

Management of ovarian endometriomas

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The efficiency of medical therapy as a unique treatment for endometrioma has not been demonstrated. Operative laparoscopic management is the ‘gold standard’ for surgical treatment, and there are no indications to prescribe medical treatment before cystectomy. Post-operative administration of low-dose cyclic oral contraceptives does not significantly affect the long-term recurrence of endometriosis after surgical treatment. In case of infertility, the management of endometriomas is controversial. Recurrent ovarian surgery is not recommended.

Key words: endometrioma/intraperitoneal cystectomy/operative laparoscopy/surgery

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Introduction

Between 17 and 44% of patients with endometriosis have ovarian endometriomas (Jenkins *et al.*, 1986; Gruppo italiano per lo studio dell’endometriosi, 1994; Redwine, 1999), and gynaecologists are frequently confronted with the problems of managing these patients. Among the different therapeutic modalities, it is well known that medical treatment alone is inadequate (Farquhar and Sutton, 1998; Jones and Sutton, 2000), and conservative medical treatment, independently of the prescribed product, may lead simply to a reduction in volume rather than complete regression of the endometriotic cyst (Dmowski *et al.*, 1989; Donnez *et al.*, 1989, 1994; Crikel *et al.*, 1995; Rana *et al.*, 1996). The failure of such conservative medical management is due to the persistence of endometriotic tissue during treatment (Donnez *et al.*, 1989). The main aim of this review was to identify, clarify and discuss non-medical modalities in the management of endometriotic cysts.

The main options of non-medical treatment of ovarian endometriomas are outlined in Table I.

Ultrasound-guided aspiration

This technique involves the insertion of a needle into the endometrioma under vaginal ultrasonographic guidance, and aspiration of the contents. The ultrasound-guided aspiration of ovarian cysts has been shown to be feasible (Zanetta *et al.*, 1993), but when applied to ovarian endometriomas this technique leads to four main problems: recurrence; complications; inadequacy of cytology; and adhesions.

Table I. Ovarian endometriomas: surgical procedures

Ultrasound-guided aspiration
Surgical treatment
Treatment by laparoscopy:
a) Conservative treatment:
Laparoscopic aspiration
Cystectomy:
Intraperitoneal cystectomy (IPC)
Transperitoneal cystectomy (TPC)
Drainage and destruction (laser or bipolar coagulation) of the inner lining
Three-stage management ^a
b) Radical treatment:
Ovariectomy
Adnexectomy
Treatment by laparotomy

^aFirst laparoscopy: drainage; GnRH agonists for 12 weeks; second laparoscopy for CO₂ laser vaporization of the internal wall.

Table II. Recurrence after ultrasound-guided aspiration of ovarian endometriomas

Reference	No. of endometrioma	No. of recurring endometrioma
Aboulghar <i>et al.</i> (1991)	21	6 (28.6)
Giorlandino <i>et al.</i> (1993)	34	18 (53.0)
Zanetta <i>et al.</i> (1995)	172	168 (97.6)
Troiano and Taylor (1998)	9	6 (66.6)

Values in parentheses are percentages.

The incidence of recurrence (Table II) ranges from 28 to 100% in four different studies (Aboulghar *et al.*, 1991; Bonilla-Musoles *et al.*, 1993; Giorlandino *et al.*, 1993; Zanetta *et al.*, 1995), and the risk of recurrence persists even with combined medical treatment (Zanetta *et al.*, 1993). In order to reduce recurrence after aspiration, some groups have combined ultrasound-guided aspiration with the in-situ injection of tetracycline (Aboulghar *et al.*, 1993), ethanol (Akamatsu *et al.*, 1988; Noma and Yoshida, 2001) or methotrexate (Mesogitis *et al.*, 2000). The results of these studies, in terms of preventing recurrence, appear better with ethanol (range 0–9%) and methotrexate (18%), though these investigations are still of a preliminary nature and require further analysis in larger patient groups. Another weak point of this procedure might be complications, mainly infections (Padilla, 1993; Muzii *et al.*, 1995; Zanetta *et al.*, 1995), the consequences of which may be very serious and sometimes justify reintervention (Padilla, 1993). The third disadvantage is the inadequacy of cytology to detect possible malignancy (Tropé, 1981; Diernaes *et al.*, 1987). The final risk is that of pelvic adhesions secondary to peritoneal inflammation stimulated by the endometrioma contents following aspiration (Muzii *et al.*, 1995; Garvey *et al.*, 1999); the consequences of such adhesions may be very serious in terms of infertility and chronic pelvic pain.

Whilst all of these factors suggest that ultrasound-guided aspiration is not a first-line choice in the management of endometriotic cysts, the technique is not totally contraindicated. Indeed, in some situations—mainly recurrence and assisted reproductive technology (ART)—ultrasound-guided puncture might offer an alternative approach, and this will be discussed later.

Modalities of surgical treatment of ovarian endometriomas

The surgical management of endometriotic cysts raises questions relating to the best operative approach for endometriomas, the modalities of surgical treatment using laparoscopy, and the combination of medical treatment before or after surgery.

The best operative approach for endometriomas

Whether surgery is performed via laparotomy or laparoscopy, the results are similar in terms of risk of recurrence (Bateman *et al.*, 1994; Catalano *et al.*, 1996; Crosignani *et al.*, 1996; Milingos *et al.*, 1999), fertility outcome (Adamson *et al.*, 1992; Bateman *et al.*, 1994; Catalano *et al.*, 1996; Milingos *et al.*, 1999; Sawada *et al.*, 1999) and pelvic pain symptomatology (Catalano *et al.*, 1996).

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Only one randomized prospective study appears to have been designed specifically to investigate surgical treatment modalities of endometriomas (Mais *et al.*, 1996). The results revealed short-term benefits of laparoscopy over laparotomy, with complication rate and operating time being similar in both groups, while numbers of analgesia-free patients at day 2 (87.5 versus 18.8%; $P < 0.05$), patients discharged at day 3 (93.8 versus 12.5%; $P < 0.05$) and those who were fully recuperated at day 15 (93.8 versus 6.3%; $P < 0.05$) were all significantly greater in the laparoscopy group. These results were confirmed by other randomized prospective studies evaluating the surgical treatment of ovarian cysts, regardless of their histological type (serous, mucinous, dermoides) (Mais *et al.*, 1995; Nitke *et al.*, 1996; Yuen *et al.*, 1997; Damiani *et al.*, 1998; Morgante *et al.*, 1998). In fact, in addition to the well-known advantages of laparoscopy over laparotomy, it was shown that laparoscopic surgery is not inherently dangerous. Recently a meta-analysis of all available prospective randomized clinical trials comparing the outcome of laparoscopic surgery and laparotomy showed that these techniques exposed patients equally to complications (Chapron *et al.*, 2002a). Although in some countries there is an equal preference for open versus endoscopic surgery (Jones *et al.*, 2002) it is possible, based on the above-mentioned arguments, to propose that operative laparoscopy be used as first-line treatment for ovarian endometriomas.

These results do not imply that laparotomy cannot be used in the management of endometriotic cysts; indeed, this approach might be indicated in cases of severe endometriosis associated with dense extensive adhesions and/or deeply infiltrating endometriosis (Crosignani and Vercellini, 1995; Saidi *et al.*, 1995; Chapron, *et al.*, 2002b).

Modalities of surgical treatment by laparoscopy

Several techniques have been proposed for the conservative laparoscopic treatment of endometriotic cysts (Table I).

The major problem of cystic drainage associated with laparoscopy, as with ultrasound-guided aspiration, involves a high risk of recurrence of 80–100% (Vercellini *et al.*, 1992; Donnez *et al.*, 1994; Marana *et al.*, 1996; Saleh and Tulandi, 1999). The administration of LH releasing hormone (LHRH) agonists after laparoscopic drainage significantly reduces the diameter of the cyst and the rate of active endometriosis (Donnez *et al.*, 1994), but does not in any way reduce the risk of recurrence (Vercellini *et al.*, 1992). Currently, it is accepted that simple drainage by laparoscopy should not be used to treat endometriomas.

Other authors have proposed a three-stage technique for the conservative treatment of ovarian endometriomas (Donnez *et al.*, 1996). This strategy consists of performing a simple drainage during a first laparoscopy with an abdominal lavage, followed by LHRH agonist administration for 3 months. Vaporization of the internal wall using a CO₂ laser is then carried out during a second laparoscopy. To date, no comparisons have been made of either randomized prospective or comparative studies using one-step surgery (drainage with laser vaporization or bipolar coagulation or intraperitoneal cystectomy) with those of three-stage management. It is possible that the three-stage approach should not be

used systematically in patients for the following reasons: (i) laparoscopy is a surgical procedure and presents a real risk of complications, even in the case of simple operation (diagnostic, drainage) (Chapron *et al.*, 1998b); (ii) the three-stage procedure is expensive, requiring treatment with LHRH agonists for several months as well as two surgical interventions, two hospitalizations and two recovery periods; (iii) until now, there has been no scientific argument offered in terms of recurrence, post-operative adhesions or fertility outcome which could justify the adoption of such a systematic strategy compared with other one-stage conservative laparoscopic techniques.

Laparoscopic cystectomy remains a first-line choice for the conservative treatment of endometriotic cysts (Beretta *et al.*, 1998). For this purpose, two principal laparoscopic techniques could be proposed: (i) intraperitoneal cystectomy (IPC) or ablation of the cystic capsule under laparoscopic control by puncturing and opening the cyst, identifying the cyst wall and removing it from the ovarian cortex by traction with grasping forceps; and (ii) transperitoneal cystectomy (TPC) or ablation of the cystic capsule outside of the abdominopelvic cavity through a mini-laparotomy. TPC, which is less elegant than IPC, is indicated only in case of intra-operative difficulties when performing an IPC in order to avoid conversion to laparotomy. It should not be proposed as a first-line treatment option.

When cystectomy is a technically difficult aspiration, drainage and destruction of the cyst wall by either laser vaporization or bipolar coagulation is an acceptable alternative.

Very few studies have compared the results of different modalities of conservative laparoscopic surgery of endometriomas (Fayez and Vogel, 1991; Beretta *et al.*, 1998; Hemmings *et al.*, 1998; Saleh and Tulandi, 1999). One group (Fayez and Vogel, 1991), in a prospective study comparing four types of conservative laparoscopy (complete excision, stripping of lining, laser ablation, drainage), reported no significant difference with regard to the post-operative risk of adhesions following IPC and aspiration with laser CO₂ vaporization. Others (Saleh and Tulandi, 1999) have reported retrospective data from 231 patients with endometriomas treated by laparoscopy, and showed the cumulative rate of reintervention to be more important following fenestration, aspiration and destruction compared with cystectomy. The reintervention rates at 18 and 48 months respectively were 6.1% and 23.6% following cystectomy and 21.9% and 57.8% following fenestration, aspiration and destruction. In a case-control study, it was reported that recurrence rates at 36 months were similar, whichever modalities of conservative laparoscopic treatment (cystectomy versus fenestration, aspiration and coagulation) had been used (Hemmings *et al.*, 1998). To the present authors' knowledge, only one randomized prospective study has compared results obtained with different modalities of conservative laparoscopic treatment (Beretta *et al.*, 1998). The median operative time, estimated blood loss, post-operative hospital stay, risk of complications and rate of conversion to laparotomy were not significantly different whether patients underwent IPC ($n=32$) or aspiration followed by bipolar coagulation ($n=32$). On the other hand, the cumulative rates of recurrence at 24 months, with regard to dysmenorrhoea [three patients (15.8%) versus nine patients (52.9%); $P<0.05$], deep dyspareunia [three patients (20%) versus nine patients (75%); $P<0.05$] and chronic pelvic pain [two patients (10%) versus nine

patients (52.9%); $P<0.05$] were significantly less for patients who had undergone IPC. The median interval between surgery and recurrence of moderate to severe pelvic pain was longer following IPC [19 (range 13.5–24) months versus 9.5 (range 3–20) months]. Although no statistically significant values regarding the global rate of recurrence have been found, it was reported in a very small group of patients that the recurrence risk was three times less important when IPC was performed (6.2%, $n=2$), but this increased to 18.8% ($n=6$; $P=NS$) in the case of aspiration and coagulation.

IPC has a further advantage over aspiration and coagulation, namely the possibility of performing histological examinations—an element which is essential with regard to the risk of neoplastic pathologies in patients aged over 40 years (Nezhat *et al.*, 1992; Fukunaga *et al.*, 1997). Histological analysis allows the detection of atypical endometriotic lesions which are observed in 1.7 to 12.2% of ovarian endometriosis cases (Czernobilsky and Morris, 1979; Fukunaga *et al.*, 1997; Nishida *et al.*, 2000). Some authors consider atypical endometriosis as precancerous lesions (LaGrenade and Silverberg, 1988; Rutgers and Scully, 1988; Moll *et al.*, 1990; Saintz de la Cuesta *et al.*, 1996; Fukunaga *et al.*, 1997) as there is a risk of transformation to malignancy of 0.6–0.8% (Corner *et al.*, 1950; Scully *et al.*, 1966; Nishida *et al.*, 2000). In case of any doubt regarding the nature of the cyst (whether benign or malignant), a surgical approach enables a choice to be made other than IPC: (i) laparoscopic adnexectomy followed by extraction into a bag in order to obtain a frozen section (Chapron *et al.*, 1998a); and (ii) conversion to laparotomy.

The risk of recurrence following cystectomy varies among series (Jones and Sutton, 2000). This variability is due to differences in the follow-up interval of the series as well as the criteria used to define recurrence (ultrasonographic recurrence, endometriomas justifying reintervention). One group did not consider age and cyst diameter to constitute risks of recurrence following drainage, aspiration and bipolar coagulation, though for patients undergoing IPC, cyst diameter was a significant risk factor for recurrence (Saleh and Tulandi, 1999). In a most detailed study (Busacca *et al.*, 1999), the authors examined risk factors for recurrence following laparoscopic cystectomy considering both clinical recurrence and reintervention. For patients presenting clinical recurrence, three risk factors were found: (i) previous history of endometriosis; (ii) stage IV rAFS classification; and (iii) score rAFS (total, adhesions and implants' scores). In addition, two main risk factors were detected for reintervention: (i) endometrioma size; and (ii) total rAFS score (Busacca *et al.*, 1999). The results obtained in four studies comparing the modalities of surgical laparoscopic conservative treatment (Fayez and Vogel, 1991; Beretta *et al.*, 1998; Hemmings *et al.*, 1998; Saleh and Tulandi, 1999) suggested that treating endometriomas by coagulation or laser vaporization without excising the pseudocapsule significantly increases the risk of recurrence (Vercellini *et al.*, in press).

Whichever modalities of laparoscopic surgery are used, the technique should not be applied without a complete pre-operative assessment and cautious time for diagnostic laparoscopy (Canis *et al.*, 1984; Chapron *et al.*, 1996). In all cases, patients should be aware that conversion to laparotomy is always possible depending on the intra-operative findings (Chapron *et al.*, 1996).

Endometriosis is a risk factor for serious urinary complications (Saidi *et al.*, 1996a) and of remnant syndrome (Nezhat *et al.*, 2000). In case of radical treatment, adnexectomy might be difficult to perform due to the presence of severe adhesions. The risk of ureteral injury is the major complication during adnexectomy (Daly and Higgins, 1988; Saidi *et al.*, 1996b), and the first step of adnexectomy would in all cases be adhesiolysis. Technically, the ureters should always be repaired, and ureterolysis and/or a retroperitoneal approach carried out whenever required (Kadar, 1995). Besides preventing ureteral injury (Daly and Higgins, 1988), this strategy allows a good presentation of the infundibulopelvic ligament, thus reducing the risk of remnant syndrome (Berek *et al.*, 1979; Hajj and Mercer, 1987; Nezhat and Nezhat, 1992). Haemostasis of the infundibulopelvic ligament is secured using a variety of techniques (bipolar coagulation, ligatures, automatic stapling devices), the efficiency of each is similar (Daniell *et al.*, 1992). In the present authors' experience, bipolar coagulation is best used to achieve secure and inexpensive haemostasis (Chapron and Dubuisson, 1995). The use of non-disposable autoclavable laparoscopic material whenever possible is necessary in order to reduce the cost of laparoscopy and to render the technique economically viable (Schaer *et al.*, 1995; Chapron *et al.*, 2000).

Should medical treatment be combined before or after surgery?

The combination of medical treatment before or after surgery, as well as the nature of the medical agent to be used, remains the subject of debate.

One group (Muzii *et al.*, 1996) found no advantages in terms of mean operating time and subsequent surgical performance to achieve cystectomy in patients by administering LHRH agonists. However, no randomized prospective studies dealing with this particular subject have been reported. Although the number of patients was limited in this study (Muzii *et al.*, 1996), no scientific arguments could clearly justify the systematic use of pre-operative medical treatment in the management of endometrioma.

By contrast, and to the present authors' knowledge, there have been no reports made which specifically studied the use of postoperative medical treatment for ovarian endometrioma. Several studies covering this subject (Telimaa *et al.*, 1987; Parazzini *et al.*, 1994; Hornstein *et al.*, 1997; Bianchi *et al.*, 1999; Vercellini *et al.*, 1999; Busacca *et al.*, 2001) analysed the results of post-operative medical treatment without considering the endometriotic lesions (superficial endometriosis, endometriomas, adhesions, deep endometriosis). With regard to the effect on pain, even if the results were controversial, post-operative drug therapy has a certain benefit (Olive and Pritts, 2001). In choosing the type of treatment (progestins, danazol, GnRH agonist), the available data suggest that the efficacy of progestins for temporary relief of endometriosis-associated pelvic pain is good and comparable with that of other, less safe treatments (Vercellini *et al.*, 1997). On the other hand, drug therapy seems to have no role in the treatment of infertility associated with endometriosis (Olive and Pritts, 2001).

Finally, one notable question is whether oral estroprogestative contraception should be administered following surgical treatment of endometriomas, or not. A recent randomized prospective study (Muzii *et al.*, 2000) showed that endometrioma recurrence, moderate to severe pain recurrence rate and mean time to recurrence of either symptoms or endometrioma, were not

significantly different for patients who did, or did not, receive post-operatively monophasic, combined, low-dose oral contraceptives. Although the 12-month cumulative rate of recurrence appears more important in those patients who received post-operative oral contraception (0.062 versus 0.101; $P=0.41$), this cumulative rate was strictly comparable at 24 (0.094 versus 0.136; $P=NS$) and 36 months (0.121 versus 0.174; $P=NS$) in both groups. Ovarian endometrioma should not be considered a contraindication to the administration of oral contraception during the post-operative period if it is necessary, or desirable.

Endometriomas and infertility

The problem of co-existing endometriomas in a context of infertility and/or pregnancy desire is a frequent situation that raises two main questions:

1. Is there a conservative laparoscopic procedure that offers better fertility outcomes?
2. Should we, or should we not, operate on endometriomas in patients scheduled for ART?

One group (Hemmings *et al.*, 1998), have reported that the cumulative clinical pregnancy rate was not statistically significant after 36 months of follow-up according to the conservative laparoscopic surgical modalities (aspiration and bipolar coagulation or cystectomy), although the time needed to obtain the first pregnancy in infertile patients was significantly shorter in those patients who underwent aspiration and bipolar coagulation (Hemmings *et al.*, 1998). A recent prospective cohort study (Jones and Sutton, 2002) reported a cumulative pregnancy rate of 39.5% following ablative laparoscopic surgery for endometrioma [after fenestration, the capsule was treated with potassium-titanylphosphate (KTP) laser or bipolar diathermy]. In a unique randomized prospective study based on a limited number of patients, better pregnancy rates were reported following laparoscopic ovarian cystectomy than after aspiration and bipolar coagulation (Beretta *et al.*, 1998). However, these results were at variance with those which suggested that endometrioma stripping might result in a loss of viable ovarian cortex during surgery (Donnez *et al.*, 1996).

With regard to the choice of strategy for patients scheduled for ART and having endometrioma, the results published to date have been controversial. Some authors have reported satisfactory results in terms of fertility in patients undergoing IVF with co-existing endometrioma (Isaacs *et al.*, 1997; Tinkanen and Kujansuu, 2000; Khamsi *et al.*, 2001), which is in favour of a 'wait-and-see attitude'. In contrast, others (Loh *et al.*, 1999) reported that, following IPC for endometriomas, the follicular response in patients aged <35 years was not significantly different from that of a normal ovary when stimulated with FSH. On the other hand, in patients aged >35 years, post-cystectomy ovaries were able to respond comparably with the normal ovary, disregarding the modality of stimulation (Loh *et al.*, 1999). Two other recent studies reported similar conclusions. The number of oocytes and embryos obtained during IVF-embryo transfer cycles were not significantly decreased after laparoscopic cystectomy compared with patients treated by laparoscopy for pelvic endometriosis but without deep ovarian endometriosis (Canis *et al.*, 2001). Other authors consider that laparoscopic cyst wall vaporization allows the preservation of a good ovarian

response to stimulation by gonadotrophins (Donnez *et al.*, 2001). Finally, ART results following ultrasound-guided aspiration of endometriomas seem satisfactory (Mittal *et al.*, 1999). In this particular context, ultrasound-guided aspiration might be considered as a good alternative as these patients are oriented towards an ART and had previously undergone laparoscopic surgery on several occasions.

Conclusion

Medical therapy is inefficient and cannot be recommended in the management of ovarian endometriomas. Whilst the surgical treatment of choice is surgical laparoscopy, for conservative treatment the preferred method is that of IPC. There are no indications for systematic pre-operative medical treatment to facilitate the cystectomy, whereas post-operative administration of monophasic combined oral contraceptives after laparoscopic surgery appears not to affect the risk of recurrence or pelvic pain. Post-operative medical treatment has no benefits in cases of infertility. When ART techniques are indicated, no rules have been established for the management of these patients, though it is recommended that recurrent ovarian surgery should not be performed in these cases.

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