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Review Article

Evidence of Best Management of Endometrioma with Regard to a Better Fertility Outcome

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Abstract

Background: Endometriomata are endometriotic deposits within the ovary. The surgical management of these blood-filled cysts is controversial. The laparoscopic approach to the management of endometriomata is favoured over a laparotomy approach as it offers the advantage of a shorter hospital stay, faster patient recovery and decreased hospital costs. Currently the commonest procedures for the treatment of ovarian endometriomata are either excision of the cyst capsule or drainage and electrocoagulation of the cyst wall. Also, conservative management of endometrioma has been proposed as a management option especially in women seeking fertility.

Objectives: The objective of this review was to determine the effectiveness and safety of surgery, medical treatment, combination therapy or no treatment for improving reproductive outcomes among women with endometriomata, prior to undergoing ART cycles. Also, to determine the most effective surgical technique for treating an ovarian endometrioma, either excision of the cyst capsule or drainage and electrocoagulation of the cyst wall, measuring the outcomes improvement in pain symptoms and fertility. The primary endpoints assessed were the relief of pain and, in women desiring to conceive, the subsequent pregnancy rate (either spontaneous or as part of fertility treatment). Secondary outcomes assessed were the recurrence of the endometrioma and the recurrence of symptoms. Also, to compare bipolar coagulation and suturing of the ovary in terms of postoperative ovarian adhesions after laparoscopic ovarian cystectomy for endometriosis. Also, to determine the impact of surgical excision of endometriosis and endometriomas compared with control subjects on ovarian reserve. Also, to evaluate the impact of different hemostasis methods on ovarian reserve in laparoscopic cystectomy in treatment of ovarian endometrioma for the long-term. At last, to evaluate laparoscopic cyst deroofing as a feasible alternative.

Keywords: *Laparoscopic ovarian cystectomy; Endometriosis; Surgical treatment; Endometrioma; Fertility outcome*

Introduction and Pathology

Endometriosis is a common condition estimated to affect around 10% of women of fertile age [1]. It is a disease characterized by the presence of endometrial tissue located in sites outside the uterine cavity. Frequent symptoms are pain during menstruation, lower abdominal pain, dyspareunia and in severe cases affection of micturition, pain or difficulties emptying the bowel. Another substantial complication to endometriosis is subfertility.

The prevalence of endometriosis among subfertile women has been reported to be 20 - 40% [2,3]. The cause for subfertility associated with endometriosis is assumedly multifactorial, possibly involving components such as inflammatory factors, adhesions involving the internal genitalia but also the presence of endometriomas.

Endometriomas are ovarian cysts containing ectopic endometrial tissue. Endometriomas have been observed in 17 - 44% of patients with endometriosis [4]. 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 [5,6], invagination of the ovarian cortex secondary to metaplasia of coelomic epithelium in cortical inclusion cysts [7] and endometriotic transformation of functional cysts [8]. The effect of the endometrioma on women's fertility is still debated and controversial.

The influence of endometriomas on fertility and *in vitro* fertilization (IVF) is not clear. Two studies reported that endometriomas are detrimental to the ovary causing lower oocyte quality and negatively affecting the number of oocytes retrieved during fertility treatment [9,10]. Current clinical practice is laparoscopic removal [11,12].

Endometriomas can be removed by several methods, such as stripping, excision, ablation or drainage. However, laparoscopy carries a risk of complications. Beyond the inherent complications to surgery and regardless of the operating technique, damage to the ovary is inevitable.

The use of bipolar cauterization for haemostasis appears to induce most damage, but a recent review suggests that all procedures used for treatment of endometriomas cause adverse ovarian damage [13].

Using various surrogate measures of ovarian function or reserve, several studies have looked into this topic.

Most frequently, ovarian reserve markers such as anti-Mullerian hormone (AMH) and antral follicle count (AFC) have been used [14]. Several studies have reported a reduced AMH after excisional surgery for endometriomas [15-17], whereas AFC does not seem to be affected to the same extent [18]. Live birth rate (LBR) is only sparsely reported as the outcome following surgical removal although this outcome is the most clinically relevant. Accordingly, controversies exist regarding whether surgical resection of endometriomas should precede assisted reproduction technology (ART) [IVF/intracytoplasmic sperm injection (ICSI)] or if conservative management or direct referral to ART is preferable in women with endometriosis.

The impact of endometrioma per se on ovarian physiology

There is growing evidence focused on assessing the potential detrimental effect of endometrioma on ovarian physiology. A systematic review by Sanchez and colleagues suggests that the presence of an endometrioma causes ovarian damage independently from its size [19] by mechanical stretching [20]. In fact the detrimental effect induced by the endometrioma is supported by the demonstration of a plethora of morphological and functional features that make the affected ovary different from the healthy one [21].

The first explanation to support the impairment of the normal ovarian function by the endometrioma per se derives from the content of the cyst that represents a potential source of 'toxicity' for the surrounding healthy tissue. Firstly, endometriotic cysts contain high levels of cellular damage-mediating factors, proteolytic enzymes, inflammatory molecules, reactive oxygen species (ROS) and iron [22-24]. The fluid content causes critical alterations to the endometriotic surrounding cells, including modifications in the expression of critical genes and genetic changes potentially initiating tumorigenesis [24,25]. Secondly, there are higher levels of oxidative stress in the healthy ovarian cortex surrounding an endometrioma compared to other benign cysts [26]. A higher amount of ROS may promote a fibrogenic response together with transforming growth factor (TGF)-b and plasminogen activator inhibitor (PAI)-1 characterized by the expansion of mesenchymal elements, synthesis of collagen and fibronectin [27-29] and collagen matrix remodelling [19]. Alterations of the oxidative stress metabolism have been associated with a detrimental effect on oocyte and embryo development, and pregnancy outcome [31-33]. Moreover, the oxidative stress imbalance has been also identified as a potential cause of oocyte apoptosis and necrosis in early follicles [34]. The relationship between the ovarian follicle and the endometrioma allows the understanding of the impact of an endometrioma on healthy ovarian tissue. Maneschi., *et al.* investigated the functional morphologic features of the ovarian cortex surrounding benign cysts. It showed that the ovarian cortex is not morphologically impaired in the presence of teratomas or benign cystadenomas, whereas,

microscopic stromal implants and decreased follicular number and activity were related to the presence of endometriomas. Other have showed that the follicular density was lower in ovarian biopsies from the healthy ovarian tissue surrounding endometriomas in comparison with non-endometriomas [10] and that the ovarian tissue inadvertently stripped during laparoscopic surgery had different morphologic characteristics in case of endometriotic cysts compared with other benign cysts [35,36]. Indeed, normal ovarian tissue was more frequently present in specimens after endometrioma excision (54%) versus non-endometriosis cysts (6%) [35]. Furthermore, regular vascular network was much less frequent in the ovarian tissue surrounding the endometrioma in comparison with other ovarian cysts, as well as the overall follicular maturation up to the antral stage [20]. Inhibition of ovarian angiogenesis and capillary loss are mediated directly by the high levels of ROS and indirectly by the cellular injury that in turn triggers over-expression of factors affecting the vascular system, such as thrombospondin (TSP)-1, a negative angiogenic regulator [21]. Qiu., *et al.* showed that endometriotic cysts are associated with decreased microvessel density and higher levels of TSP-1, which reflected ovarian interstitial microvascular injury and a decrease in blood perfusion [37].

The impact of the endometrioma per se and of its surgical treatment on the ovarian reserve

There has been a significant research interest on the impact of an endometrioma per se and its surgical removal on ovarian reserve.

The impact of the endometrioma per se on the ovarian reserve

The antral follicle count (AFC) has been largely used in research studies to estimate the ovarian reserve of women undergoing surgery for endometrioma. Two studies with unilateral endometrioma have studied the preoperative assessment of both the healthy and affected ovary [38,39].

The pooled analysis of preoperative AFC show that the mean AFC for the ovary with the endometrioma was lower than the contralateral one (mean difference 2.79, 95% confidence interval [CI] 7.10 to 1.51), but statistical significance was not reached (p = 0.20) [18]. Several studies have reported on serum (AMH) in patients with unoperated ovarian endometriomas to assess the impact of the endometrioma on ovarian reserve [40-43].

In a Taiwanese retrospective study 141 women with endometrioma were compared with 1323 infertility patients without endometrioma which showed that the mean AMH concentration in control group was significantly higher than in the endometrioma group [40]. Jim., *et al.* conducted a retrospective case-control study including 102 women with endometrioma versus 102 body mass index (BMI)-matched controls. Serum AMH and the multiples of the median for AMH (AMH-MoM) were lower in endometrioma cases than in controls, but this was not statistically significant. In addition, women with stage IV endometriosis had lower serum AMH and AMH-MoM compared with controls [41]. A Turkish prospective study included 30womenwith endometrioma > 2 cm with 30 age-matched healthy women without ovarian cysts with the primary objective of evaluating the ovarian reserve before (cases versus controls) and after surgery (cases at baseline versus cases at 1- and 6-month follow-up) showing that, at baseline, women with endometrioma had significantly lower AMH levels compared with controls [42]. Similar findings were reported in another prospective study conducted by Chen., *et al.* who evaluated the impact of the presence of endometrioma and laparoscopic cystectomy on ovarian reserve as assessed by serum AMH levels. Before surgery the endometrioma group had significantly lower AMH levels compared with the other benign ovarian cyst group and the tubal factor infertility group [43]. On the contrary, in a large retrospective French study published in 2012, Streuli., *et al.* demonstrated that both endometriosis and endometriomas per se do not decrease AMH levels. AMH levels are decreased in women with previous surgery for endometriotic cysts independently from the presence of current endometriomas [17].

The impact of endometrioma surgical treatment on the ovarian reserve

Menopausal transition occurs earlier in women with previous surgery for endometriotic cysts [35] and although rare, cases of post-surgical ovarian failure in patients operated for bilateral endometriomas have been described [45,46]. Different techniques (e.g. ablation, excision), haemostatic procedures (e.g. bipolar coagulation, sutures) and technologies (e.g. laser, plasma energy) have been proposed to treat ovarian endometriotic cysts to minimize surgical damage on healthy ovarian tissue and optimizing the preservation of the ovarian reserve and decreasing the risk of recurrence [38,47-53]. In 2014, a systematic review and meta-analysis investigated the impact of surgery for an ovarian endometrioma on the ovarian reserve assessed by AFC. Of the 24 studies considered in detail, 13 were included for data extraction and meta-analysis, including a total of 597 patients.

This study demonstrated that the AFC of the operated ovary did not significantly change after surgery (0.10, 95% CI 1.45 to 1.65; p = 0.90). Furthermore, the operated ovary showed a significantly lower AFC compared with the contralateral ovary (mean difference 1.40, 95% CI 2.27 to 0.52; p = 0.002) but this difference was already present before the operation (2.79, 95% CI 7.10 to 1.51; p = 0.20). These findings concluded that surgery for endometrioma does not significantly affect ovarian reserve assessed by AFC [30]. However, the quality of the included studies was low with significant heterogeneity [54]. Furthermore, the reliability of AFC is questionable because the visualization of antral follicles may be obscured by the endometrioma occupying a substantial portion of the ovary. The presence of the cyst also increases the distance between the ultrasound probe and the normal ovarian tissue worsening the resolution of the transvaginal ultrasound scan [53,55].

In 2012, further systematic reviews and meta-analysis investigated the impact of surgery for endometriomas on ovarian reserve as determined by serum AMH [15,16]. Somigliana., *et al.* included 11 articles and meta-analysis was not performed due to the heterogeneity of the study designs and of the reported variables.

Nine papers demonstrated a decline of AMH levels after surgery, while two studies failed to report this reduction [16]. Raffi., *et al.* identified twenty-one studies for inclusion in the systematic review, of which eight were selected for meta-analysis. The pooled analysis of 237 patients demonstrated a significant reduction in serum AMH levels after ovarian cystectomy (1.13 ng/ml, 95% CI 0.37 to 1.88), although heterogeneity was high. Sensitivity analysis for studies with a baseline AMH level of 3.1 ng/ml decreased heterogeneity but still showed a significant postoperative reduction in AMH concentration (1.52 ng/ml, 95% CI 1.04 to 2) [15].

The impact of the endometrioma per se and of its surgical treatment on spontaneous conception and pregnancy outcomes

Several studies have reported the reproductive outcome after surgical treatment of endometriomas [49,56-60], with only one paper evaluating the spontaneous pregnancy rate of patients with endometriomas without a history of infertility [61]. This prospective observational study was designed to monitor up to six ovulatory cycles the rate of spontaneous ovulation in 244 patients of reproductive age with unilateral endometriomas with 105 (43.0%) patients conceiving during the study. The overall high pregnancy rate may be explained by the selection criteria of the patients (unilateral ovarian endometriotic cysts, no risk factors for tubal disease, without history of infertility) and normal semen analysis in their partners [61].

The impact of surgical excision of the endometrioma on spontaneous conception has been documented in several studies [49,56-60]. Shimizu., *et al.* conducted a retrospective study to assess the long-term reproductive outcome after laser ablation surgery in infertile women with endometrioma. After surgery 22 women (48.9%) achieved pregnancy; however, no further information on the pregnancy outcome was reported by the authors [16]. Donnez., *et al.* undertook a prospective study combining laparoscopic excisional and ablative surgery which included 52 women with endometriomas ≥ 3 cm in size. Thirty seven women wished to conceive. At 6 months, 12 patients (32%) were pregnant, while at a mean follow-up of 8.3 months, 15women (41%) were pregnant [57]. An Italian prospective study compared stripping and cystectomy, in patients treated with the same postoperative medical therapy in terms of recurrence of endometrioma, recurrence of pain and spontaneous pregnancy rate within 2 years from surgery. Spontaneous pregnancy rate was less frequent in patients treated with the stripping technique (4.4%) compared with those who underwent cystectomy (22.3%). This difference may be due to the relatively small sample size and selection biases (i.e. lack of randomization of the patients, no information on semen analysis of the partners) [58]. Roman., *et al.* performed a prospective study to discriminate the impact of colorectal surgery for endometriosis on recurrence and pregnancy rates in women managed for ovarian endometrioma by ablation using plasma energy. The study included 52 patients with colorectal endometriosis and 72 women without colorectal nodules and the follow-up was of 48 months. Of the 83 women (66.9%) wishing to conceive (38 with colorectal endometriosis and 45 without colorectal involvement), 51 had a pregnancy (61.4%) and 33 of these pregnancies were spontaneous (64.7%). There was no difference in the rate of patients who conceived in the group with colorectal endometriosis (65.8%) and in the group without colorectal involvement (57.8%), while the percentage of spontaneous pregnancies was, respectively, 60% and 69.2%. According to the findings of this study, concomitant management of colorectal endometriosis did not affect the probability of pregnancy in women managed for endometrioma ablation using plasma energy [60]

The impact of endometrioma per se and of its surgical treatment on IVF/ICSI outcomes

Ovarian endometrioma could negatively affect the number of oocytes retrieved [62,63] as well as oocyte quality [64], embryo quality [62,65] and implantation rate [62,65,66]. Contrary to these findings other studies did not find adverse effects of the presence of the endometrioma on oocyte quality [67,68], embryo quality [63,67,68], implantation rate [63,65,67], pregnancy rate [63,65,67] and pregnancy outcome [59].

In 2006, Gupta., *et al.* performed a systematic review and meta-analysis on the effects of ovarian endometrioma on fertility outcomes with IVF evaluating the ovarian reserve, ovarian responsiveness to ovarian stimulation and assisted reproduction outcomes. This study showed that the rate of clinical pregnancy was not significantly affected in patients with ovarian endometrioma compared with controls (odd ratio [OR]: 1.07). In addition, the overall pregnancy rate was similar with an estimated OR of 1.17. Patients with endometrioma had a reduced ovarian responsiveness to ovarian stimulation and this could be explained by the lower number of follicles in these women compared with controls [9]. However, this review also included patients previously operated for endometrioma before IVF. This was a major limitation as any surgery may damage ovarian function, even when performed by an experienced surgeon [15,16]. To overcome this limitation Yang., *et al.* undertook a systematic review and meta-analysis excluding studies with women who had previous surgery for endometrioma. This study showed that the numbers of oocytes retrieved, metaphase II (MII) oocytes retrieved and total embryos formed were significantly lower in women with endometrioma than the control group. However, gonadotrophin dose, duration of stimulation, number of good-quality embryos, implantation rate, clinical pregnancy rate and live birth rate were similar. When ovaries with endometriomas and healthy ovaries of the same patients were compared, the number of oocytes retrieved, MII oocytes retrieved and total embryos formed were not statistically significantly different between the affected ovaries and healthy ovaries. Furthermore, clinical pregnancy rate and live birth rates were not affected [70]. Recently, another systematic review and meta-analysis aimed to determine the impact of endometrioma on IVF/ICSI outcomes, to determine the impact of surgery for endometrioma on IVF/ICSI outcome and to determine the effect of different surgical techniques on IVF/ICSI outcomes.

Thirty-three studies were selected for the meta-analysis; 30 retrospective and three randomized controlled trials. Women with endometrioma undergoing IVF/ICSI in comparison with those without endometrioma had similar live birth rates (OR 0.98; 95% CI 0.71 - 1.36, 5 studies, 928 women) and similar clinical pregnancy rate (OR 1.17; 95% CI [0.87 - 1.58], 5 studies, 928 women), lower mean number of oocytes retrieved (standardized mean difference [SMD] 0.23; 95% CI 0.37 to 0.10, 5 studies, 941 cycles) and higher cycle cancellation rate compared with those without the disease (OR 2.83; 95% CI 1.32 - 6.06, 3 studies, 491 women).

Patients who underwent previous surgical treatment for their endometrioma before IVF/ICSI in comparison with those without surgical treatment, had similar live birth rates (OR 0.90; 95% CI 0.63-1.28, 5 studies, 655 women), similar clinical pregnancy rate (OR 0.97; 95% CI 0.78 - 1.20, 11 studies, 1512 women) and similar number of oocytes retrieved (SMD 0.17; 95% CI 0.38 to 0.05, 9 studies, 810 cycles) [71].

General rules of choice of treatment

The first question to be raised is: shall we operate on endometrioma or shall we manage in conservatively? Apart from the previous pathology, examination and investigations, there are general factors which will make a certain choice more likely to be chosen if we eliminate other objectives of management.

A very nice and comprehensive advice was given by (Grace-Velasco JA., *et al.* Hum Reprod 2009) in the table.

Characteristics	Favours Surgery	Favours Expectant management
Previous interventions for endometriosis	None	≥ 1
Ovarian reserve	Intact	Damaged
Pain Symptoms	Present	Absent
Bilaterality	Monolateral disease	Bilateral disease
Sonographic features of malignancy	Present	Absent
Growth	Rapid Growth	Stable

What type of surgery is the best?

Surgery for ovarian endometriomas

Surgery for ovarian endometriomas may result in reduced ovarian reserve [18,36,72] by excision or destruction of the ovarian parenchyma surrounding the endometrioma cyst; this may possibly have negative effects on post-operative fertility. When the patient has one or more ovarian endometriomas, the main objective of the ovarian gesture is the preservation of ovarian reserve. This major objective outweighs that of complete eradication of ovarian cysts. In other words, the surgeon should consider the side effect or recurrent endometriosis due to incomplete treatment of ovarian lesions rather than risk a severe reduction of ovarian reserve following complete resection of endometriomas [60]. Currently two major techniques are used in the treatment of ovarian endometriomas: cystectomy respecting the wall of the cyst and ablation consisting of destruction of the internal surface of the cyst. To understand how the two techniques treat endometrioma, to the surgeon must know the histological peculiarities of ovarian endometrioma. According to Hughson's theory, an ovarian endometrioma is the result of an invagination of the endometrial tissue in the ovarian cortex along with accumulation of endometrial remnants of menstrual bleeding localized on the surface of the ovary that adhere to the peritoneum [6]. This theory holds true in more than 90% of ovarian endometriomas [7]. A second, more recent theory proposed by Donnez and Nisolle estimated that endometriomas arise from endometrioid metaplasia of the coelomic epithelium that invaginates into the ovarian cortex, a theory that is true for 100% of cases of ovarian endometriomas [73]. These two theories are of major importance for surgeons in that they show that resection of an endometrioma does not require a central incision of the ovarian parenchyma since it can be performed by a small direct incision at the level of the origin of the invagination, at a point where ovarian parenchyma is absent [74]. All surgeons who practice this procedure on young women should be familiar with the technique of ovarian endometrial cystectomy. During cyst excision, three distinct areas of the cyst can be identified, and each requires a different surgical procedure [35,74]. Zone A, circumscribing the origin of the cyst invagination, measures approximately 1 cm^2 and is discovered when the ovary is freed from its adhesions that bind it to the peritoneum of the ovarian fossa. During adhesiolysis, the origin of invagination in zone A is opened and the flow of the characteristic ''chocolate'' liquid from the cyst is observed. Scissor excision of zone A with scissors allows the surgeon to discover a plane of cleavage around the cyst, which can be followed without significant bleeding (zone B) [35]. Any adhesions that appear in the cleavage plane must be coagulated and divided to avoid tearing off ovarian parenchyma. When cleavage occurs at the level of the ovarian hilum, these adhesions are more numerous, and continued dissection requires the help of the bipolar forceps and scissors (zone C) until the cyst is completely excised. This technique is aimed at conservation of the ovarian parenchyma [75].

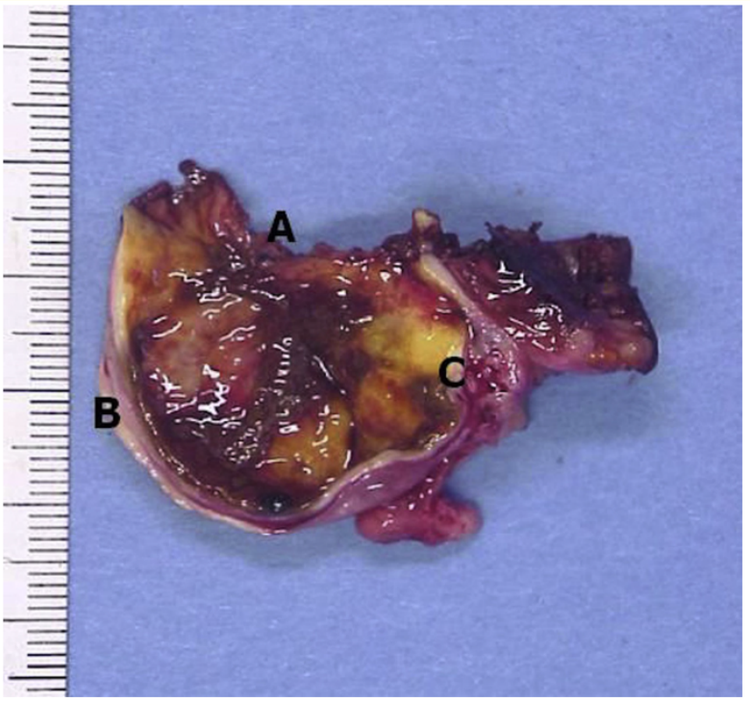

Figure: *The three distinct areas (A, B, C) of an Ovarian Endometrioma Cyst.*

Nevertheless, despite the care taken by surgeons to preserve ovarian tissue, some part of the functioning ovarian tissue is almost inevitably removed along with the cyst wall to which it is intimately attached. The technique of ovarian endometrial cyst ablation is aimed at the complete destruction of endometrial epithelium surrounded by stroma, which is responsible for the growth and recurrence of cysts. In contrast to cyst excision, the fibrotic layer surrounding the endometrial epithelium is left in place. Destruction requires the use of thermal energy, which coagulates the interior of the cyst without causing a significant diffusion of heat towards the ovarian parenchyma.

To date, the energies used for ablation of endometriomas include bipolar electric current, CO_2 laser [73] and plasma energy [60]. Due to the extent of deep diffusion of the thermal effect, monopolar energy ablation should not be used as ablative treatment in women with subsequent desire for pregnancy [50]. Several authors have described the ablation technique [60,73,76]. The point of cyst invagination is usually identified after adhesiolysis, as described in the previous paragraph. After completely aspirating the ''chocolate'' liquid, the surgeon attempts to perform a complete eversion of the cyst, in order to expose its internal surface. Removal of the surface of the cyst can be performed using several types of energy. Special attention should be given to removing the entire surface of the cyst, not forgetting the edges of the cyst opening (Zone A), as well as any adjacent implants in the broad ligament. Several studies have compared the results of ovarian cystectomy versus ablation to determine which technique is superior in terms of recurrence or post-operative pregnancy rates. The destructive ablation of endometriomas by bi-polar coagulation is definitely discouraged because of inferior results in terms of pregnancies and recurrences of endometriomas that were demonstrated by two randomized studies combined in a meta-analysis [50]. Carmona., *et al.* compared endometrioma ablation using the CO_2 laser to ovarian cystectomy in a randomized trial [50]. Five years after surgery, pregnancy rates were comparable between groups of women treated with one or the other technique. In contrast, the rate of immediate endometrioma recurrence was higher after ablation, although the difference was not statistically significant. The increase in the recurrence rate after ablation is explained by the fact that in some women, it was impossible to expose the entire interior of the cyst to laser or plasma energy rays. The study included patients with multiple cysts, or sclerotic ovaries that were difficult to evacuate or even manipulate. In the only study comparing plasma-energy ablation with cyst resection, the likelihood of post-operative pregnancy was similar between the two groups of patients, despite a significant excess of poor prognostic factors in the ablation-treated patients (higher age, two-times more frequent history of previous pelvic surgery, bilateral cysts, deep endometriosis, and colorectal endometriosis) [45]). While these studies do not demonstrate the superiority of ablation by laser or plasma energy over cyst resection, they show that ablative techniques are valid alternatives to cystectomy. Special attention should be paid to bilateral cysts, very large cysts, and recurrent cysts. Surgery of bilateral endometriomas may be particularly harmful to the ovarian reserve, with cumulative effects on both ovaries, such that 3% of patients may be immediately menopausal after surgery [77]. Endometriomas frequently recur. The probability of recurrence depends directly on the post-operative resumption of menses. In a randomized study comparing patients who underwent menstrual suppression with oral contraceptives (OC), the two-year recurrence rate of endometriomas was 29% in women without OC versus 14.7% and 8.2% in those who received OC with or without resumption of menses respectively (continuous use of OC without pause). In another randomized study, a 70% rate of recurrent endometriosis was noted in the contralateral ovary in women who did not have post-operative menstrual suppression [61]. Therefore, continuous OC administration with menstrual suppression is recommended after surgery in those patients who wish to wait before attempting to become pregnant. In case of recurrent endometrioma, the decision for re-operation with ovarian cystectomy should be carefully weighed since this may seriously aggravate the reduction of ovarian reserve. In these situations, an echo-guided transvaginal cyst puncture with sclerotherapy by intracystic instillation of alcohol [78] may be considered as an alternative solution to reduce the risk of reducing ovarian reserve. The rate of post-operative pregnancy in patients undergoing surgery for ovarian endometrioma varies in the literature in relation to duration of follow-up and associated endometriosis lesions. Generally, pregnancy rates have been reported to exceed 50% [17] in patients treated with cyst resection. In a prospective study that compared patients who underwent cyst ablation with plasma energy or cystectomy, a comparable probabilities of pregnancy of 61.3% and 69.3% at 24 months and 84.4% vs. 78.3% at 36 months respectively [45]. In the randomized trial of Carmona., *et al.* that included patients with no previous surgical history who underwent either CO_2 laser ablation or cystectomy, pregnancy rates at five years were comparable, respectively 38,1% versus 44,4 % respectively [50].

Evidence suggests that surgery to remove the endometrioma provides better results than draining and destroying the lining of the cyst with regard to the recurrence of the cyst, pain symptoms and also the chance of a spontaneous pregnancy in women who were previously subfertile. Surgery to excise the cyst should be the favoured surgical approach.

Evidence that one technique is favoured in women who desire to conceive and who seek *in vitro* fertilization (IVF) treatment is however lacking. An additional randomised trial demonstrated that in women trying to conceive the ovarian response to stimulation, as part of fertility treatment, is better in women who have undergone surgery to remove the cyst rather than draining and destroying the endometrioma. The subsequent likelihood of pregnancy was not affected.

Further research is required in this field to assess quality of life after surgery, clarify the effect of surgery on fertility with IVF treatment and to study the effect of surgery on ovarian function.

Discussion

This review addresses the controversial issue of the most appropriate surgical approach to the management of endometriomata, either excision or drainage and ablation of the cyst. This discussion focuses on the laparoscopic approach to the management of ovarian endometriomata.

Laparoscopic excision of the cyst wall of the endometrioma was associated with a reduced recurrence rate of the symptoms of dysmenorrhoea, dyspareunia and non-menstrual pelvic pain. For those women subsequently attempting to conceive, excision was also associated with a subsequent increased spontaneous pregnancy rate in women who had documented prior subfertility when compared to laparoscopic ablation of the endometrioma.

The secondary outcomes were a reduced rate of recurrence of the endometrioma and reduced requirement for further surgery in women who underwent laparoscopic excision of an endometrioma as opposed to women who underwent surgery to ablate the endometrioma.

Final Conclusion and Recommendation

Conclusions

The altered biological mechanisms related to the presence of the endometrioma per se support a detrimental effect on the ovarian cortex surrounding the endometriotic cyst and an impairment of the normal ovarian physiology. However, the available literature on this topic is conflicting. Spontaneous ovulation is not influenced by the presence of the endometrioma, independently from its size, the number and the laterality of the endometriotic cysts [61]. The presence of an endometrioma does not seem to have a significant detrimental effect on the ovarian reserve [17,36]. Conversely, there is a strong evidence for a negative effect of the surgical excision of the endometrioma on the ovarian reserve as measured by AMH concentration [15,16]. Women with unilateral endometrioma and without a history of infertility showed high rates of spontaneous conception [61]. The impact of the endometrioma per se and of its surgical treatment in women requiring IVF/ICSI suggests that although the numbers of oocytes and metaphase II oocytes retrieved and total embryos formed are significantly lower in women with endometrioma the implantation rates, clinical pregnancy rates and live birth rates are similar [70,71]. The surgical treatment of the endometrioma may be considered for cysts larger than 3 cm prior to assisted reproductive technologies to improve endometriosis associated pain or the accessibility of follicles, considering that there is no evidence that cystectomy prior to treatment with IVF/ICSI improves pregnancy rates [79].

There is no much differences between different ablation methods for treating endometrioma. There is no strong evidence about superiority of plasma energy and laser over electro surgery. Ablation is a valid alternative to surgery for treating pain symptoms and offer comparable pregnancy rate but have more risk of recurrence than surgery.

Laparoscopic cyst deroofing of endometriomas appears to be a promising alternative to laparoscopic cystectomy, with less postoperative decrease in ovarian reserve; however, the higher rate of endometrioma recurrence warrants future clinical research to determine the optimal surgical management of endometriomas.

There is good evidence that excisional surgery for endometriomata provides for a more favourable outcome than drainage and ablation, with regard to the recurrence of the endometrioma, recurrence of symptoms, subsequent spontaneous pregnancy in women who were previously infertile and ovarian response to stimulation.

Consequently, excisional surgery should be the favoured surgical approach for the management of an endometrioma. However, in women who undergo ovarian stimulation after surgery, as part of fertility treatment, there is currently insufficient evidence to favour one approach over the other with regard to the subsequent pregnancy rate. There are no studies that compare the two surgical approaches in women prior to undergoing IVF treatment.

Laparoscopic aspiration or cystectomy of endometriomata prior to ART did not show evidence of benefit over expectant management with regard to the clinical pregnancy rate. In one trial there was evidence that laparoscopic aspiration improved the ovarian response and had a positive treatment effect on the number of mature oocytes retrieved compared to a GnRH antagonist (Pabuccu 2004). One trial showed that the ovarian response to COH was greater after expectant management than after cystectomy (Demirol 2006). There is no evidence of effect that aspiration of endometriomata prior to ART provides an increase in outcome compared to expectant management on the clinical pregnancy rate and the occurrence of miscarriage.

Final Message

Treatment of endometrioma should be tailored according to patient symptoms, fertility wishes and cyst characteristics. As a general rule, independent of aim of treatment, surgery is favoured in case of pain, unilateral lesions, no previous surgery, intact ovarian reserve and no signs of malignancy. On the other hand, more conservative management plans should be in mind in case of opposite circumstances. Treatment of pain related endometriosis should be by surgery. This involves classically stripping and removal of the cyst. Deroofing is another technique which could offer better saving of ovarian reserve. Ablation methods for endometrioma offers another option for these women but recurrence is higher and is not as effective for treatment of pain. Drainage is another option for relieving pain but is to prove that it improves ART outcome, the evidence is conflicting. However, aspiration of the endometrioma cyst increases the response to IVF drugs than expectant management.

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Volume 8 Issue 7 July 2019