Management of Ovarian Endometrioma

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Abstract: The optimal conservative treatment for endometriotic cysts is unclear, particularly when treated laparoscopically. We performed a systematic analysis of the published literature on ovarian endometrioma especially focused on comparing laparoscopic cystectomy with laparoscopic drainage and coagulation of the cyst with regard to evaluating advantage and disadvantage of each method. We observed that cystectomy was superior in terms of risk of recurrent symptoms, cyst, reoperation, pregnancy: this was true in both prospective and retrospective studies previously published. Given the evidence available, excision of cyst wall in endometrioma is strongly recommended especially in infertile patients.

Key words: endometrioma, endometriosis, cystectomy, fenestration and coagulation, cumulative pregnancy rate

Introduction
Endometriosis is a common benign gynecologic condition, often presenting with infertility and pelvic pain. Its incidence ranges from 2% to 22% in asymptomatic women, but 40% to 60% in patients suffering from dysmenorrhea, and in those with infertility, it ranges from 20% to 30%. Between 17% to 44% of patients with endometriosis have ovarian endometrioma, which is an ovarian implantation of the endometrium.

Endometriomas are a common cause of gynecologic morbidity and the most common ovarian cysts encountered at surgery. Yet its etiology and management remains controversial.

The aim of this review is to clarify and discuss the best management of ovarian endometriomas.

PATHOGENESIS OF ENDOМETRIOМА
The pathogenesis of endometriotic cyst is still controversial. It is due to endometriotic deposition within the ovary. Sampson believed that this condition results from a deposit of endometrium passed through the fallopian tubes, but Hughesdon and Brosen found that endometrioma is formed by progressive invagination of the ovarian cortex after accumulation of menstrual debris that...
has derived from the shedding of superficial endometriotic active implant.\textsuperscript{11,12} According to this statement, endometrioma is a false cyst and its cyst wall is the same as the ovarian cortex. Therefore removal of pseudocyst may damage the ovary and interfere with future fertility.\textsuperscript{13}

Other theories state that primordial cells may have a role in producing endometriomas.\textsuperscript{14}

Endometriomas are more frequently located in the left hemipelvis and left ovary.

This means a left lateral predisposition of endometrioma, could be the result of the presence of sigmoid colon in the left side of pelvis, preventing endometrial cell recycling through the pelvis.\textsuperscript{15}

There is also a small risk of malignant transformation in endometriomas (0.7%).\textsuperscript{16} Clear cell and endometrioid carcinoma are the most histotypic cancer that is found in endometrioma.\textsuperscript{16–19}

**DIAGNOSIS OF ENDOMETRIOMA**

Endometrioma is detected by transvaginal ultrasound scanning (TVS) with a high degree of diagnostic accuracy. TVS is both sensitive and specific. Endometrioma has a characteristic ground-glass appearance on ultrasound. Finding a mass with an homogeneous appearance involving diffuse internal echoes on a hypoechoic background is very suspicious to endometrioma.\textsuperscript{20–22} Dogan et al\textsuperscript{21} believed that TVS has a high degree of sensitivity and specificity for diagnosing endometrioma.

It is known that endometriomas vary widely in their sonographic appearance, although a homogeneous, hypoechoic, thick-walled round-shapped mass is highly suggestive of endometrioma.\textsuperscript{21} On the other hand, endometriomas may have other sonographic appearances including echoic or heterogeneous echoes, internal septation, and fluid-fluid level. Diagnosing endometrioma before surgery, has a valuable clinical implication especially in patients for whom surgery is contraindicated or for prescribing preoperative medications to them.

**Management of Endometrioma**

There are several modalities for treatment of endometriotic cysts. These modalities include:

- medical treatment
- surgical treatment
  1. ultrasound-guided aspiration
  2. aspiration plus sclerotherapy
  3. treatment by laparoscopy
    (a) conservative treatment: laparoscopic aspiration
cystectomy (stripping method) drainage and destruction of inner lining or fenestration and coagulation
  (b) radical treatment: ovariectomy adnexectomy
  4. treatment by laparotomy.

**MEDICAL TREATMENT**

Endometriomas equal to or larger than 3 cm are known not to respond well to medical therapy.\textsuperscript{23} Very few studies have shown the effect of pure medical therapy on endometriomas.

Criel et al,\textsuperscript{24} Dmowski et al,\textsuperscript{25} and Rana et al\textsuperscript{26} compared the effects of danazol and GnRH-a on endometriomas and found a decrease of size of about 40% to 57% in endometriotic cysts and did not find any difference between these 2 drugs in decreasing the size of endometriomas.

However, Donnez et al\textsuperscript{27} showed a 25% decrease in cyst diameter after administrating GnRH-a when compared with placebo. Medical therapy may improve symptoms of pelvic pain and dyspareunia\textsuperscript{28} but it interferes with fertility treatment.\textsuperscript{29}

On the other hand, there is a small risk of cancer in those endometriomas which are left behind. Despite a 57% reduction in the size of endometriomas after medical therapy evidence suggests that
the most effective way to treat these patients is the surgical method.\textsuperscript{30}

\textbf{SURGICAL APPROACH}

Because medical therapy is not an effective treatment, endometriomas should be managed surgically. Surgery not only improves symptoms for a longer period of time, but also increases the pregnancy rate. The main surgical procedures for treatment of endometrioma include, ultrasound-guided or laparoscopy-guided aspiration, aspiration and sclerotherapy, laparoscopic surgery by means of cystectomy or fenestration and coagulation, radical treatment (ovariectomy or adnexectomy), and treatment by laparotomy. Randomized studies have demonstrated that medical therapy before or after surgery, including danazol or GnRH-a does not improve the results in terms of recurrence of pain or improvement in infertility outcome.\textsuperscript{2}

\textbf{ULTRASOUND-GUIDED ASPIRATION}

Transvaginal ultrasound-guided drainage without surgery does not seem to be effective. There are at least 5 studies that show a high recurrence rate after aspiration\textsuperscript{31–35} (Table 1). Table 1 shows recurrence rates between 28\% and 100\% in the 5 different studies.

To decrease recurrence rate, some groups combined aspiration with in situ injection of tetracycline\textsuperscript{36,37} ethanol\textsuperscript{38} or methotrexate.\textsuperscript{39} Akamatsu et al\textsuperscript{38} reported reduction of recurrence of about 0\% to 9\% by using ethanol and Mesogitis et al\textsuperscript{39} observed an 18\% recurrence rate after using methotrexate. Fisch and Sher\textsuperscript{37} found no recurrence after using sclerotherapy with 5\% tetracycline after 6 weeks of follow up.

Another problem that limits the use of simple aspiration is its complications which include: infection, abscess formation, and pain.\textsuperscript{33,40} Other disadvantages of this method are inability to rule out any malignancy and the risk of pelvic adhesion after simple aspiration owing to inflammations that occur in response to endometriotic cyst fluid.\textsuperscript{41,42} These adhesion formations may cause chronic pelvic pain and infertility. The use of GnRH-a after aspiration does not show any additional benefit, because reaccumulation of the cyst occurs in the immediate postaspiration period.\textsuperscript{43}

It can be concluded that simple aspiration of endometrioma should not be regarded as first-line treatment but in some situations, such as recurrences and before assisted reproductive technology, it could be helpful and act as an alternative approach.\textsuperscript{37}

\textbf{Surgical Modalities}

Because both laparotomy and laparoscopy have the same results in terms of pregnancy and recurrence rates, laparoscopy can be considered to be the best approach for endometriotic cysts; because blood loss during operation, the length of hospitalization, need for analgesia, and the recovery time of patients are significantly lower in the laparoscopic group.\textsuperscript{34–47} Although Jones et al\textsuperscript{50} reported that about 42.3\% of endometriomas are operated by laparotomy in the United Kingdom, this is due to lack of skill and limitation of surgical teaching.

Recently Chapron et al\textsuperscript{51} did a meta-analysis of all available prospective
randomized clinical trials comparing the outcome of laparoscopic surgery and laparotomy and showed that these techniques exposed patients equally to complications.

Despite the above mentioned argument, laparotomy should be considered for severe endometriosis associated with dense extensive adhesions or for deeply infiltrating endometriomas.\textsuperscript{51,52}

**LAPAROSCOPIC DRAINAGE OF ENDOMETRIOMA**

The major problem with laparoscopic cyst drainage is a high risk of recurrence of about 80% to 100%.\textsuperscript{53,54} Giving GnRH-a after laparoscopic drainage, significantly reduces the size of the cyst up to 50% but it has no effect on recurrence rate.\textsuperscript{55,56} Nowadays, it is accepted that simple aspiration by laparoscopy should not be used to treat endometrioma.

**LAPAROSCOPIC CYSTECTOMY**

Laparoscopic cystectomy remains the first line choice for conservative treatment of endometriotic cysts.\textsuperscript{57} In this technique, the inner lining of the cyst is dissected from the ovary by 2 atraumatic grasping forcepses that are pulled in opposite directions and the inner linings are sent for histologic examination.\textsuperscript{57}

**Table 2. Ovarian Cystectomy and Recurrence Rate**

<table>
<thead>
<tr>
<th>Author’s Name</th>
<th>No.</th>
<th>F/U (mo)</th>
<th>Recurrence Rate %</th>
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<tr>
<td>Bateman et al\textsuperscript{44}</td>
<td>36</td>
<td>12</td>
<td>11.1</td>
</tr>
<tr>
<td>Marana et al\textsuperscript{58}</td>
<td>42</td>
<td>21</td>
<td>7</td>
</tr>
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<td>21</td>
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<td>4.8</td>
</tr>
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<tr>
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<td>32</td>
<td>24</td>
<td>6.2</td>
</tr>
<tr>
<td>Fayez and Vogel\textsuperscript{61}</td>
<td>26</td>
<td>2</td>
<td>0</td>
</tr>
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<td>Hemmings et al\textsuperscript{62}</td>
<td>23</td>
<td>36</td>
<td>12</td>
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<tr>
<td>Saleh and Tulandi\textsuperscript{54}</td>
<td>161</td>
<td>18</td>
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<td>Alborzi et al\textsuperscript{53}</td>
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**Table 3. Ovarian Cystectomy With Perioperative Medication and Recurrence Rate**

<table>
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<th>Recurrence Rate</th>
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<td>5</td>
</tr>
<tr>
<td>Montanino et al\textsuperscript{60}</td>
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</tr>
<tr>
<td>Gurgan et al\textsuperscript{65}</td>
<td>19</td>
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<tr>
<td>Busacca et al\textsuperscript{66}</td>
<td>366</td>
<td>48</td>
<td>11.7</td>
</tr>
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**LAPAROSCOPIC FENESTRATION, DRAINAGE, AND ABLATION OF CYST WALL**

Difficulty of performing cystectomy and questionable effect of removal of cyst on follicular reserve, has led some surgeons to use this technique. In this method, fenestration and aspiration is done.
A 1.5 × 1.5 cm biopsy is taken and sent for histologic examination followed by bipolar coagulation of the inner lining.\textsuperscript{57,63} It has been suggested that coagulation or ablation of cyst wall may induce thermal injury to underlying ovarian cortex, hence a functional loss in ovarian reserve may occur.\textsuperscript{71} But Donnez\textsuperscript{72} has stated that laparoscopic fenestration and coagulation of cyst wall allows the preservation of ovarian follicular reserve with good response to stimulation by gonadotropins. On the other hand, this method is associated with incomplete destruction of endometrioma.\textsuperscript{71}

Table 4 shows the cyst recurrence rate after ablation and fenestration with or without preoperative medication.

There are different techniques for doing fenestration and coagulation. Some authors do fenestration and coagulation in 2 steps, using luteinizing hormone releasing hormone agonists before the second laparoscopy.\textsuperscript{68} Others use the above mentioned technique without preoperative or postoperative medication.\textsuperscript{67} Other groups use a single step method for fenestration and coagulation by electroceutry or laser.\textsuperscript{57,63}

### WHICH PROCEDURE IS BETTER FOR THE MANAGEMENT OF ENDOMETRIOMA: CYSTECTOMY OR FENESTRATION AND COAGULATION?

To find the best technique for the treatment of endometriomas, we searched MEDLINE from January 1970 to January 2005.

As Vercellini et al\textsuperscript{13} have also mentioned, very few articles have been published on the comparison of cyst excision versus drainage and coagulation by laparoscopy. Two of these articles evaluated only the recurrence rate of endometrioma\textsuperscript{54,61} and 3 others discussed both the above factor and the postoperative conception rate.\textsuperscript{57,62,63} Only 2 of them were true prospective randomized controlled clinical trials.\textsuperscript{57,63}

For evaluating these 2 techniques and comparing the recurrence rate of symptoms and endometrioma, we did 2 meta-analyses. One meta-analysis was done on the 2 recent prospective randomized trials, by Alborzi et al\textsuperscript{63} and Beretta et al.\textsuperscript{57} Another meta-analysis was performed on 5 prospective and retrospective studies that compared 2 different approaches for operating endometriomas.\textsuperscript{54,57,61-63}

In the first meta-analysis data of the 2 studies (Alborzi and Beretta) were combined together and the 2 laparoscopic techniques were compared with each other and we found that the laparoscopic excision of endometrioma was associated with a significant decrease in the recurrence of dysmenorrhea [odd ratio (OR) 0.15 confidence interval (CI) 95% 0.06-0.38].

On the other hand, Beretta reported a lower recurrence rate of dyspareunia
Recurrence of endometrioma was observed in 48 out of 267 (17.9%) endometriomas treated with coagulation or laser vaporization and in 28 out of 355 (7.8%) who underwent cystectomy. The OR of recurrence of endometriotic cyst for the 5 considered studies ranged from 1.41 to 9.1 with 95% CI.

The common OR was 2.54 (2.24-2.89), suggesting that treating endometriotic cysts with fenestration and coagulation increases the risk of recurrence about 2.5-fold when compared with excision of cyst wall.

In Fayez’s study, 4 different methods for the treatment of this cyst were evaluated: complete excision of the cyst, stripping of the lining, CO2 laser ablation of the lining and drainage of the cyst. It was not explained in Fayez studies whether there was any difference between complete removal and excision of the cyst with stripping of the lining. Fayez also used danazol for 8 weeks after the operation which could have interfered with the results. Hemmings et al showed that there was no significant difference in recurrence rate among the 3 groups who underwent fenestration and coagulation, laparoscopic cystectomy and cystectomy by laparotomy. Their results are similar to those obtained by Alborzi et al and Beretta et al.

The other purpose of this meta-analysis, was to evaluate reoperation rate in these 2 methods of treatment. Only 2 of the 5 previous studies, have compared the rate of reoperation in the 2 treatment modalities for endometrioma. By combining the data obtained by Saleh and Alborzi, we found that reoperation rate was significantly lower in the cystectomy group than in the fenestration and coagulation group (OR 4.36 CI 95% 3.17-5.99). Saleh and Tulandi also found that rate of reoperation after cystectomy was higher in patients with larger cysts. However, Saleh’s study was retrospective and the number of patients

(OR 0.08 CI 95% 0.01-0.51) and non-menstrual pelvic pain (OR 0.1 CI 95% 0.02-0.56) in the cystectomy group when compared with the fenestration and coagulation group. Also, the interval for recurrence of pain was significantly longer in Beretta’s cystectomy group.

Significant reduction in the recurrence rate of endometrioma in the cystectomy group is another advantage of cystectomy when compared with fenestration and coagulation (OR 0.41 CI 95% 0.18-0.93) and this was observed in our analysis. The other advantage of cystectomy is that the chance of reoperation is significantly lower in the cystectomy group versus the fenestration and coagulation group (OR 0.21 CI 95% 0.05-0.79).

Saleh and Tulandi also found similar results. The most important advantage, obtained by cystectomy of endometrioma is the pregnancy rate, which was significantly higher after a 1 year follow-up in the cystectomy group as compared with the fenestration and coagulation group after combining the data of the 2 mentioned studies (OR 5.24 CI 95% 1.92-14.27). The overall subsequent spontaneous pregnancy rate was higher in the excision group (OR 5.21 CI 95% 2.04-13.29).

Two other retrospective studies, have showed a higher conception rate in the cystectomy group.

For better evaluation of the 2 surgical modalities, we also did another meta-analysis on 5 previous studies, including both retrospective and prospective studies. For evaluating the recurrence of symptoms such as dysmenorrhreal and dyspareunia, we only had data from 2 prospective studies (Alborzi, Beretta) that were discussed before.

Figure 1 shows range and means of odd ratios of endometrioma recurrence rate in the 5 different studies and depicts the common odd ratios.
in the excision group was much higher than in the fenestration and coagulation group (161 vs 42).

Finally for evaluating the pregnancy rate after these 2 surgical approaches for endometrioma, we only had data from 3 of the 5 previous studies (Hemming, Beretta, and Alborzi).

By combining these data, we found that pregnancy rate was significantly higher in the excision group as compared with the fenestration and coagulation group (OR 2.03 CI 95% 1.57-2.64).\(^\text{57,62,63}\)

It is interesting to note that, Hemmings et al\(^\text{62}\) reported that the average time interval to the first conception was significantly shorter in the coagulation group than in the cystectomy group. However, Hemmings report was retrospective and the number of patients in the fenestration and coagulation group was much higher than in the excision group (80 vs 23) and they did not mention the medication and methods used for the treatment of infertility after surgery.\(^\text{62}\)

**FIGURE 1.** Overview of articles that shows range and means of odd ratio of endometrioma recurrence rate comparing 2 surgical approaches (excision vs. coagulation) with 95% CIs. Data related to study of Fayez are number of cysts.

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RADICAL TREATMENT FOR ENDOMETRIOMA
This technique includes adnexectomy and ovariectomy, which is done by laparoscopy or laparotomy. The choice of operation (laparotomy and laparoscopy) is made based on the presence of pelvic adhesion and the experience of the surgeon in performing endoscopic surgery.
Although using each of these 2 methods, it is essential to maintain hemostasis and avoid urinary tract injury.

**ENDOMETRIOMA AND INFERTILITY**

The association between endometriosis and infertility is well known, but its mechanism is unclear. The best surgical technique for obtaining a better pregnancy rate is still controversial.

Hemmings has reported that the cumulative clinical pregnancy rate was not statistically significant after 36 months of follow-up by laparoscopic fenestration and coagulation, although the time to achieve the first pregnancy in infertile patients was significantly shorter.62

In a recent prospective cohort study, Jones and Sutton76 reported a cumulative pregnancy rate of 39.5% at 12 months follow-up while according to the 2 randomized clinical trials,57,63 comparing the 2 different techniques, better pregnancy rate was achieved with ovarian cystectomy.

This result is supported by other studies.13,47,66 Several studies have shown that both cystectomy and fenestration and coagulation do not impair ovarian response to controlled ovarian hyperstimulation, if care is taken to avoid damage to the remaining ovarian tissue.72,77,78

**Conclusions**

Endometrioma is the most frequent ovarian mass that is encountered by gynecologists. There are controversies on the pathogenesis, risk of malignant transformation, modalities of treatment, and effect on fertility.

The possibility of malignant transformation together with recurrence of pain and fertility problems indicates that ovarian cystectomy may be a better option.

This suggestion is result of our meta-analysis which showed that women underwent fenestration and coagulation are about 2.5 times as likely as those underwent cystectomy to experience a recurrence of endometrioma. Also, the recurrence rate of symptoms such as dysmenorrhea and pain were significantly lower in patients for whom the cysts wall was excised. Additionally, requirement for further surgery was significantly lower in the cystectomy group and this technique was associated with better pregnancy rate when compared with the fenestration and coagulation techniques.

Therefore, the excision of cyst wall in endometriomas is strongly recommended especially in infertile patients.

Further studies are needed to compare cystectomy with fenestration to evaluate the effect of these techniques on the quality of life, ovarian function after surgery, and the relationship between type of laparoscopic treatment and the outcome of further assisted reproductive technique.

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