystectomy or cystotomy). The application of the therapy with GnRH analogues shows a statistically significant correlation with the recurrence of endometriosis. This suggests that the recurrence of endometriosis occurred later in the group of patients in which the treatment GnRH analogues was applied after the surgical treatment. The application of therapy with GnRH analogues in the group of patients with more severe stages of endometriosis shows a significant correlation with the recurrence of endometriosis. This suggests that the recurrence of endometriosis in more severe stages (stages III and IV) occurs later in the group of patients in which the treatment GnRH analogues is applied after the surgical treatment.

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