Endometriosis Infertility

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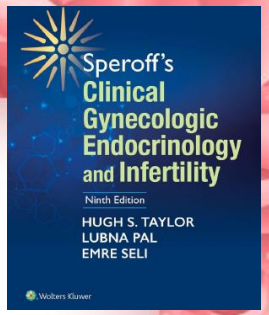
Endometriosis affects 6% to 10% reproductive age women, but is present in 25% to 50% women with unexplained infertility .

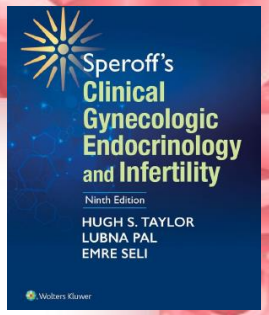
It is characterized by the presence of endometrial glands and stroma located outside of the uterine cavity and is found primarily on the peritoneum, ovaries, and rectovaginal septum .

Fecundability rates in affected patients are estimated at 2% to 10% per month.



The overall prevalence of endometriosis is greater in infertile than in Fertile Women.

Although reduced to a similar extent in untreated women with minimal and mild endometriosis and women with unexplained infertility, monthly fecundity decreases further with increasing severity of disease.



Monthly fecundity of women with minimal and mild endometriosis

Receiving treatment with exogenous gonadotropin stimulation and intrauterine insemination (partner sperm) is lower when compared to women without disease.

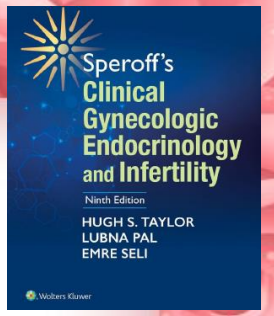
Women with minimal and mild endometriosis are significantly more likely to conceive after surgical treatment than untreated women.

IVF pregnancy rates are negatively correlated with endometriosis severity.

Possible mechanisms for infertility among women with endometriosis include:

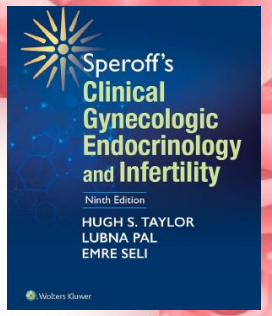
- **Anatomic distortion from adhesions or fibrosis**
- **The impact of chronic inflammation on gametes, embryos ,tubal fimbria and eutopic endometrium**

Laparoscopic visualization and histologic confirmation of biopsied lesion(s) remains the gold standard for the diagnosis of endometriosis.



Taken together, these observations support the conclusion endometriosis decreases fertility to an extent that correlates roughly with the severity of disease.

Furthermore, decreased fertility in women with advanced endometriosis also could result from premature depletion of the ovarian follicular pool (due to ovarian surgery or destruction). The association between endometriosis is likely multifactorial, involving mechanical, inflammatory, cell signaling, and epigenetic origins



Excess production of prostaglandins, metalloproteinases, cytokines, and chemokines results in chronic inflammation that impairs ovarian, tubal, or endometrial function, leading to disorders of folliculogenesis, fertilization, or implantation.

The presence of endometriomas (and resultant inflammation) affects oocyte production and ovulation, while the peritoneal inflammatory milieu itself can also damage oocytes and sperm,decrease tubal motility, and have toxic effects on an embyro

- **Vaginal US has excellent specificity for endometriomas and other deep disease .**
- **It is unclear whether the mere presence of endometriosis negatively affects IVF outcomes.**
- **Endometriosis patients have similar rates of embryonic aneuploidy and live birth with ARTs as compared to unaffected patients.**
- **However, more severe disease (stages III and IV) and previous endometriosis surgery are associated with fewer oocytes retrieved and reduced pregnancy /live birth rates (by 30% to 40%) compared to patients without endometriosis .**

MANAGEMENT

- **Hormonal suppression of endometriosis typically has minimal benefit for endometriosis-related infertility.**
- **For minimal to mild disease, laparoscopic ablation appears to significantly improve pregnancy rates when compared to diagnostic laparoscopy alone as evidenced by a large randomized trial reporting 31% (treated) versus 17% (untreated) pregnancy rates .**
- **A subsequent meta-analysis supported the effectiveness of laparoscopic treatment in stages I to II endometriosis associated infertility**

- **Number needed to treat analysis suggests that eight laparoscopies involving treatment of mild or minimal endometriosis would need to be performed for each pregnancy gained.**

- **A Cochrane review found moderate evidence in favor of particularly excisional laparoscopic treatment of minimal-mild endometriosis for spontaneous pregnancy in the 9 to 12 months postoperatively .**

- **Although removal of endometriomas may be indicated prior to IVF, when they would interfere with oocyte retrieval ,endometrioma resection during IVF/ICSI treatment is associated with decreased ovarian function in up to 13% of cases , reduced quantity of dominant follicles, and fewer retrieved oocytes compared to unoperated patients in a meta-analysis of 2,649 IVF cycles.**
- **Furthermore, 40% of endometriomas recur postoperatively .**
- **Therefore, IVF is considered a reasonable first-line therapy for endometriosis associated infertility because of the short time to pregnancy and avoidance of surgery.**

Sclerotherapy, whereby the endometrioma is drained via transvaginal puncture and a sclerotic agent such as ethanol is instilled into the cyst cavity, was associated with higher numbers of retrieved oocytes and similar pregnancy rates as compared to laparoscopic management, in a meta-analysis of 18 studies, and may be an alternative to surgery

Background: The influence of previous conservative surgery for endometriomas on IVF-ICSI outcome is debated. Conflicting information emerging from the literature may be consequent to the fact that endometriomas are mostly monolateral. The contralateral intact ovary may adequately supply for the reduced function of the affected one. To clarify this point, we assess IVF-ICSI outcome in women operated on for bilateral endometriomas.

Methods: Women selected for IVF-ICSI cycles who previously underwent bilateral endometriomas cystectomy were matched (1:2) for age and study period with patients who did not undergo prior ovarian surgery.

Results: Sixty-eight cases and 136 controls were recruited. Women operated on for bilateral endometriotic ovarian cysts had a higher withdrawal rate for poor response ($P < 0.001$). In these patients, despite the use of higher doses of gonadotrophins, the number of follicles ($P = 0.006$), oocytes retrieved ($P = 0.024$) and embryos obtained ($P = 0.024$) were significantly lower. The clinical pregnancy rate per started cycle in cases and controls was 7% and 19% ($P = 0.037$) and the delivery rate per started cycle was 4% and 17%, respectively ($P = 0.013$).

Conclusions: IVF outcome is significantly impaired in women operated on for bilateral ovarian endometriomas.

IVF–ICSI outcome in women operated on for bilateral endometriomas

Edgardo Somigliana [1], Mariangela Arnoldi, Laura Benaglia, Roberta Iemmello, Anna Elisa Nicolosi, Guido Ragni

Affiliations + expand

PMID: 18441346 DOI: 10.1093/humrep/den133

Abstract

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ethanol sclerotherapy for treating endometrioma: A retrospective cross-sectional study

Abbas Aflatoonian [1], Nasim Tabibnejad [1]

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PMID: 33349801 PMCID: PMC7749973 DOI: 10.18502/ijrm.v13i11.7960

Free PMC article

Abstract

Background: Endometrioma is a common high-recurrence gynecological disease that affects infertility. Surgical resection using laparotomy or laparoscopy is applied as a standard treatment. Moreover, sclerotherapy is reported to be effective as a non-invasive method for treating endometrioma.

Objective: To evaluate whether the ethanol retention or aspiration after sclerotherapy improve pregnancy outcome in infertile women with endometrioma.

Materials and methods: In a retrospective study, hospital records of 43 women with recurrent or bilateral endometrioma who had been undergone transvaginal ultrasound sclerotherapy were reviewed. They were selected to receive either ethanol for 10 min, ethanol injection, irrigation, and then aspiration or total retention without aspiration based on the surgeon's decision. The participants were followed-up for 3, 6 and 12 months for natural or artificial conception as well as for cyst

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Results: Chemical pregnancy was positive in 52% of the women in the aspiration group and 53.8% in the retention group. Ongoing pregnancy (44% vs 46.2%, p = 0.584) and live birth (40% vs 46.2%, p = 0.490) were reported marginally higher in the retention group compared with the aspiration group, and the differences were not statistically significant. Moreover, the recurrence rate were found to be 48.1% and 37.5% in the aspiration and retention groups, respectively (p = 0.542). The cysts size in the retention group was significantly correlated to the recurrence rate.

Conclusion: Both the aspiration and left in situ of ethanol 95% sclerotherapy have the similar impact on the treatment of ovarian endometrioma regarding pregnancy and recurrence rate. However, larger randomized studies with strict inclusion criteria are needed.

Keywords: Ethanol; In vitro fertilization; Pregnancy rate.; Sclerotherapy; Endometrioma.

eCollection 2017.

Weigh the pros and cons to ovarian reserve before stripping ovarian endometriomas prior to IVF/ICSI: A meta-analysis

Xin Tao [1], Lei Chen [1], Shuqi Ge [2], Lisi Cai [1]

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PMID: 28574993 PMCID: PMC5456033 DOI: 10.1371/journal.pone.0177426

Free PMC article

Abstract

Purpose: To explore the effects of conservative surgery for endometriomas on ovarian responsiveness during assisted reproductive technology (ART) and provide reproductive and gynecological doctors with a more reliable reference program for the treatment of endometriomas.

Methods: A literature search was performed by searching the PubMed, Embase, Cochrane Library, Web of Science and Science Direct databases. Studies with inter- and intra-patient comparisons of ovarian responses and oocyte quality between operated and unoperated ovaries and that met the inclusion criteria were retrieved, and the data from the outcome measures were extracted and pooled for this meta-analysis

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Results: Twenty-one published studies (2649 ART cycles) were included. The total amount of gonadotropin (Gn) used (inverse variance (IV):0.48; 95% confidence interval (CI): [0.13, 1.82], P = 0.0007) was significantly increased in the women with endometriomas who had a history of cystectomy. The estrogen (E) level on the day of hCG administration (IV: -0.29; 95% CI: [-0.41, -0.17], P<0.00001), the number of mature or dominant follicles (IV: -1.17; 95% CI: [-1.51, -0.82], P<0.00001) and the total number of oocytes retrieved (IV: -1.78; 95% CI: [-2.38, -1.17], P<0.00001) were significantly decreased in the women with endometriomas who had a history of cystectomy. The duration of stimulation (IV: 0.02; 95% CI: [-0.09, 0.13], P = 0.77), the total number of formed embryos (IV: -0.06; 95% CI: [-0.17, 0.04], P = 0.25), the pregnancy rate(IV:0.98;95%CI[0.82,1.18], P = 0.83) and the live birth rate(IV:0.93;95%CI[0.70,1.23], P = 0.61)were not statistically different between the two groups. Similar intra-patient results were found in the number of mature or dominant follicles (IV: -0.88; 95% CI: [-1.25, -0.52], P<0.00001) and the total number of oocytes retrieved (IV: -3.48; 95% CI: [-4.77, -2.19], P<0.00001).

Conclusion: ART might be a better therapeutic method for ovarian endometrioma-related infertility

Bilaterality of ovarian endometriomas does not affect the outcome of in vitro fertilization/intracytoplasmic sperm injection in infertile women after laparoscopic cystectomy

Hsing-Tse Yu [1], Hong-Yuan Huang [1], Hsiao-Jung Tseng [2], Chin-Jung Wang [3], Chyi-Long Lee [1], Yung-Kuei Soong [1]

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PMID: 29179885 PMCID: PMC6138598 DOI: 10.1016/j.bj.2017.06.009

Free PMC article

Abstract

Background: To assess whether the unilateral or bilateral lesions can affect ovarian reserve and pregnancy outcome in in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) in infertility patients underwent laparoscopic cystectomy.

Methods: A total of 148 IVF/ICSI cycle in patients who had undergone laparoscopic cystectomy for unilateral or bilateral endometriomas were reviewed retrospectively. There were 103 cycles where

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Background: To assess whether the unilateral or bilateral lesions can affect ovarian reserve and pregnancy outcome in in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) in infertility patients underwent laparoscopic cystectomy.

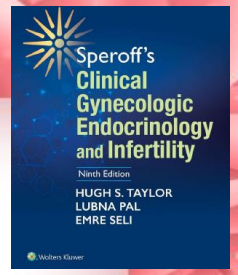
Methods: A total of 148 IVF/ICSI cycle in patients who had undergone laparoscopic cystectomy for unilateral or bilateral endometriomas were reviewed retrospectively. There were 103 cycles where laparoscopic cystectomy had been carried out for unilateral endometriomas and 45 cycles after bilateral-side surgery. Primary outcome measures were ovarian reserve and ovarian response. Secondary outcome measures were the implantation rate, clinical pregnancy rate, and live birth rate.

Results: The number of dominant follicle on the day of human chorionic gonadotropin (hCG) administration (5.2 ± 3.1 vs. 4.2 ± 2.7; p = 0.048), and oocytes retrieved (10.0 ± 6.9 vs. 7.6 ± 6.6; p = 0.047) were significantly lower in the bilateral-side group compare with the unilateral-side group. However, the mean number of antral follicle count, metaphase II oocytes, the doses of gonadotropin used, fertilization rate, the rate of good quality embryos transferred, implantation rate and clinical pregnancy, live-birth rate and miscarriage rate were similar between the two groups.

Conclusion: There were no associations among the bilaterality of ovarian endometriomas, ovarian reserve and pregnancy outcomes in IVF/ICSI cycles. However, bilateral ovarian endometriomas after laparoscopic cystectomy may impair ovarian response as compared to unilateral ovarian endometrioma.

Keywords: Bilaterality; Endometrioma; Intracytoplasmic sperm injection; In vitro fertilization; Laparoscopy

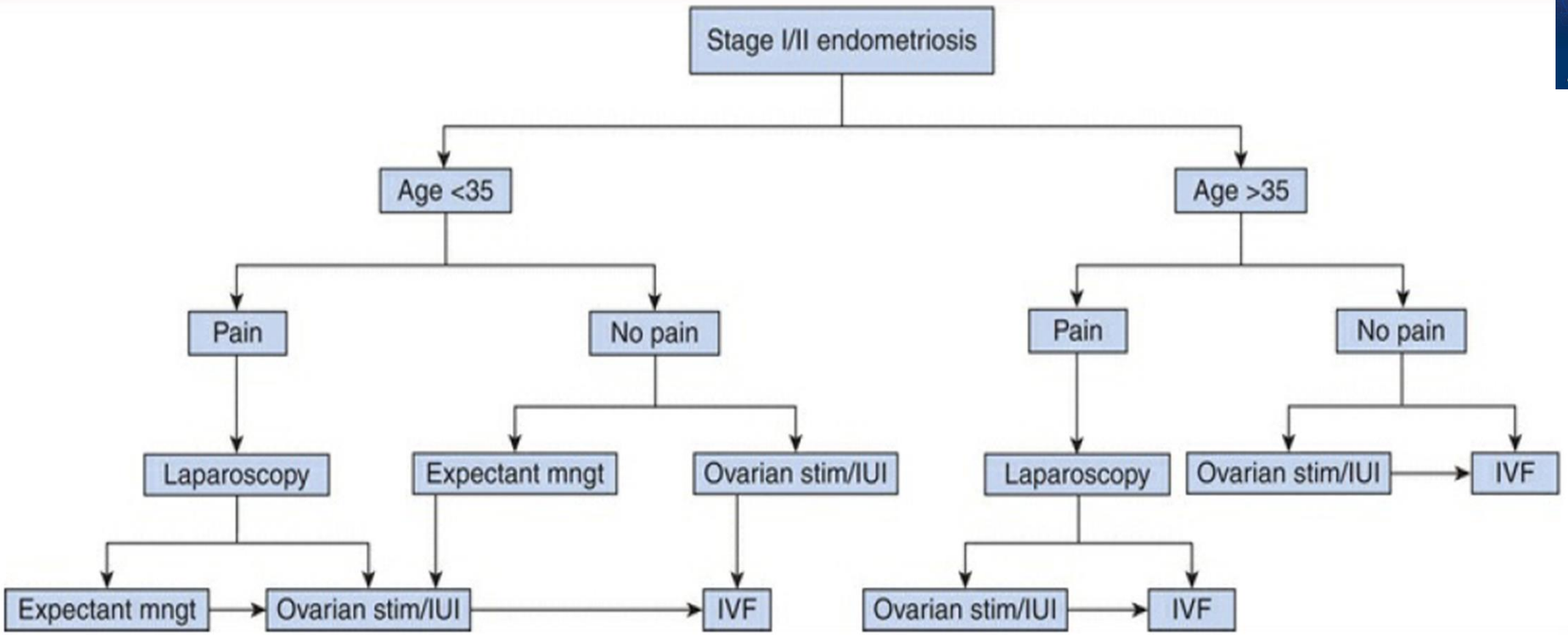
TREATMENT OF ENDOMETRIOSIS ASSOCIATED INFERTILITY



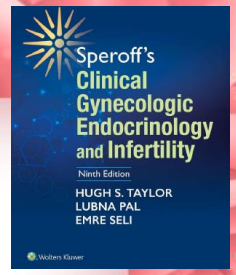
While not routinely recommended, expectant management is an option for women who are hesitant to pursue ovarian stimulation with or without intrauterine insemination (IUI) or IVF.

As mentioned earlier, the fecundity rate of women with endometriosis is lower than in the noninfertile reproductive population; however , women with endometriosis can conceive without intervention.

As the overall likelihood of success with expectant management is less, it should only be considered in women who do not have advance-stage disease and who are <35 years age.



Current strategies for endometriosis management. Obstet Gynecol Clin North Am 42(1):87, 2015, with permission from Elsevier

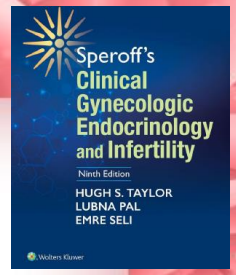


Medications used to treat endometriosis-associated pain are predominantly hormonal and suppress ovulation.

In a Cochrane review of 25 trials using ovulation suppressive agents (COCs, progestins, danazol, GnRH agonists) in an effort to improve fertility in women with endometriosis, there was no benefit to use of ovulation suppression.

Use of ovulation suppression agents increased time to conceive.

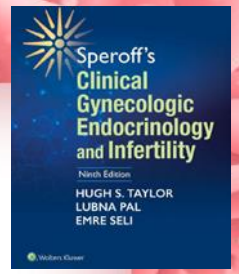
The one exception is the use of GnRH agonists or COCs for suppression of endometriosis in patients undergoing IVF.



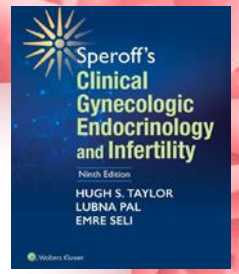
A review of three randomized controlled trials using a GnRH agonist for 3–6 months prior to IVF found that both the clinical pregnancy and live birth rates were significantly higher in the GnRH agonist group compared to the control group.

In a pilot trial assessing effect of 6–8 weeks of COC use prior to IVF in women with endometriosis, it was found that COC use significantly increased the odds of pregnancy.

Furthermore, COC use may be as effective as GnRH agonist, although larger randomized trials are needed to confirm this.



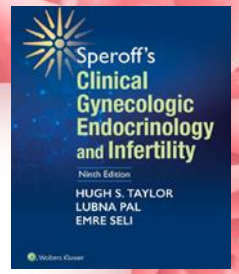
The effects of surgery on fertility in women with minimal and mild endometriosis have been examined in two randomized controlled trials. In a multicenter Canadian trial, women with unexplained infertility had diagnostic laparoscopy, and those with minimal or mild endometriosis were randomized to treatment (excision or ablation of disease) or expectant management and followed for 36 weeks or until 20 weeks of gestation if pregnancy occurred during follow-up.



The chance of pregnancy in treated women was twice that in untreated women (OR = 2.03, CI = 1.28–3.24).

Overall, 50/172 (0.29) women randomized to treatment achieved an ongoing pregnancy, compared to 29/169(0.17) of those managed expectantly, yielding a treatment effect of 0.12 and a number needed to treat (the inverse of the treatment effect) of 8.3, rounded upward to 9.

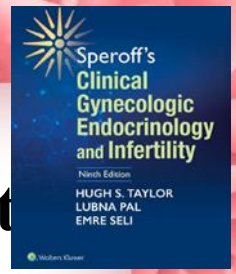
The results suggest that approximately nine infertile women with minimal or mild endometriosis must undergo surgical treatment to achieve one additional pregnancy.



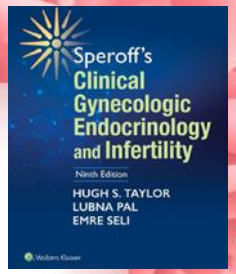
However, in a second smaller Italian trial of similar design (n = 96), no difference between treatment and no treatment was observed.

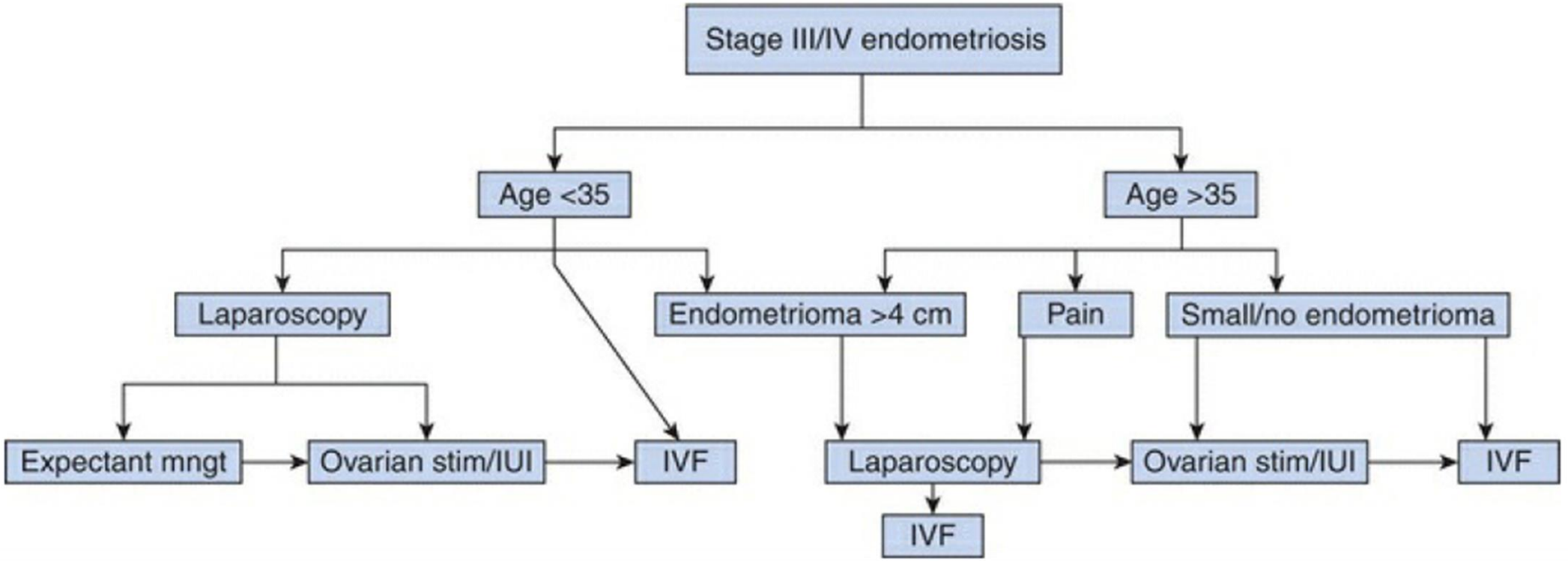
A meta-analysis combining the data from both studies concluded that surgical treatment of minimal and mild endometriosis may improve fertility (OR = 1.64, CI = 1.05–2.57); the number needed to treat was 12.

In women with mild to moderate disease, surgical treatment with removal of endometrial implants has the potential benefit of decreasing inflammation, which may improve fertility



For women with endometriomas, the literature is clear—the cumulat pregnancy rate 1–3 years after surgical treatment is approximately 50% for women with endometriomas, and response to gonadotropins is also improved.





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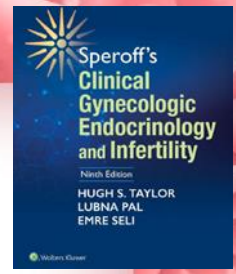
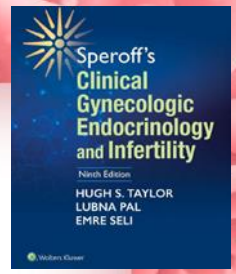


In severe disease, potential benefits of surgery include:

- **lysis of adhesions**
- **ideally resultant restoration of normal pelvic anatomy.**

Two randomized controlled trials demonstrated that laparoscopy was beneficial for advance-stage disease.

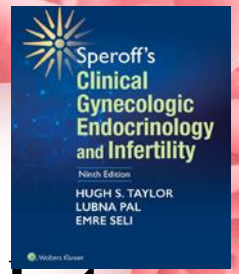
In addition, for women who are in pain and attempting to conceive, surgical intervention should be an option prior to proceeding with ovarian stimulation /IUI or IVF, as available regimens can exacerbate pain



In a prospective cohort study involving 169 infertile women under age

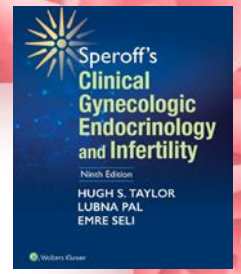
38 with symptomatic deep infiltrating endometriosis, the pregnancy rate achieved with IVF was significantly higher in women who chose to have preliminary surgical treatment.

Although the advantages of surgical treatment in infertile women with severe endometriosis seem obvious, there are few randomized controlled trials assessing the potential benefits, and more research is needed.



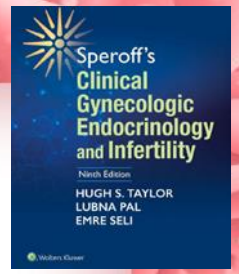
The use of adhesion barriers reduces adhesion formation after surgical treatment in infertile women , but there is no convincing evidence that adhesion barriers or other adhesion prevention strategies improve pregnancy rates after surgical treatment.

OVARIAN STIMULATION & ASSISTED REPRODUCTIVE TECHNOLOGY



In patients with minimal to mild endometriosis with patent tubes, ovarian stimulation (with clomiphene citrate, letrozole, or gonadotropins) with or without intrauterine insemination can be tried, as fertility rates are increased.

This method is preferred when the patient does not have distorted anatomy; however, no more than four cycles are recommended, as each can stimulate endometriotic lesions.



As mentioned earlier, IVF success rates in women with endometriosis are similar to those with tubal and male factor and unexplained.

It still remains unclear how much endometriosis affects pregnancy rates when compared to other causes of infertility.

However, in vitro fertilization is currently the most effective treatment of endometriosis-associated infertility, especially in women with advanced disease.