

Ovarian Endometrioma Surgery - How to Safeguard the Follicular Reserve

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Abstract

Ovarian endometrioma is a particular anatomopathological entity in the context of endometriotic pathology. The ovary is the organ most frequently affected by endometriosis and in 30% of cases, the pathology is bilateral. The effect of endometriosis on fertility is varied; however, women with severe endometriosis and the presence of endometriomas appear to have significantly lower pregnancy rates, also following IVF treatment, when compared with women with severe endometriosis but without endometriomas. Surgical treatment is indicated if the endometrioma becomes symptomatic and increases in size despite medical therapy, and in cases of related infertility. However, endometrioma surgery can reduce the follicular reserve either through stripping that does not take into account the correct cleavage plan and involves an exaggerated “traction-counter traction”, or with an indiscriminate electro-hemostasis or, with a too narrow suture that causes ischemia. In consideration of this important issues, we have organized a surgical-excision technique that tries to safeguard as much as possible the follicular reserve of the ovary affected by endometriosis.

Keywords: Ovarian Endometriosis – Laparoscopic Surgery – Follicular Reserve

Introduction

Endometriosis is defined by the presence of a tissue similar to uterine endometrium that is located in places other than physiologically appropriate. These endometrial heterotopic islets contain glands and stroma and are functionally capable of responding to exogenous, endogenous, or local hormonal stimuli. The clinical and social impact of the disease is particularly high. Suffice it to say that, to date, an estimated 170 million women worldwide suffer from endometriosis.

Endometriosis occurs in four different entities [1]:

- Superficial peritoneal endometriosis
- Ovarian endometriosis (endometrioma)
- Deep Infiltrating Endometriosis DIE
- Adenomyosis

Each with specific characteristics.

Pathogenesis of ovarian endometriotic cysts.

It is controversial

Brosens defines the endometrioma as an ‘extraovarian pseudo-cyst’ because the majority of these lesions are extra-ovarian, and the wall of the cyst is lined by gonadal cortex [2]. Hughesdon suggests that endometriomas are the result of progressive invagination and duplication of the ovarian cortex, secondary to adhesion of the gonad to the pelvic sidewall.

At odds with the previous theory, Nisolle and Donnez hypothesized that the pathogenesis of endometriotic cysts is different from that of peritoneal implants, as the former do not derive from regurgitated endometrium but, rather, from invagination of the superficial ovarian coelomic epithelium, which subsequently undergoes metaplasia in typical glandular epithelium and stroma [3].

Another theory, also supported by Vercellini, originates from the evidence that often the fluid content in the endometriomas is formed by the accumulation of menstrual debris [4]. However, if this is true, the “chocolate” fluid would have to be found in all endometriotic lesions, while it is specific to ovarian disease. Consequently, a relationship between ovulation and endometriomas seems possible, since both are exclusive to ovarian pathophysiology. In fact, a possible alternative source of “trapped” blood is a cystic corpus luteum that develops in an ovarian cortex adhering to the pelvic wall.

The Surgery

If it is true that: to surgically remove or not to remove an endometrioma for the best fertility outcome is a key question without a clear answer, we must try to give an answer and do it by asking three key questions: Why do I perform the surgery? When do I perform the surgery? How do I perform the surgery?

First question: WHY do I perform the surgery?

The endometrioma transforms the macro- and microenvironment in the ovary to a highly inflammatory one. The endometriotic tissue may secrete a number of inflammatory products that can activate

specific pathways in the follicular cells, until a premature follicular development and accelerated atresia [4, 5].

The Donnez Group had shown a significant reduction in the number of primitive follicles in the cortical stroma adjacent to the endometrioma and, after two years, the same group formulated the “burnout hypothesis” [6, 7]. The formation of endometrioma may cause focal inflammation in the ovarian cortex. This inflammation could result in massive fibrosis and loss of cortex-specific stroma that maintains follicular nests. Focal loss of follicular density may be associated with a dysregulated folliculogenesis that results in burnout of the stockpile of dormant follicles.

Muzii’s study also tells us that Anti-Muellerian Hormone levels in the presence of an endometrioma are lower than in a healthy ovary [8]. A recent study done in Germany by Nicolaus indicates that endometriosis reduces the “follicular output rate” and the number of metaphase-II oocytes after controlled ovarian hyperstimulation independently of women’s age, antral follicle count and anti-Müllerian hormone [9].

From this data it is clear that endometrioma can damage the follicular reserve, even if many authors disagree [10, 11]. But we also know that with surgery, dysmenorrhea and dyspareunia decrease and sometimes serious complications are avoided:

- Risk of rupture of the endometrioma and/or the development of a pelvic abscess
- Missing an occult early-stage malignancy
- Difficulties during oocyte retrieval
- Follicular fluid contamination with endometrioma content
- Progression of endometriosis [12, 13].

Second question: WHEN do I perform the surgery?

Some Authors and many guidelines indicate that in the presence of pelvic pain or infertility it is necessary to undergo surgery for the endometrioma which has a diameter equal to or greater than 3 to 4 cm. ESHRE itself in 2017 does not limit the size of the endometrioma and reiterates what was indicated in 2014, giving only information on the type of surgery used by the various reference centers [14-19].

The article by Sato and Coll. suggests that it is useful to intervene before the mesosalpinx are affected by endometriosis: the study in fact shows that the number of pre-surgical antral follicles is much lower compared to the number of antral follicles without involving the mesosalpinx [20].

ESHRE 2014, NICE 2017 and the Guidelines of the Italian Society of Gynecology and Obstetrics of 2018 show that surgical intervention will be performed in case of:

- patients with painful symptoms resistant to medical therapy
- contraindications or refusal of medical therapy
- severe organ impairment or damage as in case of late ovarian cysts or intestinal or urinary tract obstruction
- ovarian cysts suspected of malignancy
- Infertility

But there is another big problem: what does surgery, however correctly performed, determine on the ovary? In 2002 Muzii and Coll [20-22]. already shown that removing an endometrioma also removed healthy ovarian tissue in 54% of cases, but this happened much less when removing cysts of another nature [23]. The amount

of healthy ovarian tissue is related to the severity of the pathology, probably due to the presence of an important adhesion-syndrome secondary to the chronic inflammatory state [24]. Removal of healthy tissue can lead to a 50% reduction in ovarian volume [25]. Furthermore, Roman has shown that the loss of healthy tissue is related to the size of the endometrioma, with a maximum of surgical damage when the diameter of the cyst is equal to or greater than 7 cm [26].

In this regard, before operating large endometriomas, progestinic therapy could be useful to reduce the size of the endometrioma by up to 70% [27]. At the end of this chapter, it should be noted how important it is to try to avoid relapses, because second surgery can damage the residual ovary even more seriously [28].

Third and biggest question: “HOW” to perform surgery?

It is now established that the best and the most effective surgical approach is definitely the laparoscopic one [18]. It is necessary to reiterate with Somigliana e Coll, how important it is to use surgery that respects the ovarian reserve, reduces the formation of adhesions and that tries to reduce the recurrence rate of the endometrioma. Four studies on a total of 507 patients conclude that coagulation or laser vaporization significantly increased the risk of cyst recurrence compared to excision, and that cystectomy increased the cumulative pregnancy rate [29, 30]. These results are also confirmed by Cochrane which emphasizes above all the possibility of improving fertility of women suffering from ovarian endometriosis and who were previously sub fertile [31]. We will subsequently deal with the problem about surgical excision, because these premises contrast with the fact that in the various Reference Centers the most frequent surgical technique is ablation.

Ablation

Donnez proposes a “combined” technique: an initial stripping with resection of the cyst near the ovarian hilum where an ablative technique is performed [32]. Donnez himself then proposes the “three-stage procedure”, that provides for a first laparoscopy with endometrioma drainage, a medical treatment with GnRH analogs and a second laparoscopy with laser-vaporization [33]. The “plasma-energy” used by Roman allows the ablation of endometrial tissue with minimal damage to the ovarian parenchyma and is useful in women where the risk of worsening the ovarian reserve is very high [34].

In recent years, laser-vaporization is being used in the San Raffaele Hospital in Milan. This technique provides optimal respect for healthy ovarian tissue, because the vaporization depth can be standardized to 0.4-0.6 mm, to stop at the peri-cystic fibrous area. Compared to stripping, the reported data confirms a greater respect of the follicular reserve, evaluated with the antral follicle count [35]. Some authors reported good results with ultrasound-guided ethanol sclerotherapy [36]. In Policlinico Gemelli in Rome, ethanol sclerotherapy is performed in laparoscopy.

Excision/stripping

Let’s go back to what was stated at the beginning of this chapter: the excision technique.

Because if it’s true that the comparison between the excision with stripping and the vaporization or coagulation techniques represents the main point of debate on what is the best procedure to remove

ovarian endometrioma, it's also true that the excision technique is associated with a higher pregnancy rate and a lower rate of recurrence [19, 29].

It must be said that the stripping technique may determine severe injury to the ovarian reserve and that there is no doubt that this surgical technique is to be improved [37]. Gurkan Uncu and Coll. indicate the various steps that are foreseen by the excision of the endometrioma. There are many technical problems to be addressed in the excision of the endometrioma, but the most important are:

- the correct cleavage plan must be identified
- stripping must be mild
- hemostasis must be targeted and used as little as possible .

Some studies compare the possible ovarian damage secondary to electro hemostasis versus suture and show that the suture is definitely safer, even if a too tight suture can cause ischemic damage [38, 39]. An exaggerated and sometimes senseless electrohemostasis (especially if performed in correspondence of the ovarian hileus) causes irreversible tissue damage with frequent total loss of the follicular reserve [40].

Our technique

For our experience it was particularly important the article of Taejong Song and Coll, in which the authors performed the use of a hemostatic sealant with less damage on the ovarian reserve rather than the use of bipolar coagulation [41].

So we thought this could be the first step in trying to develop a surgical technique to really minimize the ovarian damage caused by stripping. WE also thought about the many Italian hospitals that, like us, do not have plasma energy or laser equipment. It was necessary to put together sporadic and disjointed indications of some colleagues who had my own problem at heart: "operating the endometriotic cyst and safeguarding the ovary".

Admission protocol

Together with gynecologists from our department, I created this protocol:

All women with ovarian endometriosis, who have a "desire for pregnancy", are admitted, therefore regardless of age and parity. These patients must have a documented ultrasound of mono- or bilateral ovarian endometrioma with diameter equal to or greater than 4 cm.

At admission the following is performed:

Clinical evaluation with vaginal and / or rectal exploration

Transvaginal Ultrasound for the study of:

- Morphology and volume of both ovaries - endometrioma measurement with 3 diameters
- Myometrial ecostructure and endometrial pattern
- Rectovaginal septum and Douglas pouch with sliding sign
- Bladder-uterine septum with sliding sign

In case of endometrioma fixation on the pelvic wall: renal ultrasound.

In case of suspected multifocality of endometriosis or association with DIE: Nuclear Magnetic Resonance

Surgical technique

After positioning the bladder catheter and uterine manipulator, four trocars were inserted like in the classic laparoscopic gynecological surgery.

- Firstly, we performed pelvic adhesiolysis with excision of loose adhesions that are sent for histological examination (the presence of fibroblasts can lead to suspicion of active endometriosis).
 - Then, we open and drain the endometrioma, which often occurs spontaneously during mobilization maneuvers,
 - Meticulous identification of the correct cleavage plan.
 - Detachment (no stripping) with mono or bipolar coagulation of the vascular connections as close as possible to the capsule of the cyst and not on the ovarian parenchyma.
 - Application of one of two hemostatic factors witch act in same way: a bovine gelatin-thrombin matrix and an absorbable hemostatic powder derived from purified plant starch.
 - Place wet gauze on the cyst-bed for exactly 2 minutes.
 - Hemostasis control, which is very often satisfactory: possible targeted bipolar coagulation by water-test.
 - Transcutaneous ovarian suspension. I put a monofilament stitch with a double purpose: bringing the margins of the cystic bed closer together and bringing the ovary out of the pelvis (the ovary must be remain outside the pelvis for 48 hours).
 - Peritonectomy of the area of adhesion of the endometrioma to the pelvis (often the histological examination detects endometriotic implants which could affect the ureteral course) and excision of all suspicious areas due to the presence of endometriotic foci.
 - Pelvic washing with Lactated Ringer's solution. Another 250 ml are left in the pelvic cavity to avoid adhesions.
- 48 hours after surgery, we discharge the patients - after removing the wires of the ovarian suspension - with anti-inflammatory therapy for 10 or 15 days and hormonal therapy (progestinic or estro-progestinic) for 6 months.

Follow-up

Three months from surgery, we perform the trans-vaginal ultrasound for Antral Follicle Count on the operated ovary. We perform AFC on both ovaries only in women with immediate pregnancy desire to assess the need for referral to PMA centers. We know that Antral Follicle Count and Anti-Mullerian Hormone are parameters that are widely used in the prediction of ovarian functional reserve, but for our evaluation, we have chosen the Antral Follicle Count. We have also confirmed the correctness of our choice from the study published last year by Zeynep Ozturk Inal which concludes by claiming that no perfect marker exists in the evaluation of ovarian reserve and response, but that there is a strong assumption that AFC is a better reflection of ovarian response in women with endometrioma [42].

Our cases until thirty first of December 2019:

We performed our surgery technique on 46 patients

The age of the women was between 21 and 39

In 11 cases, the endometrioma was in the right ovary and in 26 cases in the left ovary. In 9 women the endometrioma was bilateral. The endometrioma diameter was between 4.3 to 8.2 cm with average diameter: 4.7 cm

We found superficial implants on the Douglas Pouch surface in 36 women and superficial implants on the bladder-uterine fold in 28 cases.

In 8 cases, we found the Fallopian tubes involvement and in 12 cases we removed nodules in the utero-sacral ligaments and / or in the round ones.

In 9 women there is an association of DIE in the anterior or posterior compartment?

Home therapy:

Dienogest to 9 women, Norethisterone acetate to 11, Desogestrel to 5 and estrogenic to 10 women. No therapy was prescribed to 11 patients due to their desire for pregnancy, patients completed the 3-month follow-up [42]. AFC in the 3rd month from 3 to 6, with 4 as the average value.

Conclusions

We are aware that we didn't create anything extraordinary, but we are also sure that our ovarian endometrioma surgery achieves the intended purpose: to safeguard the follicular reserve of an ovary already damaged by endometriosis. The safeguard is possible thanks to cystectomy with disconnecting or mild stripping, vascular connection coagulation directly on the cystic wall during cystectomy and, especially, to the use of hemostatic sealant or powder that allows us to remove the thermal damage of healthy part of the ovary.

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