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The Effect of Surgery on Endometriomas in Fertility (2nd edition)

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This guidance is for healthcare professionals who care for women, non-binary and trans people with ovarian endometriosis, also known as an ovarian endometrioma.

Plain language summary

Endometriosis is a condition where the lining of the uterus (womb) is found in other locations such as, but not limited to, the ovaries, bowel, and bladder. It is a common condition that can affect up to 1 in 10 women and people, and can be found in up to 3-5 in 10 women with a diagnosis of infertility.

Women with endometriosis often present with painful periods, heavy periods, pain while opening their bowels or passing urine, pain during sexual intercourse and difficulty in conceiving. A proportion of women with endometriosis remain asymptomatic of the disease and as such, care should be tailored to each individual.

The significant improvement in diagnostic technology has increased the detection rate of endometriosis. Women with ovarian endometriosis, also known as an ovarian endometrioma, can be diagnosed using a transvaginal (internal) or transabdominal (via the tummy) ultrasound scan. The detection rates have been reported in up to 90% for routine ultrasound scans.

Ovarian endometriomas can impact fertility outcomes, and these women, therefore, require a multidisciplinary approach to their care. The presence of an ovarian endometrioma and endometriosis is known to have a negative impact on the ovarian reserve (egg count and quality) and overall, chance of successful conception. Women with known endometriosis should therefore be counselled about the various options available for fertility preservation.

The treatment for ovarian endometrioma(s) in women wanting to conceive can be broadly divided into two categories, expectant (watch and wait approach), and surgical, involving most commonly keyhole surgery.

Expectant management carries with it the reduced risk of surgery and a general anaesthetic, along with no further surgically related reduction in ovarian reserve. It also reduces the delay from diagnosis to starting fertility treatment. The disadvantages of this approach, however, would be the persistence of pain symptoms, and ongoing difficulty with accessing the ovary during assisted fertility treatment such as in vitro fertilisation.

Surgical treatment for ovarian endometrioma(s) in the context of women trying to conceive is often approached with caution. Surgery has been shown to reduce the ovarian reserve further, and clinicians would attempt to limit the degree of impact by reducing the amount of surgical stress to the ovary. The benefits of this approach, however, would be an improvement in symptoms and access to the ovary for fertility treatment.

Current best practice is a multidisciplinary team approach to managing women with endometriosis and early involvement of a fertility expert in the care of these women.

1. Background

Endometriosis is increasingly recognised as a systemic inflammatory condition extending beyond the pelvis.[1] It is characterised by the presence of endometrium-like epithelium and/or stroma outside of the endometrium and myometrium.[2] It is estimated that 5-10% of women[1] mainly of reproductive age, are affected by the condition, with a reported higher prevalence in certain subgroups, such as those affected by infertility, 30-50%.[3-4] Endometriotic ovarian cysts (known as 'endometriomas') can be found in up to 17-44% of women with endometriosis and are often associated with the severe form of the disease.[5-6] While the pathognomonic mechanisms of endometriosis per se remain elusive, it is widely believed that most endometriotic lesions develop from retrograde menstruation and are possibly associated with immune dysfunction, which can interfere with endometrial implant clearance.[7] Ovarian endometrioma(s) are mostly thought to occur through the invagination of endometriotic tissue/cells on the ovarian serosa, for example, during remodeling of the ovarian cortex after ovulation.[8]

The presence of an endometrioma(s) can often present a clinical dilemma during fertility treatment. For example, there can be uncertainty regarding the decision to operate or to manage conservatively, balancing the potential detrimental effect of surgery on ovarian reserve largely reflected by a lower anti-mullerian hormone (AMH) level, antral follicle count (AFC) and oocyte yield, against the potential benefit that may be gained from surgery, such as an improvement in symptoms aiding natural conception or improved follicular access during assisted reproductive techniques. Ovarian reserve and its parameters, however, do not reflect the chances of natural conception but provide information and largely represent how the woman or person would respond to controlled ovarian stimulation in assisted reproductive treatments such as in vitro fertilisation (IVF).

The optimal intervention for the management of endometriomas is largely debated. Many different techniques exist, with the recommendation for treatment needing to be individualised to the woman's specific circumstances, such as the presence of concomitant pain, unilateral or bilateral disease and the location of the follicles in relation to the site of the endometrioma. Fertility preserving surgical management options of an endometrioma include ultrasound-guided or laparoscopic-guided cyst aspiration, cystectomy or fenestration and coagulation. In the presence of bilateral disease, a more conservative approach may be favoured to help preserve as much normal ovarian tissue as possible. In an asymptomatic individual, as long as the endometrioma does not prevent access to the follicles, it can be left untreated.[9] However, the removal of endometriomas larger than 4cm in diameter have been linked to higher spontaneous pregnancy rates.[10]

Current guidelines often rely on evidence from historical studies, which tend to be either small and/or retrospective in design. This Scientific Impact Paper will review the current evidence for management of endometriomas within the context of infertility treatment and offer an opinion of how best to counsel patients in their journey, taking into consideration improvements made with stimulation protocols and laboratory techniques as well as advancements made in benign laparoscopic surgery.

Within this document we use the terms woman and women's health. However, it is important to acknowledge that it is not only women for whom it is necessary to access women's health and reproductive services in order to maintain their gynaecological health and reproductive wellbeing. Gynaecological and obstetric services and delivery of care must therefore be appropriate, inclusive

and sensitive to the needs of those individuals whose gender identity does not align with the sex they were assigned at birth.

2. Potential mechanisms for endometriosis-associated infertility

Fecundity rates may be reduced in women with endometriosis, with a nearly two-fold increased risk of infertility in women aged under 35 years, with an approximately 2-10% fecundity rate per month compared to 15-20% per month in healthy couples,[3, 11] potentially related to the severity of the disease (revised American Society for Reproductive Medicine [rASRM] classification).[12] The presence of ovarian endometriomas is usually associated with rASRM staging of moderate or severe disease.[5] A number of theories for endometriosis-related infertility have been proposed, including chronic inflammation and reduced endometrial receptivity, tubo-peritoneal anatomic distortion, compromised oocyte and embryo quality, reduced ovarian reserve, but the precise mechanism has yet to be determined.[13]

2.1 Chronic inflammation

Endometriosis is associated with dysregulation of the immune system. Peritoneal fluid from women with endometriosis has been found to contain increased numbers of immune cells, including macrophages, and mast, natural killer and T cells, as well as elevated levels of growth factors, chemokines and cytokines.[14-16] The enhanced inflammatory state might affect the quality of the oocytes and impair ovarian function, resulting in defective folliculogenesis and fertilisation.[17]

2.2 Endometrial receptivity

Implantation and trophoblast invasion can be disrupted in the presence of endometriosis by the dysregulation of signaling pathways and molecules (proteins) in endometrial stromal cells, differential endometrial gene expression, alterations in cell physiology and vascular abnormalities. Inflammation, a consequence of endometriosis, is known to alter endometrial receptivity.[18] Implantation and clinical pregnancy rates have been shown to be significantly reduced by 7.67% and 13.33% respectively, in women with endometriosis compared to women without endometriosis.[19] This finding, however, has been shown to be overcome by employing the freeze-all strategy where all suitable embryos are cryopreserved and no fresh embryo transfer is undertaken, increasing both the clinical pregnancy rates (13.4%) and cumulative ongoing pregnancy rates (17%) in frozen cycles compared to fresh cycles.[20-21]

2.3 Oocyte and embryo quality

Oocyte and embryo quality are key determinants of reproductive outcomes. Oocyte competence (growth and maturation) is influenced by the follicular fluid, which is composed of many substances, such as hormones, cytokines, immune cells (including natural killer cells, lymphocytes, and macrophages), enzymes, anticoagulants, electrolytes, reactive oxygen species, lipids, cholesterol, and antioxidants. In endometriosis, dysregulation of molecular mechanisms may alter the follicular microenvironment, represented by elevated concentrations of progesterone and interleukin-6 and decreased concentrations of vascular endothelial growth factor,[22] inhibiting embryonic development by affecting the mRNA, mitochondria, lipid and protein reserves. Furthermore, the degree of apoptosis of the granulosa cells surrounding the oocyte, alterations of the cell cycle and incidence of oxidative stress has been suggested to be greater in women with endometriosis than in women with other causes for their infertility.[3] Embryo development with autologous oocytes is slower in women with endometriosis than in women with tubal factor infertility.[23] Women with moderate-to-severe disease, however, receiving eggs from a donor without endometriosis have a similar pregnancy rate

to other egg recipients.[24-25] The implantation rate has been shown to be reduced by 4.2-16.6% and the pregnancy rate by 16.7-33% if oocytes are donated by women with endometriosis compared with no endometriosis.[25]

2.4 Ovarian reserve

The presence of ovarian endometriomas, especially if bilateral, can affect the ovarian reserve, impacting the ovarian response to gonadotrophins during assisted reproductive techniques (ART). A histological study[26] reported a significant reduction in the primordial follicle cohort in affected ovaries. Follicle depletion may be secondary to damage induced by the endometriosis-associated inflammatory reaction and by increased tissue oxidative stress leading to fibrosis.[27] A group of potentially toxic agents, such as free iron, that can diffuse through the cyst wall of the endometrioma, as well as long-lasting mechanical stretching of the ovarian cortex, might all detrimentally impact the ovarian reserve.[28] Most importantly, however, is the negative effect of ovarian surgery on ovarian reserve, especially if repeated surgical interventions are undertaken (see sections 3.1.2 and 3.2.2).

3. Management options

While the options include expectant and surgical management in the context of fertility, the recommended treatment should be guided by: the woman's symptoms; fertility prognostic factors, including age and ovarian reserve; previous treatment history with specific reference to past surgical interventions; size and nature of the cyst; unilateral or bilateral, and the wishes of the woman or person.[29] Treatment of incidental disease in otherwise asymptomatic women is currently not recommended, as the development and natural progression of endometriomas is not well understood.[30]

3.1 Natural conception

3.1.1 Conservative management for natural conception

Women with regular menstrual cycles and an incidental finding of an ovarian endometrioma without suspicion of malignancy, who wish to conceive, should be encouraged to try natural conception before seeking fertility treatment. While the evidence of the impact of an endometrioma on spontaneous conception is limited, a prospective observational study[31] (n=244) reported a 43% spontaneous pregnancy rate during the 6-month follow-up period in the presence of unilateral endometriomas of varying sizes (diameter 5.3$\pm$1.7cm [mean$\pm$SD]). The study also reported similar ovulation rates in the affected ovary to the healthy ovary (49.7% versus 50.3%), not influenced by the laterality of the endometriomas, their number and size, or by the presence of deep endometriosis diagnosed by ultrasound scan. This finding contradicted previously reported data in a smaller prospective study (n=70),[32] of reduced ovulation in the affected ovary (31% versus 69%). Conservative management for fertility should be weighed against the potential benefits and risks of surgery or fertility treatment. The dilemma is most acute for those who have a low ovarian reserve and are potential poor responders.

Women with known endometriosis should be advised to attempt natural conception for 6-months and if they do not become pregnant, to seek specialist consultation. For those with a known diminished ovarian reserve, a six-month delay to their IVF treatment has not been shown to detrimentally impact their overall outcome.[33]

3.1.2 Surgical treatment for natural conception

There is controversy regarding surgical management of endometriomas in women with an incidental finding. Surgery in the form of laparoscopic excision or ablative treatment of peritoneal endometriosis (rASRM stage I [minimal endometriosis with a few superficial implants]/II [mild endometriosis with a greater number and deeper implants than stage I] endometriosis) has been shown to improve the clinical pregnancy rate compared to a diagnostic laparoscopy alone (odds ratio [OR] 1.89, 95% CI 1.25 to 2.86; three randomised controlled trials [RCTS] including 265 patients who underwent surgical intervention versus 263 who underwent a diagnostic laparoscopy only).[34] However, by restoring pelvic anatomy, it remains unclear as to whether surgical intervention on the ovary itself is beneficial. It is not believed to reverse the inflammatory and biomolecular changes shown to influence fertilisation and implantation.[35] No comparative studies evaluating the spontaneous conception rate after surgery for an endometrioma or deep endometriosis compared to no surgical intervention have been identified.[30]

Furthermore, there are concerns regarding the safety of surgical treatments, with a reported reduction in ovarian reserve[36-37] and the small added risk of requiring an oophorectomy. In contrast, concerns have been raised about the effect of an endometrioma on oocyte quantity and quality. This conflict suggests that management should be individualised and based upon clinical factors, including pain symptoms, size of the cysts and concerns over potential malignancy. Consideration should be given to surgical treatment being undertaken by a gynaecologist with specific expertise in endometriosis and fertility, to minimise the impact on ovarian reserve and provide a holistic assessment regarding future fertility management.

When performing surgery, ovarian endometriomas are best managed by performing a cystectomy, as opposed to drainage with adjuvant therapy such as coagulation. Preoperative assessment of AMH levels may be beneficial in knowing the baseline ovarian reserve before embarking on surgery, and helping clinicians and women in making an informed decision, as a cystectomy may potentially reduce the ovarian reserve. A cystectomy is associated with an overall lower risk of recurrence and less endometriosis-associated pain, especially if the cyst is 3cm or more in diameter.[38] The rate of recurrence after laparoscopic ovarian cystectomy is approximately 6-67%, while the rate of recurrence after aspiration is 28-98%, reducing to approximately 15% after surgery in conjunction with sclerotherapy.[39] Hart et al[38] summarised two RCTs where a beneficial effect of excisional surgery of an endometrioma compared to drainage or ablation on spontaneous pregnancy rates (OR 5.24, 95% CI 1.92 to 14.27; n=88; 2 trials) in infertile women was demonstrated. This finding is further supported by a comparative study that demonstrated higher spontaneous pregnancy rates after a laparoscopic ovarian cystectomy (55.5%) compared with cyst vaporisation with CO_2 laser (35.9%).[40]

3.2 Assisted conception

3.2.1 Effect of endometriosis and endometriomas on IVF outcomes

Evidence of the impact of an endometrioma on ovarian response during IVF is equivocal. Systematic reviews including controlled studies have reported similar ovarian response in women with and without endometriosis.[41] Similar outcomes in ovarian response are also seen when a unilateral ovarian endometrioma is compared to a normal contralateral ovary in the same women.[42] The live birth rate (OR 0.96, 95% CI 0.82 to 1.12; 8 studies; n=4157), clinical pregnancy rate (OR 0.84, 95% CI 0.69 to 1.03; 15 studies; n=9692) and mean number of oocytes retrieved per cycle (-0.58, 95% CI 21.16 to 0.01; 11 studies) have been shown to be comparable in those with stage I/II endometriosis and no endometriosis. In contrast, the live birth rate (OR 0.77, 95% CI 0.64 to 0.92; 8 studies), clinical pregnancy rate (OR 0.60, 95% CI 0.44 to 0.81; 15 studies; n=9471) and mean number of oocytes

retrieved (21.76, 95% CI 22.73 to 0.79; 14 cycles; n=9172) were significantly lower in women with stage III (moderate endometriosis with a number of deep implants, including small endometriomas on one or both ovaries and the presence of filmy adhesions)/IV (severe endometriosis with a number of deep implants, including large endometriomas on one or both ovaries and the presence of dense adhesions) endometriosis compared to no endometriosis.[43] However, the live birth rate (OR 0.98, 95% CI 0.71 to 1.36; 5 studies; n=928 women), clinical pregnancy rate (OR 1.17, 95% CI 0.87 to 1.58; 5 studies; n=928 women) and miscarriage rate (OR 1.70, 95% CI 0.86 to 3.35; 3 studies; n=171 pregnancies) were similar between women with and without an endometrioma, but the mean number of oocytes retrieved (mean difference -0.23, 95% CI -0.37 to -0.10; 5 studies; n=941 cycles) was significantly lower and the cycle cancellation rate (OR 2.83, 95% CI 1.32 to 6.06; 3 studies; n=491) significantly higher in those with an endometrioma compared to those without.[44] Furthermore, studies[45-48] have reported on the potential detrimental effect of the size of the endometrioma on ovarian response, especially when it is 3cm or more in diameter. These findings have been replicated by Alshehre et al (2020)[48,] who compared reproductive outcomes following ART in women with an endometrioma and controls, including those without an endometrioma, tubal factor or male infertility. The number of oocytes (n=428 women had an endometrioma and 523 controls) (weighted means difference [WMD] -2.25, 95% CI 3.43 to -1.06) and the number of mature oocytes retrieved (n=140 women had an endometrioma and 186 controls) (WMD -4.64, 95% CI 5.65 to -3.63) were significantly lower in the presence of an endometrioma compared to the control group. In contrast, the gonadotrophin dose (n=178 women had an endometrioma and 249 controls) and total duration (n=173 women had an endometrioma and 241 controls), number of high-quality embryos created (n=156 women had an endometrioma and 185 controls), clinical pregnancy rate (n=152 women had an endometrioma and 251 controls), implantation rate (n=241 women had an endometrioma and 361 controls) and live birth rate (n=76 women had an endometrioma and 134 controls) were comparable.[48] Of note, no pelvic abscesses were recorded in a series of 214 women undergoing oocyte retrieval in the context of endometriomas under antibiotic prophylaxis.[49]

When comparing women with an intact endometrioma with those with peritoneal endometriosis only, there was no differences in the live birth rate (OR 0.92, 95% CI 0.92 to 1.79; two studies; n=353 women), clinical pregnancy rate (OR 0.87, 95% CI 0.56 to 1.35; 3 studies; n=518 women), miscarriage rate (OR 0.86, 95% CI 0.18 to 4.17; two studies; n=175 pregnancies), mean number of oocytes retrieved (mean difference -0.31, 95% CI -1.03 to 0.42; three studies; n=539 cycles) and cancellation rate (OR 0.82, 95% CI 0.23 to 2.93; one study; n=46 cycles).[44]

Different ovarian stimulation protocols in ART cycles have not been shown to affect the outcomes in women and people with stage III/IV disease. In contrast, an observational retrospective cohort study (n=386) has demonstrated a higher biochemical, clinical pregnancy and live birth rate (42.8% vs. 26.7%) in women with stage I/II disease with gonadotrophin releasing hormone (GnRH) agonist protocols compared to antagonist protocols.[50]

Basal follicle stimulating hormone levels were higher in women with an endometrioma compared to women with no evidence of endometriosis (mean difference 0.20, 95% CI 0.02 to 0.38; three studies; n=491 cycles) but similar to women with peritoneal endometriosis (mean difference 0.41, 95% CI -0.29 to 1.10; 2 studies; n=190). The antral follicle count (mean difference -0.02, 95% CI -0.21 to 0.18; two studies; n=433 cycles) and total stimulation dose (mean difference -0.07, 95% CI -0.27 to 0.12; two studies; n=433 cycles) were comparable in those with an endometrioma and no evidence of endometriosis.[44] Although equivocal, most studies[51-52] report that the observed reduced ovarian response, especially in the presence of larger endometriomas, is related to an overall reduced ovarian reserve in women with an endometrioma.

An adverse impact of endometriomas and endometriosis on oocyte quality has been suggested by

Simón et al[53] who reported on data from an oocyte donation programme. Within this, women with endometriosis were shown to have the same chance of implantation and pregnancy as other oocyte recipients, when the oocytes came from donors without known endometriosis. However, the implantation rates were reduced in healthy recipients when the oocytes came from donors with endometriosis, suggesting the condition had a negative effect on oocyte quality. Nevertheless, the European Society of Human Reproduction and Embryology (ESHRE) guideline for the management of endometriosis,[29] published 20 years after Simón et al[53], has not identified such differences. ESHRE are reassured by the reproductive outcomes demonstrated in large databases that include more recent IVF cycles, such as the Human Fertilisation and Embryology Authority and the Society for Assisted Reproductive Technology.

3.2.2 Surgical treatment prior to IVF

Surgical treatment of endometriomas prior to IVF is widely practised,[54] although debatable on its effect and need. The live birth rate (OR 0.90, 95% CI 0.63 to 1.28; five studies; n=655), clinical pregnancy rate (OR 0.97, 95% CI 0.78 to 1.20; 11 studies; n=1512) and miscarriage rate (OR 1.32, 95% CI 0.66 to 2.65; four studies; n=195 pregnancies) were found to be comparable between women who underwent surgical treatment of an endometrioma prior to ART and conservative management of an intact endometrioma.[44] A further systematic review and meta-analysis did not demonstrate an advantage of surgical pre-treatment of an endometrioma on live birth rates (OR 1.08, 95% CI 0.80 to 1.45; seven studies).[55] While the mean number of oocytes retrieved (mean difference -0.17, 95% CI -0.38 to 0.05; nine studies; n=810 cycles) and the cancellation rate per cycle (OR 1.17, 95% CI 0.69 to 2.00; four studies; n=647 cycles) were comparable, women who underwent surgical pre-treatment of an endometrioma had a lower antral follicle count (mean difference -0.53, 95% CI -0.88 to -0.18; four studies; n=558 cycles) and required higher doses of gonadotrophins for ovarian stimulation (mean difference 1.45, 95% CI 0.23 to 2.68; four studies; n=635 cycles).[44] Women who had undergone surgical management of a unilateral endometrioma had a lower number of oocytes retrieved from the surgically-treated ovary (mean difference -2.59, 95% CI -4.13 to -1.05; four studies; n=222 cycles)[44] when compared with the contralateral normal ovary, indicating a reduction in the ovarian reserve following surgical intervention, as has been reported in several other studies.[35, 45, 51] The potential physiological compensation by the normal ovary for the compromised ovary, in conjunction with the higher follicle stimulating hormone doses required for ovarian stimulation, may account for the similar IVF outcomes noted in women who have undergone surgical treatment for their endometriomas.[46]

Furthermore, no difference in the live birth rate (OR 0.72, 95% CI 0.37 to 1.37; two studies; n=371), clinical pregnancy rate (OR 0.99, 95% CI 0.71 to 1.38; six studies; n=893) and miscarriage rate (OR 0.80, 95% CI 0.17 to 3.72; two studies; n=69 pregnancies) was seen between women who had undergone surgical pre-treatment of an endometrioma versus peritoneal endometriosis. The total gonadotrophin dose required for ovarian stimulation (mean difference 0.18, 95% CI -0.25 to 0.61; two studies; n=167 cycles) was not different, but the mean number of oocytes retrieved (mean difference -0.33, 95% CI -0.53 to -0.13; 7 studies; n=1101 cycles) was significantly lower in those who underwent surgical pretreatment of an endometrioma compared to peritoneal endometriosis.[44]

Different surgical techniques have been employed to manage an endometrioma with no superiority demonstrated for one approach over another.[30] A Cochrane review incorporating two small RCTs has reported similar pregnancy rates for surgical (cystectomy or aspiration) and expectant management.[56] While no differences in pregnancy rates have been shown between a cystectomy and aspiration of an endometrioma, a cystectomy is associated with a lower ovarian response following controlled stimulation, with a lower number of mature oocytes retrieved, raising concern about the potential adverse influence of a cystectomy on ovarian reserve. A retrospective cohort

study found a higher cancellation rate following an ovarian cystectomy compared to conservative management.[57] In contrast, a meta-analysis incorporating controlled studies (including non-RCT studies) reported similar ovarian responses (mean difference in the number of oocytes retrieved -0.17, 95% CI -0.56 to 0.22; four studies; n=289 cycles) and clinical pregnancy rates (OR 0.98, 95% CI 0.57 to 1.69; three studies; n=232 women)[44] following IVF in women with an endometrioma surgically managed with a cystectomy compared to transvaginal aspiration. The total gonadotrophin dose required to achieve ovarian stimulation (mean difference -0.02, 95% CI -0.42 to 0.38; two studies; n=100 cycles) was also comparable.[44]

Ethanol sclerotherapy is a potential adjuvant to the management of endometriomas that are aspirated. In this treatment, the endometrioma is first aspirated, followed by the instillation and flushing through of the cyst with 96% ethanol for 10mins. The ethanol is then re-aspirated and removed completely.[58] A systematic review and meta-analysis evaluating the effect of ethanol sclerotherapy with ovarian cystectomy demonstrated a similar clinical pregnancy rate (OR 1.63, 95% CI 0.91 to 2.9; three studies; n=214 women) but significantly higher oocyte yield (mean difference 2.7, 95% CI 0.98 to 4.4; three studies; n=178 women) with sclerotherapy. No difference was seen in the clinical pregnancy rate (OR 1.1, 95% CI 0.57 to 2.12; three studies; n=164 women) and oocyte yield (mean difference −0.51, 95% CI −2.23 to 1.21; three studies; n=148 women) between those treated with sclerotherapy or conservatively.[59] In contrast, a very small retrospective study reported a more than two-fold higher chance of a live birth following ethanol sclerotherapy compared to conservative management (OR 2.68, 95% CI 1.13 to 6.36; n=74).[60]

A review based on the combined results of eight studies (n=553 women) demonstrated no significant difference in the clinical pregnancy rate of women with endometriosis managed with either surgery alone (43.8%, 95% CI 22.5 to 66.4), surgery plus assisted reproductive techniques (ART) (38.3%, 95% CI 32.3 to 44.7), aspiration ± sclerotherapy plus ART (40.8%, 95% CI 27.7 to 54.6) or ART alone (32%, 95% CI 15.0 to 52.0).[39]

Based on the available evidence, the ESHRE guideline concluded that a cystectomy for an endometrioma larger than 3cm, before undergoing IVF treatment, does not improve live birth rates and is likely to have a negative impact on ovarian reserve.[30] However, surgery before ART can be considered for the management of endometriosis-associated pain, for increasing the accessibility of the follicles during the oocyte retrieval procedures, or to ameliorate any concern for malignancy. No one surgical technique is considered superior in terms of reproductive outcomes. Ovarian reserve is largely said to be impacted by repeated surgical procedures on the same ovary compared to the first surgical intervention.[61] The management of bilateral endometriomas can have a greater negative effect on ovarian reserve compared to surgical treatment of unilateral disease.[62]

Despite the lack of evidence of the clear benefit of surgical treatment for the management of an endometrioma on reproductive outcomes, and the various potential drawbacks and risks, conservative management in women with an endometrioma undergoing IVF treatment has been questioned. The presence of an endometrioma may theoretically interfere with ovarian responsiveness to controlled stimulation and oocyte competence, as well as pose potential risk and technical difficulties during oocyte retrieval, including the associated risks to injury to adjacent organs due to altered pelvic anatomy with the presence of adhesions, infection and abscess formation, follicular fluid contamination with endometrioma content, progression of endometriosis, further growth and rupture of the endometrioma, missed occult malignancy and cancer development in later life. A systematic review evaluating the potential risks of conservative management in women with a known endometrioma undergoing IVF concluded that there was insufficient evidence on the risks of reduced ovarian responsiveness and reduced oocyte competence.[42] Furthermore, surgery for an endometrioma may potentially reduce ovarian reserve,

as evidenced by a decrease in the AMH levels[37] and subsequent responsiveness to gonadotrophin stimulation.[63]

While the risk of technical difficulties during oocyte retrieval is low, based on very limited reports, there are no data to suggest that surgery for an endometrioma will prevent adhesion reformation and facilitate oocyte retrieval effectively. While the available data exclude a clinically relevant effect of IVF on progression of pelvic endometriosis and ovarian endometriomas,[64] the risks of infection from an endometrioma (0-1.9%) and follicular fluid contamination (2.8-6.1%) are very small, and do not justify surgery for the presence of an endometrioma before IVF treatment.

The ESHRE guideline discusses the importance of women being appropriately counselled about the risk of reduced ovarian function following surgical intervention and even the possible risk of an oophorectomy.[30] The decision to proceed with surgery for an endometrioma should be carefully considered, including the various prognostic factors that can influence the success of an ART cycle, such as the age of the woman, ovarian reserve status, unilaterality or bilaterality of the disease, number and size of the cysts, symptoms, presence or absence of suspicious radiological features, extent of extraovarian disease and history of previous ovarian surgery.[65] Asymptomatic women, women of advanced reproductive age, those with reduced ovarian reserve, bilateral endometriomas or a history of prior ovarian surgery may benefit from proceeding directly with IVF, as surgery may further compromise ovarian function and delay the start of treatment. Surgery may be considered first-line in highly symptomatic women, those with an intact ovarian reserve, unilateral and large cysts, and should be considered for cysts with suspicious radiological and clinical features. Endometriomas may be associated with extraovarian disease, including bowel involvement and deep endometriosis. Reproductive outcomes have not been shown to be improved by the excision of deep endometriosis in randomised trials, with surgical excision of endometriotic nodules providing symptomatic benefit albeit potentially exposing the woman or person to significant surgical risks, to which the women should be appropriately counselled.[28]

4. Fertility preservation in the presence of endometriosis

Fertility preservation in the context of a cancer-related diagnosis or treatment that is likely to render women infertile is well established. Recent advancements in the field have seen fertility preservation using ovarian tissue cryopreservation with now successful pregnancies following orthotopic transplantation in women who have been cured of their disease. Women receiving this complex diagnosis have often alluded to the positive impact the option of fertility preservation brings to their treatment pathway.

Fertility preservation, however, for women with endometriosis is less well explored and discussed. The negative impact of endometriosis on ovarian reserve and the associated infertility has been greatly discussed.[66] Women with known endometriosis who are not planning to conceive imminently should be offered an early opportunity to discuss reproductive planning.

While AMH has not been shown to be a viable predictor of spontaneous pregnancy;[67] a baseline fertility assessment should be considered to inform this discussion. Discussion regarding the various forms of fertility preservation such as oocyte and embryo cryopreservation should be included. There is increasing awareness and engagement including fortune 500 companies offering women the option for early fertility preservation in the context of social oocyte or embryo freezing due to an age-related decline in fertility. Therefore, clinicians treating women with endometriosis will need to allow a pragmatic approach to consider women with this diagnosis to explore this further with an appropriate subspecialist.[68]

5. Opinion

- Endometriomas are associated with reduced monthly fecundity rates, although a direct causal relationship has not been well established.
- Endometriomas are known to impact the ovarian reserve and as such, women in the reproductive age group considering surgical treatment should have their ovarian reserve parameters assessed before surgery to aid fertility related discussions.
- Surgical management of an ovarian endometrioma has been shown to significantly reduce the ovarian reserve regardless of the surgical method employed, drainage of an endometrioma, cystectomy or ablative therapy.
- Repeated or extensive ovarian surgery has a detrimental impact on ovarian reserve, and this should be considered when deciding on treatment and specifically, further surgery.
- Surgery may reduce endometriosis-associated pain. The theoretical benefit of performing surgery to improve pelvic anatomy and accessibility is plausible but has not been supported with substantive scientific evidence.
- Surgery can be used as an adjunct to aid fertility treatment when transvaginal access to the ovaries for egg collection is suboptimal and likely to impact on the IVF outcome. Surgery performed in this setting would be fertility optimising and err on the side of caution for risk of disease recurrence and persistence.
- Until robust evidence from large RCTs incorporating modern treatment modalities is available, many uncertainties will remain on the optimal treatment of an endometrioma. Meanwhile, management decisions should be based on individual circumstances, such as patient choice, age, ovarian reserve, and associated symptoms.
- Women and people should be offered an opportunity to discuss reproductive planning with a specialist in the field.

Appendix I: Risks and benefits of expectant and surgical management of an endometrioma for women undergoing assisted reproductive treatment.

	Expectant management	Surgical management
Potential benefits	• Avoids surgery and its associated complications • No further compromise to ovarian reserve • Avoids delay in commencing assisted reproductive treatment	• Alleviates symptoms • Histological confirmation of diagnosis (excludes malignancy) • Reduced risk of cyst complications • Facilitates ovarian access
Potential risks	• Symptoms (pain) • Cyst rupture • Difficult ovarian access during oocyte retrieval procedures • Infection of an endometrioma • Follicular fluid contamination • No histological diagnosis • Accelerated progression of the disease	• Surgical risks • Reduced ovarian reserve • Postoperative adhesions • Potential delay of assisted reproductive treatment

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The guideline will be considered for update 3 years after publication, with an intermediate assessment of the need to update 2 years after publication.

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