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Review Article

# Surgical Management of Endometriomas: The Link Between Pathophysiology and Technique

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## Abstract

Endometriosis is a common condition that affects 6-10% of reproductive age women. The surgical management may be excisional versus ablative surgery. Cystectomies remain first line of treatment as they provide better pain relief, reduced recurrence rates, higher spontaneous pregnancy rates and comparable IVF pregnancy rates when compared to ablative procedures. Stripping the cyst wall damages part of the ovarian tissue, owing to dense extensive adhesions between the pseudocyst formed by invagination and the normal ovarian tissue. Special attention is required during the dissection of the surface of the hilum ovarii. Another important aspect of endometrioma surgery is achieving hemostasis that might be difficult to achieve after the stripping operation and lysis of adhesions. There is growing attention as to whether the hemostasis of bipolar coagulation and ultrasound scalpel will affect the ovarian reserve through thermal damage. The best method to achieve good hemostasis is to optimize dissection by identifying the correct plane of cleavage during surgery. Suturing is effective and less damaging to the ovary and the ovarian reserve in expert hands when compared to the use of other methods. In this literature review we discuss surgical approach to treatment of endometriomas and their impact on ovarian reserve.

**Keywords:** Ablative Technique; Cystectomy; Endometrioma; Hemostasis; Stripping

## Introduction

Endometriosis is a common condition that affects 6-10% of reproductive age women [1] and is defined as presence of viable, estrogen sensitive, endometrial like glands and stroma outside the uterus associated with inflammatory response. Endometriosis is characterized by three specific phenotypes: peritoneal endometriosis, ovarian endometrioma and Deeply Infiltrating Endometriosis (DIE). Endometriomas can be found in 17-44% of women with endometriosis [2]. According to widely used American Society for reproductive medicine Revised classification of endometriosis endometrioma of 1cms or greater defines stage III disease or moderate to severe endometriosis. The most common presentation is pelvic pain and subfertility [3]. Management for endometriomas can be medical and/or surgical. The surgical management may be excisional versus ablative surgery. The objective of this literature review is to summarize the surgical approach to endometriomas and its' implications on ovarian function.

## Pathophysiology

Since first description of endometriosis by Von Rokitansky in 1860 several theories for pathogenesis of endometriosis have been described in literature but the most accepted one is the transplantation theory proposed by Sampson in 1927 which describes endometriosis results from regurgitation of endometrial cells by the fallopian tubes during menstruation [4]. Recent evidence supports the presence of endometrial stem/progenitor cells in menstrual blood is responsible for pathogenesis of endometriosis. The theory of endometrial stem cells or transient amplifying progenitor cells claims that circulating stem cells originating from bone marrow or from basal layer of endometrium could differentiate into endometriotic tissue at different anatomical sites [5]. Progesterone resistant endometrial mesenchymal stem cells are colonogenic and can differentiate to various lineages and have been proposed to be progenitors of endometrial stromal fibroblast -the key cells in pathogenesis of endometriosis [6]. The pathogenesis of ovarian endometriosis has been controversial and is different from other forms of endometriosis. Sampson described that perforation of chocolate cyst led to spillage of cyst contents and spread of peritoneal endometriosis [4]. Hughesdon [7] described that inside of the chocolate cyst is the outside of ovary as ovarian endometriomas arise from active invagination of ectopic endometrium into ovary .Latter studies suggested that the adhesions were not the result but the cause of endometriosis. They described that 90% of typical endometriomas were formed by invagination of the cortex after accumulation of menstrual debris from bleeding of endometrial implants which were located on the ovarian surface [7-9] (Figure 1).

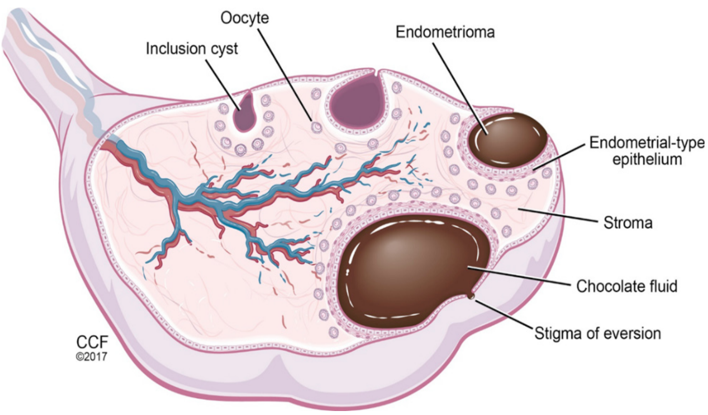


**Figure 1:** Pathogenesis of Endometriosis.

Another proposed theory is that celomic metaplasia of invaginated inclusions could be responsible for this pathogenesis similar to theory suggesting rise of ovarian cancer from cells at fimbrial end of fallopian tube [10]. The pelvic mesothelium has a high metaplastic potential [11]. Nisolle, et al. [11] described that the epithelium covering the ovary can invaginate into the ovarian cortex and under the influence of unknown growth factors undergoes metaplasia to form endometriomas. When the mesothelium invaginates the follicles located at the site of invagination are also pushed concomitantly with the mesothelium. Thus, the internal lining of endometrioma histologically represents glandular epithelium, endometrial glands and stroma and there is an interface of fibrosis between the glandular epithelium and the underlying cortex. Hence careful removal of endometriomas is necessary as removal of cyst wall might remove normal ovarian tissue and affect future ovarian reserve [12-14].

The technique of vaporization involves concentrating on the inner cyst wall and leaving the fibrotic capsule surrounding the endometrioma so as to avoid removal of oocytes. Muizii et al. [15] studied the histologic nature of endometrioma wall to determine the appropriate surgical management and stated that 60% of the inner surface of cyst wall was covered with endometrial tissue and the mean value of maximal depth of penetration of endometrial tissue in the cyst wall was 0.1 to 2.0mm (mean depth of 0.6mm). The penetration of endometrial tissue into the cyst capsule was greater when thickness of wall was more as such both techniques of superficial vaporization of inner surface up to 0.2mm with KTP laser and low power bipolar coagulation of endometrial implants would be insufficient to treat endometrioma completely. Muizii et al. in their study stated that in specimens obtained during cyst excision via stripping technique the endometriotic tissue did not reach the deepest portion of excised specimen and margins clear of pathology were always found. Hence concluding that cyst excision and stripping of wall would provide more complete removal of pathology. As the plane of cleavage in stripping procedure runs through the interface between the fibrotic capsule and the normal ovarian tissue they found that when endometriomas penetrate deeper into the cyst capsule(>1mm), the thickness of excised cyst is also greater in that part of specimen which yields more complete removal of pathology.

## Surgical Management of Endometriomas

Different surgical techniques have been proposed for the treatment of endometriomas and have been surrounded with controversies. The laparoscopic approach is favored over laparotomy with advantages of shorter hospital stay, faster patient recovery and reduced health care costs. The surgical management varies from excision of cyst capsule or drainage of cyst with ablation of cyst wall or three step approach [16,17] (includes first step of operative laparoscopy with drainage of endometrioma followed by GnRH therapy to shrink the cyst followed by second look laparoscopy and ablation of cyst wall) . The aim of successful management is to have the maximum removal of endometrioma to alleviate pain, improve fertility, exclude malignancy and to prevent recurrence- with minimal damage to ovarian function. As ovarian endometrioma presenting with severe pain are found to be associated with DIE, proper preoperative imaging is required to evaluate the deep nodules and to plan the appropriate surgical technique [3]. All these procedures differ in terms of recurrence of symptoms, effect on ovarian reserve, impact on IVF outcomes and spontaneous pregnancy rates.

## Ovarian Cystectomy

Laparoscopic cystectomy is most commonly used initial treatment of endometriomas. This surgical technique involves mobilization of cyst with lysis of adhesions. Once mobilized the cyst is grasped at the cortex with forceps and then incised at the antimesenteric surface sparing the hilus using an energy form such as bipolar energy, laser, harmonic energy or scissors without energy. The incision is extended, and the cyst wall is separated from the ovarian stroma either bluntly with traction and counter traction on the cyst wall or in some cases via hydroids section with saline (Figure 2).

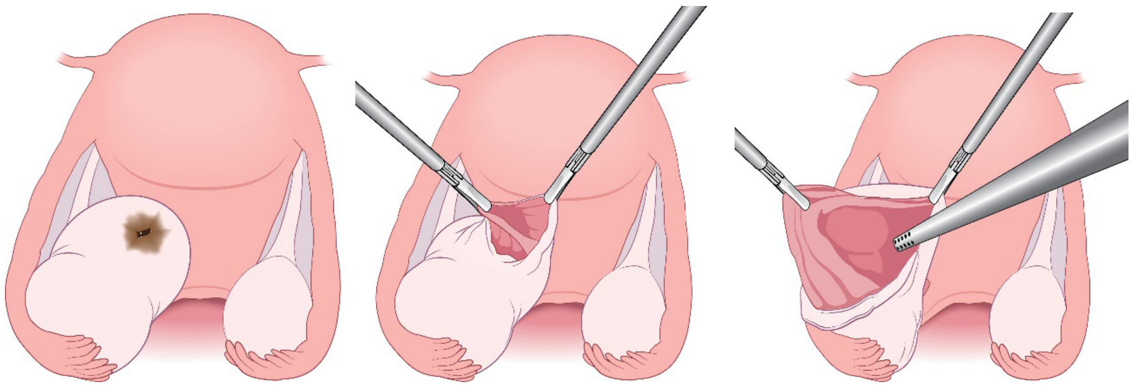

**Figure 2:** Technique of laparoscopic ovarian cystectomy.

An important part of ovarian cystectomy would thus be to differentiate normal ovarian tissue from the cyst wall by paying attention to their color distinction and contour of the capsule wall. Normal ovarian tissue appears as pink-white compared with gray or gray-yellow color of the capsule wall. The plane of cleavage during the stripping procedure thus follows interface between fibrotic capsule and normal ovarian tissue. This area is firmly adherent to the cortex. Care must be taken not apply too much tension as normal ovarian tissue can be removed. and never to dissect through pathology to ensure complete removal.

Spillage is common during dissection and can be easily lavaged. After stripping the cyst wall from the normal ovarian tissue, the bed of the cyst is inspected carefully for bleeding and good hemostasis is achieved with bipolar coagulation, hemostatic agents or suturing. The endometrioma is then removed with endobag and sent for pathology. With literature supporting risk of malignancy with endometriomas [18] ,removal of specimen in containment bag reduces the chances of possible malignancy [19] and port site implantation. Another important aspect of laparoscopic procedure is to improve fertility by restoring normal anatomy with adequate adhesiolysis but importance should be given to preserve the blood supply to the ovary. Saito et al. [20] evaluated the anatomical condition of mesosalpinx during laparoscopic cystectomies in 53 patients and classified them into involved or intact mesosalpinx depending on whether the mesosalpinx that is responsible for blood supply to the surgery was involved or not prior to cystectomy and measured the effect on decrease in ovarian reserve by comparing AMH levels pre-operatively and post operatively. They found that pre-existing mesosalpinx disturbance in combination with adhesiolysis may be involved in medium and long-term decrease in ovarian reserve after laparoscopic cystectomy. As such care should be taken during the lysis of adhesions during cystectomy to minimize the disruption of mesosalpinx especially in cases where surgery indication for surgery is infertility.

Muzii et al. [21] described that recognizable ovarian tissue was inadvertently excised together with the endometriotic cyst wall in most cases during stripping for endometrioma excision. Close to the ovarian hilus there is an absence of a clear plane of cleavage, hence the ovarian tissue removed inadvertently with the endometrioma wall contained primordial, primary, and secondary follicles in 69% of cases. Away from the hilus, no follicles or only primordial follicles were found in 60% of specimens. When compared to ablative procedures studies have shown that cystectomy has higher success rate [22,23]. Hart et al. performed meta-analysis comparing short term and long-term outcomes of excisional versus ablative procedure for endometriomas of 3cms or greater and looked at 2 RCT with 164 patients and concluded that the relative risk of recurrence of dyspareunia, dysmenorrhea and non-menstrual pelvic pain were lower in group that underwent cystectomy as compared to the patients in ablative group [24]. Studies have also looked at effect of excisional surgery on future fertility at 1year and 2years follow up period in women with subfertility and demonstrated that laparoscopic cystectomy and excision of cyst wall is associated with increased spontaneous pregnancy rates in patients with subfertility as compared to the ablation techniques [22,23]. As per Cochrane review subsequent spontaneous conception rates are higher after excisional surgery as compared to ablative procedures, OR-5.21 (95% CI: 2.04-13.29) [24].

For pathological cyst like endometriomas which need surgical intervention an important concern is effect of surgery on ovarian reserve. Ovarian reserve is the reproductive potential of any individual at certain point of time and is usually determined by the number of resting primordial follicles than grow up to develop primary, antral and eventually ovulatory follicles. Markers of ovarian reserve used in various studies include anti-mullerian hormone, antral follicle count, ovarian volume and ovarian flow and clinical markers like response to ovarian stimulation and pregnancy rates (Table 1).

| Name of study | Type of study | Inclusion criteria | Study Size | Cyst characteristics | Type of Surgery | Outcomes |
|---|---|---|---|---|---|---|
| Roman, et al. 2014 [25] | RCT | Age 18-45yrs, no prior ovarian surgery, Non-pregnant, Surgical treatment required for pain or Infertility, Unilateral endometrioma >3cms | 22 | Unilateral endometriomas, mean diameter >3cms | Plasma energy ablation | AMH at 3mo post-op significant decreased |
| Ferrero, et al. 2012 [26] | RCT | Reproductive age, Bilateral endometriomas >3cms, Infertility for >1year with male partner with normal semen analysis, No prior ovarian surgery, No h/o PCOS, No known endocrine disorder | 100 | Bilateral endometriomas, mean diameter 7cms | LC and suturing versus bipolar | AMH significantly dropped in both groups at 3,6 and 12mo pre- v/s post-op. AMH drop post-op between the 2 groups not significant. |
| Tsolakidis, et al. 2010 [16] | RCT | Age 22-40yrs, Endometrioma >3cms, BMI<30, No prior ovarian surgery, No prior hormone therapy | 20 | Not reported, mean diameter >3cms | Three stage technique vs cystectomy | Less reduction in AFC and AMH with three step techniques |
| Donnez, et al. 2010 [27] | Prospective | Reproductive age women, Unilateral endometrioma >3cms | 52 | Unilateral cyst, mean diameter 5.2cms | Partial cystectomy and laser vaporization | AFC and OV post-op no difference between groups. |
| Var, et al. 2011[28] | RCT | Age 20-35 yrs., Bilateral endometrioma, Similar endometrioma sizes, Endometriomas between 4 and 6 cm | 48 | Bilateral cyst, mean diameter 4-6cms | Cystectomy versus bipolar coagulation | Lower AFC and OV in cystectomy v/s bipolar coagulation. |
| Hwu T, et al. 2011 [29] | REC | Age 22- 46-yr, Infertility with or without ovarian endometrioma | 1642 | Unilateral and bilateral, mean diameter not reported | LC | Both post cystectomy patient and patients with endometrioma unoperated had lower AMH levels |
| AFC- Antral Follicle Count, AMH- Anti-mullerian Hormone, LC- Laparoscopic Cystectomy, OV-Ovarian Volume, RCT- Randomized Controlled Trial, REC-Retrospective Comparative, Yrs.- Years. | | | | | | |

**Table 1:** Effect of endometrioma surgery on ovarian reserve.

Several mechanisms have been proposed for decreased ovarian reserve post-cystectomy. As endometrioma is a pseudocyst with surrounding fibrous tissue layer has no proper plane of cleavage, cystectomy always removes some normal ovarian tissue [12]. Cystectomy specimens have revealed that ovarian tissue was detected in 40% of endometrioma specimens with direct correlation between cyst size and amount of ovarian tissue lost [12]. Greater the cyst burden greater is the impact of surgery on ovarian reserve. Another important factor may be presence of bilateral endometriomas. A prospective cohort study demonstrated statistically significant decrease in AMH at 1month after cystectomy or ablative procedure as compared to pre-operative AMH levels and also decline was even more in the cystectomy group when the surgery involved removal of bilateral endometriomas [30]. Goodman et al. conducted study on bilateral endometriomas and found that endometrioma cyst size and bilateral cyst at presentation result in significantly greater decline in AMH levels postoperatively [13]. Studies have demonstrated a significant fall in AMH levels 3months post-operatively when cyst removed was 5cms or greater in size (30) [14]. Ergun et al. [31] studied the effect of cyst size on ovarian reserve during cystectomy.

The study demonstrated that low AMH levels were seen pre-operatively and postoperatively in patients having endometriomas 7cms or greater when compared to those with cyst size less than 7cms. However, no comparison was made in pre-and post-operative values in each group as such no comments could be made on impact of cyst size on impact of surgery on AMH values.

Studies have demonstrated recovery of AMH levels to 65% of preoperative value at 3months after cystectomy [32]. However, some studies report slower return of AMH levels postoperatively when followed up to 1-year post-op [13-24, 30-33]. This could be explained by transient effect of ischemic and inflammatory insult on ovary followed by recovery by phenomenon of follicular cohort rearrangement that occurs as compensatory mechanism to the ovarian damage [32] with some permanent damage which could be very important in patients with low baseline reserve As AMH levels do not give a qualitative measure of ovarian reserve clinical response to ovarian hyper stimulation of ovaries treated with cystectomy or ablation versus normal ovaries have been studied. While several retrospective studies have shown diminished response of ovaries post cystectomy to gonadotrophins [34,35] a RCT in 2006 on 81 patients with endometriomas who were operated via cystectomy or fenestration and coagulation and underwent ovulation induction with single method found that there was no difference in response of diseased ovaries treated with cystectomy or fenestration compared to response of contralateral normal ovaries [36]. Cystectomy does not appear to improve IVF outcomes as suggested in recent studies including a Cochrane review [37,38]. A systematic review [39] reported similar live birth (OR 0.9; 95% CI 0.63-1.28), clinical pregnancy (OR 0.97; 95% CI 0.78-1.2) and miscarriage rates (OR 1.32; 95% CI 0.66-2.65) following IVF treatment in women with surgically-treated endometriomas compared to those with intact endometriomas. While the number of oocytes retrieved, and the cancellation rates were comparable, women with a surgically-treated endometrioma had a lower antral follicle count and required higher doses of gonadotrophins for ovarian stimulation. As such surgical treatment does not significantly improve pregnancy outcomes in patients who plan to take IVF/ICSI treatment [39]. Pregnancy rates after controlled ovarian hyperstimulation when comparing excisional surgery and ablative surgery show no difference as per recent Cochrane review, OR 1.4(95% CI-0.47-4.15) [23]. The European society of human reproduction and embryology guidelines (2014) states that there is not enough evidence supporting specific surgical management for infertility patients planning to undergo Assisted Reproductive technology.

American society of reproductive medicine [40] also states that in women with asymptomatic endometriomas who are undergoing IVF/ICSI there is insufficient evidence to support removal of endometriomas to improve IVF outcomes and there have been no studies evaluating impact of size of endometriomas on outcomes. However, ASRM suggests risks versus benefits should be discussed with the patient in case of large endometriomas (>4cms) as surgical removal might be necessary for histological confirmation, to improve access to follicles during oocyte retrieval and possibly improve ovarian response. On the other hand, extensive surgery might also reduce ovarian reserve and negatively impact response to ovarian stimulation [40] *Loss of ovarian reserve by endometriosis itself or repeated surgeries has led to exploration of role of fertility preservation technologies in patients with endometriomas not trying to attempt pregnancy in near future. Ovarian tissue cryopreservation can be done with healthy cortical tissue inadvertently removed with the capsule or from cortical tissue that's loosely adherent to the ovary after dissection [41].*

## Ablative Treatments

Another approach to treating ovarian endometriomas is ablation or vaporization of endometriotic implants. For small endometriomas <1cms on ovary are vaporized until no further pigmented tissue is visible or follicles with clear fluid are encountered. For larger endometriomas (>4cms) small portion of top of the cyst is excised and all chocolate colored fluid is aspirated followed by completely opening the cyst wall and washing it with irrigation fluid. After washing the cyst is carefully examined grossly to confirm endometrioma and the inner cyst wall is then vaporized till no further pigment seen to destroy the inner mucosal lining of the cyst wall. The vaporization is usually carried out with bipolar electrosurgery which allows quick and easy vaporization. Plasma energy has also been used for ablative procedures where ablation of cyst wall is carried out using plasma jet set in coagulation mode at 10-40 and with a mean distance of 5mm from tip with 1-2seconds exposure time at each site. Roman et al. in their study on 55 women with ovarian endometriomas solely with ablation with plasma energy and found that recurrence and pregnancy rates were comparable to cystectomy and can be important method to spare ovarian parenchyma such as bilateral endometriomas or history of ovarian surgery [25,42,43]. However ablative techniques using plasma jet also cause decrease in AMH levels up to 3months after surgery followed by slow rise in subsequently [38]. Unlike cystectomies ablation techniques do not remove the entire wall hence are associated with higher recurrences at 12months and 60months follow up period as supported by studies [44] and are also associated with lower spontaneous pregnancy rates [30,45].

## Combined Techniques

Three step techniques have also been described in studies for large endometriomas >5-6cms where first at diagnostic laparoscopy the endometrioma cyst is drained and completely opened followed by second step where GnRH therapy is given for 12weeks to decrease the cyst size and then three months later at second look laparoscopy ablation is carried out using $CO_2$ laser or plasma energy [16,17,37]. The GnRH therapy makes cyst wall atrophic and so vaporization is quick with minimal damage to ovarian parenchyma. Patient undergoing three step techniques had better AMH values at 6month follow up and AFC also increased compared to patients undergoing cystectomy alone. However, the study did not focus on infertility patients and does not describe effects on resolution of symptoms or recurrences. Another form of combined technique involves first performing an excisional procedure where cyst wall is opened and stripped from underlying cortex with good hemostasis and while approaching the hilus where more functional tissue is present and plain of cleavage is less visible resection of the dissected tissue is performed that removes around 80-90% of cyst wall (partial cystectomy). And after the first step ablation with $CO_2$ laser or plasma energy is carried out for vaporization of remaining 10-20% of cyst wall. Muzzi et al. [46] in a multicenter RCT with 51 patients with bilateral endometriomas larger than 3cms with each patient serving as their own control compared combined technique (stripping/ablation) to traditional stripping alone and found lower recurrence rates with combined technique but results were not statistically significant, moreover while there was no difference in AFC among two techniques the ovarian volume was significantly reduced after combined technique at 6month follow up.

## Hemostasis During Surgery

One of the reasons for diminished ovarian reserve after ovarian cystectomy is damage suffered by the primordial follicles mainly due to damage to ovarian vasculature and blood supply during hemostatic procedures. Suturing and bipolar electro surgery are two most commonly used and studied methods for hemostasis during ovarian cystectomies however several hemostatic sealants like FloSeal have also been used as alternative methods. Bipolar coagulation is the most common hemostatic method due to the characteristics of convenience and efficiency. However, the best method to achieve good hemostasis is to optimize dissection by identifying the correct plane of cleavage during surgery and performing in plane dissection. Suturing in expert hands allow good hemostasis with minimal ovarian tissue damage. The idea is to reapproximate but not to strangulate the ovarian tissue as suturing under tension can tear ovarian tissue and very tight knots can compromise the ovarian blood supply. Studies have compared the impact of suturing versus cauterization for hemostasis on ovarian reserve (Table 2).

| Author & year | Type of study | Method used | Number of participants | Exclusion Criteria | Inclusion criteria | Age (yr.) | Cyst characteristics and size (cm) | Outcomes |
|---|---|---|---|---|---|---|---|---|
| Ferrero, et al. 2012 [26] | RCT | ES followed by hemostasis with BC 20-30W vs IOS with 2-0 vicryl | BC:50 IOS:50 | Age>40y, Prior ovarian surgery, Prior endometriosis surgery, PCOS, Premature ovarian failure, Endocrine disorders, Uterine malformation, Bilateral tubal occlusion, Suspicion for malignancy, Hormonal theory 4mo before surgery, Desire to use hormonal therapy after surgery | Bilateral endometrioma >3cms, Infertile for >12mo with partner with normal semen analysis | BC:31.9+-5.2 IOS:32.1+-3.7 | Bilateral endometrioma BC:7.4+-2.9, IOS:7.5+-2.4 | AMH and FSH at 3,6 and 12mo Post-op: AMH decreased in both BC & IOS (statistically significant).FSH increased in both BC & IOS. FSH increased more in BC v/s IOS at 3 & 6mo (statistically significant) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Kumakiri, et al. 2012 [47] | Prospective non-randomized | ES followed by IOS v/s BC after stripping with vasopressin prior to stripping | BC with vasopressin before stripping:18 Suturing:20 | Not reported | Reproductive age women with endometrioma | Reproductive age group | Not reported | Time to hemostasis and total blood loss were significantly shorter and less in BC with vasopressin than in IOS (419 ± 207 sec vs. 1,188 ± 541 sec, p < 0.001; 41 ± 13 mL vs. 62 ± 29 mL, p = 0.005). AMH at 3 mo. after surgery significantly decreased (p < 0.001) in both groups. Rate of decline in AMH no significant difference (IOS: 44% ± 28% vs. BC+Vasopressin: 58% ± 24%; p = 0.15). Rate of AMH decline significantly correlated with time required for hemostasis in both groups. |
| Qiong-Zhen, et al. 2014 [48] | RCT | LC performed via stripping without injection (C), stripping with saline injection (S) & stripping with vasopressin injection (VIT) | C: 29 S: 28 VIT: 29 | Not meeting inclusion criteria | Bilateral endometriotic cysts 4.0 to 6.0 cm, 30 to 38 years; Regular menstrual flow (cycle duration of 28-30 days in the 6 months before surgery) No previous surgical treatment of endometriosis; No medical treatment of endometriosis in the previous 9 mo.; No intent to become pregnant for 1 to 2 yrs. after the operation; No endocrine disease. | Mean age C:34.5 S: 34.6 VIT:34.1 | C:5.2 S:5.2 VIT:5.2 | Rate of ovarian tissue in the endometrioma wall specimens, the thickness of the tissue specimens, and the thickness of ovarian tissue inadvertently excised. VIT & S v/s C statistically significant (all p < .001). VIT v/s S (p> .05) Coagulation events VIT (4.4) & S (10.8) v/s C (17.8) significantly lower (p < .01). Coagulation events VIT v/s S statistically lower. FSH 3mo post-op, S v/s VIT higher (p < .05), C v/s S & VIT higher (p < .01). |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Saeki, et al. 2010 [49] | RCT | LC without injection (C) v/s saline injection (S) versus vasopressin injection (VIT) and number of pinpoint bipolar coagulations on ovarian cortex required to achieve hemostasis | C-5 S-5 VIT-5 | Not reported | Single-lobular endometriotic cysts with mean diameter 4.5 to 5.4 cm | C:30±3.1<br>S: 32±5.4<br>VIT:31±2.9 | C:4.76±0.201<br>S:4.92± 0.335<br>VIT:4.79±0.366 | Pinpoint coagulation events VIT v/s C statistically fewer (p = .041). VIT v/s S statistically fewer (p = .041). Time for stripping and hemostasis C:745.0 ± 139.3, S;697.8 ± 127.6 VIT:584.6 ± 110.6 |
| Song, 2015 [50] | RCT | LOS with BC v/s PS with 2.0 V-Loc barbed suture | BC:62; PS:63 | Suspicion for malignancy, Menopausal state, Pregnancy, Lactation, Hormonal treatment in past 3mo, Endocrine disorders | Age 18-39, Ovarian cyst 3-12cms, ASA 1-2, Regular menses | BC:31.2±4.8<br>PS:30.8±5.2 | Unilateral and bilateral cyst<br>BC:6.4±1.6<br>PS:6.8±2.2 | AMH decreased in both groups pre-op vs post-op (statistically significant). AMH 3mo postop BC decreased more than PS (statistically significant). |
| Zhang, et al. 2016 [51] | RCT | OS with BS with 25W v/s US v/s IOS with 2.0 vicryl | BC:69<br>US:69<br>IOS:69 | Prior ovarian surgery, Endocrine disorders, Prior OCP or hormonal therapy, Hysterectomy, Excision of adnexa, ovarian malignancy | Age 18-45 Unilateral or bilateral ovarian endometrioma, Regular menses for last 6mo, | BC:30.9±8.2,<br>US:31.4±8.5,<br>IOS:33.1±7.2 | BC:5.3±2.6<br>US:4.9±2.9<br>IOS:5.3±2.7 | AMH, FSH, AFC and OV compared at 1,3,6 and 12mo. AMH, AFC & OV BC & US v/s IOS decreased significantly at all post op times. FSH levels BC & US v/s IOS increased significantly at all post op times. |
| AFC- Antral Follicle Count, AMH- Anti-Mullerian Hormone, BC- Bipolar Coagulation, C-Control, ES- Excision via stripping, FSH- Follicle Stimulating Hormone, VIT-Vasopressin injection, IOS- Intraovarian Suturing, LC- Laparoscopic cystectomy, LOS- Laparoscopic Ovarian Stripping, OS- Ovarian Stripping, OV- Ovarian Volume, PS- Parenchymal Suturing, RCT- Randomized Controlled Trial, S- Saline, US- Ultrasonic scalpel. | | | | | | | | |

**Table 2:** Comparison of various hemostasis techniques and their impact on ovary.

Peters, et al. [52] in their meta-analysis described improved conservation in AMH levels post-operatively in suturing group compared to bipolar coagulation group and state that these levels drop anywhere from 27-53% in ovaries treated with bipolar coagulation or ultrasonic scalpel. Also, studies have demonstrated a significant decrease in ovarian volume and diameter in the bipolar and ultrasonic scalpel group compared to suturing used for hemostasis [16,53].

Zhang, et al. [51] in their study compared the effects of method used for hemostasis in endometrioma surgery in 207 patients between 18-45yrs of age and randomized them into three groups: bipolar coagulation versus ultrasonic scalpel versus suturing and found that FSH levels at the 1st month, 3rd month, 6th month, and 12th month follow up were higher in bipolar electrocoagulation and ultrasonic scalpel group compared to group which underwent suturing with 3-0 absorbable suture to achieve hemostasis ($p < 0.05$). AMH was significantly lower in groups where energy was used to control bleeding compared to suturing ($p < 0.05$) during the same period. No difference in AFC was observed at the 1st month and 3rd month ($p > 0.05$), whereas at the 6th month and 12th month, AFC in suturing group was higher than the other two groups ($p < 0.05$). PSV (peak systolic velocity) was also significantly lower in the electrocoagulation and ultrasonic scalpel hemostasis compared to suturing (p<0.05) Hemostatic agents that are mixture of flowable gelatin matrix (bovine or porcine) and a human-derived thrombin component for example, FloSeal® (Baxter Healthcare Corporation Fremont, CA 94555, USA) and Surgiflo® (Ethicon Endo-Surgery, part of Johnson & Johnson Company, New Jersey 08876, USA) are also used for hemostasis when suturing or coagulation needs to be avoided for impact on ovarian reserve. FloSeal under direct vision with a laparoscopic applicator is applied on the bleeding sites. Studies comparing use of FloSeal® to bipolar electrocoagulation have shown that FloSeal® yields a shorter, but not statistically significant, time to hemostasis, less blood loss and a lower decrease in postoperative hemoglobin [54]. Another study demonstrated that acute ovarian damage was less common with FloSeal® during the first postoperative month, but the ovarian reserve was replenished in the bipolar electrosurgical coagulation group by the third month [55]. (Table 1) describes the studies that compare the various hemostasis techniques.

Studies have also evaluated the effect of mode of hemostasis on menstrual cycles and future fertility. It has been demonstrated that age <27years, FSH>10IU/L was significantly increased in patients undergoing coagulation with unilateral ovarian cystectomy (bipolar energy-26.5%, ultrasonic scalpel-27.5%, suturing-10.8%) but increase was much more in females with bilateral endometriomas [56]. Ferrero et al. [26] reported pregnancy rates in their study on 100 women with bilateral endometriomas and showed a nonsignificantly different pregnancy rate of 30% in suturing group versus 36% in bipolar cautery group with median time to pregnancy of 5months in both the groups. AMH levels were higher both preoperatively and 3months postoperatively in females who conceived compared to those who did not. Another study demonstrated similar pregnancy rates in patients undergoing in vitro fertilization after ovarian cystectomy and undergoing hemostasis with cauterization versus suturing [57].

## Conclusion

Cystectomies remain first line of treatment for management of ovarian endometriomas as they provide better pain relief, reduced recurrence of cyst, have a higher spontaneous pregnancy rates and comparable IVF pregnancy rates when compared to ablative procedures [58]. Although the pathogenesis of an endometriotic cyst is still controversial, one hypothesis is that endometrioma was formed by progressive invagination of the ovarian cortex after accumulation of menstrual debris originating from the shedding of superficial endometriotic active implants. Stripping the cyst wall will hence inevitably damage part of the ovarian tissue, owing to dense extensive adhesions between the pseudocyst and normal ovarian tissue. The cleavage plane between the cyst wall and the adjacent ovarian cortex once identified, the cyst wall is completely stripped off from the normal ovarian tissue by opposite traction, preserving the normal ovarian tissue as much as possible. Special attention is required during the dissection at the hilum ovarii. Another important aspect of endometrioma surgery is achieving hemostasis. Bipolar coagulation is the most common hemostatic method with benefits of convenience and efficiency, causes less scab, provides exact effect and clear vision. However, there is growing attention as to whether the hemostasis of bipolar coagulation and ultrasound scalpel will affect the ovarian reserve through thermal damage. At expert hands suturing is equally effective but less damaging to the ovary and the ovarian reserve when compared to the use of surgical energy for achieving hemostasis [52]. Hemostatic sealants have been evaluated as adjuncts to use of energy or suturing and might be useful in patients with medical indications like those with bleeding disorders or active disseminated intravascular coagulation.

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