



Surgical management of endometrioma for ovarian safety

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ABSTRACT

Objectives: The effect of laparoscopic surgery for endometrioma on ovarian function is debated and controversial. The aim of the study was to address the impact of preoperative parameters and surgical technique for the removal of endometrioma on the ovarian reserve.

Methods: This was a retrospective cohort study of outpatient women referred to the Fertility Center of the University of Campania "Luigi Vanvitelli" in Naples undergoing laparoscopy for enucleation of endometriotic cysts. The evaluation of the ovarian reserve was performed before the intervention and at the third month after the intervention by the count of antral follicles (AFC), FSH and AMH dosage. Surgery was performed by operative laparoscopy by stripping technique and ablation. Hemostasis was performed with two kinds of bipolar forceps, according to the feasibility of self-regulating coagulation.

Results: 46 patients were analyzed. The data showed a greater impact of the surgical technique on the ovarian reserve of patients in advanced reproductive age or with a recurrent endometrioma ($p < 0.05$). Patients undergone surgery with the use of forceps without self-regulation showed a statistically significant impairment ($p < 0.05$) of AFC, FSH, and AMH.

Conclusions: Our data showed equal hemostatic effectiveness for the two forceps, but a lower impact on the ovarian reserve with the one with self-regulating coagulation ($p < 0.05$). However, more studies with a longer follow-up period are required to clarify the fertility outcome better.

Keywords: : endometriosis; endometrioma; fertilization in vitro; infertility; bipolar forceps; laparoscopy; AFC; FSH; AMH

INTRODUCTION

Endometriosis is defined as endometrial tissue outside the uterine cavity and is considered as a chronic recurring disease. Its prevalence in infertile women is relevant and is estimated to be between

SOMMARIO

Obiettivo: L'effetto della chirurgia laparoscopica per endometrioma sulla funzione ovarica rappresenta ancora un tema dibattuto e controverso. Lo scopo dello studio è valutare l'impatto di parametri preoperatorio e tecnica chirurgica per la rimozione dell'endometrioma sulla funzione ovarica.

Metodi: È stato svolto uno studio retrospettivo di coorte su pazienti afferite al Centro di Fertilità dell'Università della Campania "Luigi Vanvitelli" di Napoli (Italia) candidate alla laparoscopia per l'enucleazione di cisti endometriose. La valutazione della riserva ovarica è stata eseguita prima dell'intervento e al terzo mese dopo l'intervento attraverso la conta dei follicoli antrali (AFC), il dosaggio di FSH e di AMH. L'intervento è stato eseguito mediante laparoscopia operativa con tecnica stripping e ablazione. L'emostasi è stata eseguita con due tipi di pinze bipolari: una con la possibilità di autoregolazione ed un'altra senza.

Risultati: 46 pazienti sono stati analizzati. I dati hanno mostrato un maggiore impatto dell'intervento sulla riserva ovarica nelle pazienti in età riproduttiva avanzata o con recidiva dell'endometrioma ($p < 0.05$). I pazienti sottoposti a chirurgia con l'uso di una pinza senza autoregolazione hanno mostrato una differenza statisticamente significativa ($p < 0.05$) di AFC, FSH e AMH.

Conclusioni: I nostri dati hanno mostrato un'efficacia emostatica uguale per le due pinze, ma un impatto minore sulla riserva ovarica con quella con autoregolazione ($p < 0.05$). Tuttavia, sono necessari più studi con un periodo di follow-up più lungo per chiarire meglio il risultato sull'outcome riproduttivo.

20 and 50 %⁽¹⁻²⁾. The most common symptom of endometriosis is long-term pelvic pain [3]. However, the pathogenesis of endometriosis is widely accepted as multifactorial⁽⁴⁻⁷⁾. About 17-44% of women with endometriosis will have an endometrioma, a cystic structure located on the outer wall of the ovary. One ovary is usually involved, while bilateral localization is less frequent and is present in about

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50% of patients⁽⁸⁾. However, the pathogenesis of endometrioma is controversial, and three main theories have been proposed to explain its origin: invagination of ovarian cortex secondary to bleeding of superficial implants, invagination of the ovarian cortex secondary to metaplasia of coelomic epithelium in cortical inclusion cysts and endometriotic transformation of functional cysts⁽⁹⁻¹²⁾. The effect of the endometrioma on women's fertility is still debated and controversial, although severe endometriosis is associated with reduced fertility outcome⁽¹³⁻¹⁴⁾. However, Coelho et al. hypothesized that the ovarian reserve acts as a major factor to predict fertility outcomes than endometriosis alone⁽¹⁵⁾. The diagnosis of endometrioma is achieved by a rectovaginal pelvic examination, a transvaginal ultrasound examination and, above all, a laparoscopic evaluation combined with histopathological confirmation⁽¹⁶⁻¹⁸⁾. A clinical history of chronic pelvic pain could help for diagnosis. Instead, to predict ovarian reserve, before an intervention, AFC and AMH levels are commonly used⁽¹⁹⁻²⁰⁾. The indications for surgical therapy should be personalized in relation to the age of woman and impact of the disease on the quality of life and currently are represented by the presence of debilitating pain symptoms, infertility, cysts with a diameter greater than 4 cm even in the absence of relevant symptoms⁽²¹⁾. The surgical approach is represented by operative laparoscopy, and the most effective surgical technique is ovarian cystectomy using the stripping technique and ablation⁽²²⁾. However, some studies concerned about the negative impact of cystectomy on fertility and anti-Mullerian hormone (AMH) level⁽²²⁻²⁵⁾. Nevertheless, ovarian cystectomy has been found to be superior to ablation regarding recurrence of endometrioma, pain symptoms, and reproductive outcomes rate on subfertile patients⁽²⁶⁻²⁷⁾. Moreover, researches are inconclusive about which surgical method is the less harmful to the ovarian reserve in the long term⁽²⁸⁻³⁰⁾. The aim of our study is to assess the impact on the ovarian reserve of preoperative parameters and surgical technique for the removal of endometrioma.

MATERIALS AND METHODS

This was a retrospective cohort study of outpatient women referred to the Fertility Center of the University of Campania "Luigi Vanvitelli" in Naples (Italy) and undergoing laparoscopy for enucleation of endometriotic cysts. Local Institutional Review Board approved the study. All participants before enrollment signed a comprehensive written consent form. The study was conducted in accordance with the principles of the Helsinki Declaration. The

inclusion criteria were: age between 18 and 40 years, regular menstrual cycle, size of the cyst > 4 cm in diameter, negative history of hormonal therapy in the 6 months before surgery. Two gynecologists performed the ultrasound examinations with the Voluson 730 Expert GE ultrasound machine using a transvaginal probe (3.3-10.0 MHz). The evaluation of the ovarian reserve was performed before the intervention and in the third month after the intervention by:

- Count of antral follicles (AFC) or follicles that appear at transvaginal ultrasound with a diameter between 2 and 10 mm on the II/III day of the menstrual cycle; the reference values for reduced ovarian reserve were less or equal than six as the sum of the antral follicles present on both ovaries.

- FSH (mU/ml) and AMH (ng/ml) dosage by blood sampling on the II-III day of the cycle. Reference values for reduced ovarian reserve were above 16 mU/ml for FSH and below 1ng/ml for AMH.

Laparoscopic surgery, performed by two gynecologists specialized in endometriosis, was planned in the follicular phase of the menstrual cycle. The laparoscopic surgical technique was as follows: the ovarian cyst was mobilized, and the content aspirated. The cystic wall was stripped and, after identification of the cleavage plane, was separated from the residual ovarian parenchyma by tractions exerted in opposite directions with two traumatic forceps, such as "Manhes". After the incision of the cystic wall, hemostasis was performed with bipolar forceps. The passage of current necessary for hemostasis is strictly limited to the area of tissue between the two branches reducing the damage to the surrounding ovarian tissue. For this purpose, for every procedure, we used one of the following forceps between:

- Robi Kelly grasping forceps, Clermont-Ferrand model (Karl Storz), size 3.5 mm, length 360 mm, with a 360° adjustable stem capable of coagulation, grasping and dissecting, connected to Ergo VAIO electro-surgical units 300 and pre-set for bipolar coagulation with 60 Watt effect 1, modifiable according to the needs of the operator but without the possibility of self-regulation;

- BiClamp LAP forceps Maryland (Erbe), semi-deep ribbed, shaft 5 mm, non-adhesive coating, length 340 mm, connected to Ergo VAIO 200 electro-surgical units and capable of automatically measuring the impedance of the tissue to which it is applied and therefore of supplying the lowest wattage necessary for hemostasis.

Histological examination of tissue removed was performed for every patient. Data were shown as

means \pm standard deviation. Comparisons between the two groups were assessed with Student's t-test. A p-value <0.05 was considered statistically significant. The study was performed according to the strengthening the reporting of the observational studies in epidemiology (STROBE) guidelines⁽³¹⁾.

RESULTS

Data for 48 women who underwent endometrioma excision were analyzed. Two patients were excluded: 1 was lost to follow up, and 1 was no data recorded. The main characteristics of the patients are shown in **Table 1**.

Table 1
Main characteristics of the patients

Main characteristics of the patients (n=46)	
	Mean \pm SD or percentage
Age (years)	33 \pm 4.6
BMI (kg/m ²)	23.5 \pm 3.8
Ethnicity	Caucasian (100%)
Diameter of the endometrioma excised (mm)	53.2 \pm 5.7
Laterality of endometrioma-excised ovary	Left: 22 (47.8 %) Right: 14 (30.4 %) Bilateral: 10 (21.8 %)
History of previous intervention on endometrioma	First intervention: 36 (78.3%) Recurrent intervention: 10 (21.7%)
Main ovarian values before intervention:	
AFC	7.9 \pm 2.1
FSH (mU/ml)	8.5 \pm 2.6
AMH (ng/ml)	1.9 \pm 1.3

In all cases, the intervention was decisive for the complete excision of the endometriotic tissue adjacent to the ovary. No surgical or post-surgical complications occurred. For each sample, the anatomopathological diagnosis was consistent with the clinical and ultrasound diagnosis. The patients were divided into four different comparison groups based on the following criteria: age less than or equal to 35 years old vs. over 35, first intervention vs. recurrence, monolateral cysts vs. bilateral cysts, diathermocoagulation with classic bipolar forceps Robi Kelly vs. BiClamp LAP forceps Maryland.

In the first group we made a comparison

between patients aged less than or equal to 35 and those with a higher age: the data showed a greater impact of the surgical technique on the ovarian reserve of patients in advanced reproductive age. In fact, AFC and FSH values showed a statistically significant difference (<0.05) before and after the intervention (6.2 \pm 2.0 vs. 3.3 \pm 1.0 and 9.6 \pm 1.6 vs. 14.5 \pm 4.2, respectively). On the contrary, under the age of 35, the reduction in ovarian function after surgery is not statistically significant, with values of AFC, FSH, and AMH, even if reduced, however within the limits (8.3 \pm 2.3 vs. 7.1 \pm 2.7; 6.8 \pm 2.5 vs. 7.3 \pm 3.1; 2.1 \pm 1.0 vs. 1.8 \pm 1.0, respectively). Data are shown in **Table 2**.

Table 2
Ovarian function according to age

	Patients aged less than or equal to 35 (n=28)			Patients aged more than 35 (n=18)		
	pre-intervention	post-intervention	P-value	pre-intervention	post-intervention	P-value
AFC	8.3 \pm 2.3	7.1 \pm 2.7	ns	6.2 \pm 2.0	3.3 \pm 1.0	<0.05
FSH (mU/ml)	6.8 \pm 2.5	7.3 \pm 3.1	ns	9.6 \pm 1.6	14.5 \pm 4.2	<0.05
AMH (ng/ml)	2.1 \pm 1.0	1.8 \pm 1.0	ns	1.5 \pm 1.0	1.0 \pm 0.8	ns

In most cases the endometrioma is presented in the unilateral form: among our patients, 22 (47.9 %) presented endometrioma in the left ovary, 14 (30.4 %) in the right one and 10 (21.7%) had bilateral endometrioma. In fact, in the second group, we made a comparison between the removal of unilateral cyst vs. bilateral cysts. In the case of patients suffering from bilateral endometrioma, AFC and AMH values were lower in the pre-intervention phase than patients

with unilateral endometrioma. Otherwise, in patients with unilateral endometrioma, we observed a good ovarian response to surgical therapy in terms of preservation of function: AFC pre-intervention vs. post-intervention (7.2±2.6 vs. 6.0±3.5) was not statistically significant. FSH and AMH pre-intervention vs. post-intervention were not statistically significant (7.5±2.5 vs. 8.5±5.3 and 1.9±0.9 vs. 1.6±1.0) too. Data are shown in **Table 3**.

Table 3
Ovarian function according to the numbers of surgery for endometrioma

	Patients with unilateral endometrioma (n=36)			Patients with bilateral endometrioma (n=10)		
	pre-intervention	post-intervention	P-value	pre-intervention	post-intervention	P-value
AFC	7.2±2.6	6.0±3.5	ns	6.6±2.3	4.4±2.5	ns
FSH (mU/ml)	7.5±2.5	8.5±5.3	ns	9.9±1.7	12.1±3.2	ns
AMH (ng/ml)	1.9±0.9	1.6±1.0	ns	1.6±1.3	1.0±1.3	ns

In the third group, we made a comparison between first intervention for endometrioma vs. intervention for recurrence. Our data showed a decidedly greater reduction in the ovarian reserve in patients after the second endometrioma excision operation: AFC and AMH values were

particularly compromised (6.5±1.7 vs. 3.5±1.2 and 1.2±0.4 vs. 0.5±0.4) and the difference is statistically significant (p<0.05). Also, FSH values before and after reoperation showed a statistically significant difference (9.2±1.6 vs. 12.1±3.5) (p<0.05). Data are shown in **Table 4**.

Table 4
Ovarian function according to the numbers of surgery for endometrioma

	Patients with a negative history of previous intervention (n=36)			Patients after the second endometrioma excision operation (n=10)		
	pre-intervention	post-intervention	P-value	pre-intervention	post-intervention	P-value
AFC	7.5±2.5	5.8±3.1	ns	6.5±1.7	3.5±1.2	<0.05
FSH (mU/ml)	7.7±2.6	9.0±3.2	ns	9.2±1.6	12.1±3.5	<0.05
AMH (ng/ml)	2.0±1.0	1.6±1.1	ns	1.2±0.4	0.5±0.4	<0.05

In the fourth group, we made a comparison between patients undergone surgery with classic forceps (without autoregulation) vs. patient operated with Maryland clamp forceps (with self-regulation). Our data showed an equal hemostatic efficacy for the two instruments, but a lower impact on the ovarian reserve for the Maryland forceps: AFC, FSH, and AMH values before and after surgery, in fact, did not show a statistically significant difference (8.8±2.2 vs. 7.5±2.0, 7.2±2.3 vs. 7.6±3.0 and 2.2±0.8 vs. 2.0±0.7, respectively). Patients who underwent

surgery with the use of classic/traditional bipolar showed, instead, a statistically significant variation (p<0.05) of AFC before the intervention and after the intervention (6.6±2.2 vs. 4.3±2.9). Also, FSH and AMH values were particularly compromised (8.4±2.6 vs. 11.3±5.4, 1.6±1.1 vs. 1.0±1.1) (p<0.05). Otherwise, AMH values, after the intervention, showed a statistically significant difference (p<0.05) between the two groups while, before the intervention, did not show a statistically significant variation between them. Data are shown in **Table 5**.

Table 5
Ovarian function according to the kind of bipolar forcep

	classic/traditional bipolar (n = 30)			Maryland clamp (n=16)		
	pre-intervention	post-intervention	P-value	pre-intervention	post-intervention	P-value
AFC	6.6±2.2	4.3±2.9	<0.05	8.8±2.2	7.5±2.0	ns
FSH (mU/ml)	8.4±2.6	11.3±5.4	<0.05	7.2±2.3	7.6±3.0	ns
AMH (ng/ml)	1.6±1.1	1.0±1.1	<0.05	2.2±0.8	2.0±0.7	ns

DISCUSSION

The effect of the endometrioma on women's fertility is still debated and controversial, and the approach in the reproductive age patient should be conservative^(2,32-35). Since the surgical removal of the endometrioma capsule is potentially associated with damage to the ovarian function, and therefore can further negatively impact the ovarian reserve of these patients, it is essential to evaluate the factors that may affect the outcome of surgical therapy in the risk terms for residual ovarian function^(21,36). Our study has highlighted the importance of the age of the patient as a predictor of post-operative ovarian function: patients under the age of 35, in fact, responded much better to surgical therapy and ovarian reserve seems less damaged by surgery than in older patients. This is in line with the evidence that the ovary is involved in a physiological aging process after the age of 35 and therefore more susceptible to damage in case of invasive therapies⁽³⁷⁻³⁹⁾. The bilaterality of the cyst or in any case the recurrence had a significant impact on the post-surgical ovarian reserve, reducing the possibility of successful IVF techniques. On the contrary, when the cyst is unilateral or in cases when is the first diagnosis of endometrioma, the ovarian reserve appeared less affected by the intervention. As proposed by other Authors, it is conceivable that the contralateral ovary could partially compensate the anatomic-functional damage suffered by the other ovary and, although the ovarian reserve is worse, it is not to be considered completely compromised⁽⁴⁰⁻⁴¹⁾. Instead, in the case of patients suffering from bilateral endometrioma, the ovarian reserve appeared from the pre-intervention basal control compromised by the presence of cysts and further damaged by the surgical insult. It is therefore desirable in these cases, as in relapses of endometrioma, an accurate evaluation and counseling of patients about the risks and

benefits of the intervention, concerning the potential ovarian damage connected and the possibility of bilateral early ovarian failure⁽⁴²⁻⁴³⁾. Several studies have been conducted to investigate the causes of frequent recurrences of the endometrioma: it had been seen that they are mostly related to the surgical technique, greater for the fenestration vs. excision of the cyst, and to the experience of the surgeon⁽⁴⁴⁻⁴⁵⁾. However, our data showed a decidedly greater reduction in the ovarian reserve in patients undergoing surgery for recurrence of endometrioma: AFC and AMH values were particularly compromised, parameters that are directly related to each other. In any case, even for this type of patients with recurrent endometrioma, accurate counseling is necessary in relation to two fundamental parameters: the risk faced by the patient in terms of significant reduction of ovarian function, up to an early menopause and, on the other hand, the possible presence of malignant degeneration which in any case cannot be excluded except by anatomic-pathological examination^(43,46-48). As is known, technological evolution has led to the development of more efficient instruments, on the one hand, in terms of coagulation effect and, on the other, less invasive for the distance thermal effect. Our data showed an equal hemostatic efficacy for the two instruments, but a lower impact on the ovarian reserve for the Maryland forceps ($p < 0.05$). Moreover, while our data were consistent with those reported in the literature about the post-intervention ovarian reserve regarding the first three groups of patients, for the latter group IV our study was innovative in comparing patients and their ovarian response based on a parameter that had not been taken into account so far⁽⁴⁹⁻⁵⁰⁾. However, this study had some limitations. The choice of classic bipolar forceps as an alternative to BiCision did not consider the variables that

distinguished the various groups. Furthermore, this was a retrospective analysis, and we did not consider the long-term effects on fertility outcome. In conclusion, preoperative ovarian reserve status should be studied in women performing ovarian cystectomy, especially if in fertile age. However, more studies with a more extended follow-up period are required to

understand the effects of different methods of hemostasis on the ovarian reserve and also on fertility outcome.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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