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Received Date : 01-Nov-2016

Revised Date : 01-Feb-2017

Accepted Date : 08-Feb-2017

Article type : State-of-the-art review

An update on the diagnosis, surgical management, and fertility outcomes for women with endometrioma

Running: Endometrioma and fertility: an update

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Declarations of Interest

All authors have declared no conflicts of interest.

Abstract

Endometriosis is estimated to affect up to 50% of infertile women, and severity of endometriosis stage appears to correlate with reduced fertility. Ovarian endometrioma are found in up to 44% of women with endometriosis, and are significantly associated with the presence of pelvic deep infiltrating endometriosis, ovarian adhesions, and pouch of Douglas obliteration. Through the use of MEDLINE and PubMed databases, we conducted a literature review of all available research related to the diagnosis, surgical management and fertility outcomes for women with endometrioma. The evolving use of specialized transvaginal ultrasound for the diagnosis of endometrioma and related endometriotic pathologies can allow for pre-operative mapping/staging of the disease, as well as appropriate surgical planning and fertility counselling. Surgical management of endometriomas appears to reduce markers of ovarian reserve, such as AMH, prompting concern of reduced fertility following surgery. Ovarian cystectomy appears to be superior to ablation in terms of endometrioma recurrence, pain symptoms and increased spontaneous conception rate amongst subfertile patients. Research is inconclusive as to which surgical method least damages ovarian reserve in the long term, however bipolar hemostasis appears to be the most damaging technique and should be avoided. Surgical management should be individualized for women with endometrioma, and strong consideration should be given to the pre-operative ovarian reserve status prior to performing ovarian cystectomy. Current evidence suggests that ovarian cystectomy does not improve reproductive outcomes for women with endometrioma undergoing assisted reproductive technology, however, the majority of studies have been performed retrospectively and more prospective studies are needed.

Keywords

Endometrioma, Ovarian reserve, Fertility, Transvaginal ultrasound, Magnetic resonance imaging, Cystectomy.

Abbreviations

AFC: antral follicle count
AMH: anti-Mullerian hormone
ART: assisted reproductive technology
BMI: body mass index
DIE: deep infiltrating endometriosis
ICSI: intracytoplasmic sperm injection
IVF: in vitro fertilization
MRI: magnetic resonance imaging
POD: pouch of Douglas
POR: poor ovarian response
RCT: randomized controlled trial
TVU: transvaginal ultrasound
UBESS: ultrasound based endometriosis staging system
USL: uterosacral ligament

Key Message

Surgical management of ovarian endometrioma does not appear to improve reproductive outcomes for subfertile women undergoing assisted reproductive technology. Pre-operative specialized ultrasound for disease complexity should be considered if endometrioma surgery is planned, and ovarian stripping is the recommended surgical technique.

Introduction

Endometriosis is defined as the growth of endometrial glands and stroma in aberrant foci, and can present in a multitude of ways, from incidental discovery during surgery, to chronic pelvic pain and infertility. The prevalence of endometriosis in infertile women is substantial; estimated to be between 20 to 50 percent (1, 2) and approximately 17-44% of women with endometriosis will have an endometrioma (3, 4). The mechanisms in which endometriosis affect infertility are not fully understood, but have been attributed to more than just distortion of pelvic anatomy as is seen in advanced disease. A chronic inflammatory response that impairs ovarian, tubal, endometrial and/or even spermatic function has been suggested as another cause for reduced fertility, as evidenced by both laboratory based studies (5), and

observational studies showing a reduced success rate of in vitro fertilization (IVF) in patients with endometriosis as compared to those with tubal infertility (6).

Transvaginal ultrasound (TVU) has a high diagnostic accuracy for endometrioma, and continues to evolve as the first-line imaging modality for the prediction of deep infiltrating endometriosis (DIE) (7, 8) and endometriosis-related pelvic adhesions, such as ovarian fixation and pouch of Douglas (POD) obliteration (9, 10). A significant relationship has been demonstrated between endometrioma and pelvic DIE (4) and pelvic adhesions (11-13). In addition, infertility is known to be affected not only by the presence of endometrioma, but also by the stage of endometriotic disease (14). Given the ability to stage endometriosis pre-operatively with TVU, this imaging modality may not only aid in surgical planning (15), but also in fertility counselling for women with endometrioma.

The standard surgical management for endometrioma is ovarian cystectomy; however researchers have expressed concern regarding the negative effect of cystectomy on fertility and anti-Mullerian hormone (AMH) level (16-20). It has been suggested that surgical technique for cystectomy may play a role in fertility preservation (21). Through the use of MEDLINE and PubMed databases, we conducted a literature review until September 2016 on the diagnosis and surgical management of endometrioma, as well as the impact of other factors such as disease severity and different surgical techniques with regard to fertility outcome for women with ovarian endometrioma. Searches were not restricted based on study design, publication date or language. Search terms included endometriosis, endometrioma, deep infiltrating endometriosis, diagnosis, imaging, ultrasound, transvaginal ultrasound, magnetic resonance imaging, fertility, ovarian reserve, antral follicle count, anti-Mullerian hormone, pregnancy, surgery, cystectomy, ablation and laparoscopy.

Endometrioma and fertility

Endometriosis is primarily a disease of the pelvis, although in rare cases it has also been found above the diaphragm (5). Ovarian endometriosis can manifest as superficial implants on the ovarian surface or deep deposits with associated endometriomas. Endometriomas, otherwise known as ‘chocolate cysts’, can range from less than 1 to greater than 15cm in size, and are associated with more severe endometriotic disease (22).

The effect of endometriosis on fertility is varied, however worsening stage of disease appears to correlate with reduced fertility (23). A systematic review and meta-analysis recently revealed a significant reduction in both implantation rates and clinical pregnancies in patients with severe endometriosis (Stage III/IV) undergoing IVF treatment (6). Furthermore, women with severe endometriosis and the presence of endometriomas appear to have significantly lower pregnancy rates following IVF treatment when compared to women with severe endometriosis but without endometriomas (14). In a recent study by Coelho et al., the researchers found that although women with endometriosis are more likely to have reduced ovarian reserve compared to controls, the chance of conceiving by IVF/ intracytoplasmic sperm injection (ICSI) is similar to women without endometriosis, when both groups have reduced ovarian reserve (i.e antral follicle count ≤6) (24). These findings suggest that ovarian reserve likely plays a more important role than the presence of endometriosis alone, per se, when predicting fertility outcomes.

Antral follicle count (AFC)

Factors commonly used to predict ovarian reserve are antral follicle count (AFC) and anti-Mullerian hormone (AMH) level. The vast majority of research with regard to endometrioma and fertility has focused on pregnancy outcomes in women undergoing assisted reproductive technology (ART). The AFC, measured with TVU during the follicular phase, is reported as the total number of follicles measuring 2-10mm. AFC is commonly used as a predictor of ovarian responsiveness following ovarian stimulation, and is thought to be reduced in women with endometriomas. A possible explanation for reduced AFC in these women may be due to local inflammation caused by the endometrioma (25). More recently, it has been suggested that the reduced AFC associated with endometrioma may be at least partially due to the inability to adequately visualise antral follicles with TVU, due to distorted ovarian anatomy and increased attenuation caused by endometrioma (26).

Studies have reported conflicting results with regard to the relationship between endometrioma and AFC. In a systematic review and meta-analysis by Hamdan et al., the researchers included 33 studies with subfertile women with endometrioma who underwent IVF/ICSI and found that women with intact endometrioma had a similar AFC to women without endometrioma. This review also demonstrated that women with endometrioma had a similar live birth rate and clinical pregnancy rate compared to women without endometrioma; however, the cancellation rate for women with endometrioma was significantly higher (27).

Lima et al. performed a retrospective cohort study in 37 women who underwent IVF/ICSI with unilateral endometrioma to determine the difference between AFC and the number of oocytes retrieved per ovary. The researchers found reduced AFC in the ovary with endometrioma, however, the number of oocytes retrieved in the contralateral normal ovary was similar to the endometriotic ovary, providing further evidence supporting the theory that the AFC may be underestimated during the TVU assessment of ovaries with endometrioma (28).

Anti-Mullerian hormone

The use of AMH as a measurement of ovarian reserve is well recognised regarding its usefulness in predicting ovarian response in ART (29). AMH levels indirectly represent the total number of follicles, as estimated by the number of pre-antral and small follicles (30). The effect of endometrioma on AMH is not currently clear, with available studies differing in their results when comparing the AMH levels of women with endometrioma against their age and BMI matched controls (31).

The general consensus is that AMH levels are reduced in women with stage IV endometriosis and/or endometrioma, however, a large retrospective study by Streuli et al. found that AMH was not significantly decreased in women with endometriosis/endometrioma. Factors significantly associated with decreased AMH were age ($P < 0.001$) and previous surgery for endometrioma ($P < 0.05$). It is important to note from this study that the participants included were referred for benign gynecological conditions rather than infertility; therefore women with a history of infertility may have been underrepresented in this study (32).

Ovarian response to stimulation appears to be a better predictor of clinical pregnancy rate than the presence of endometrioma per se. Coehlo et al. performed a retrospective study of 517 women undergoing IVF/ICSI. Poor ovarian response (POR), defined as ≤3 oocytes retrieved, was significantly higher in women with endometrioma (38.5%vs. 17.2%, p=0.002). However, reasonable pregnancy rates (37.5%) were observed in women with endometriomas when ≥4 oocytes were retrieved. The authors concluded that although endometrioma is associated with POR, endometrioma alone is not an independent predictor of pregnancy (33).

Diagnostic approach of endometrioma

As has been the case for some time, the gold standard in the diagnosis of endometriosis and localisation of lesions remains laparoscopy, combined with histopathological confirmation. Laparoscopy has the benefits of direct visualisation of the pelvis, allowing for diagnosis and staging of the disease, and treatment of endometriosis and adhesions (34). The need for non-invasive tools to assist in the diagnosis of endometriosis location and severity has and continues to be the subject of much research.

History and clinical examination

A thorough clinical history and examination should form the basis of every patient encounter. In addition to infertility, symptoms such as chronic pelvic pain, dysmenorrhea, and/or dyspareunia may be associated with the presence of endometrioma. A vaginal examination is useful in the diagnosis of endometriosis deposits in the vagina and deep implants in the rectovaginal space, with a positive/negative predictive value of 80%/97% for vaginal endometriosis and 78%/98% for endometriosis of the rectovaginal space (35). However, physical examination alone performs poorly in the diagnosis of endometrioma and endometriotic deposits elsewhere (i.e rectum, uterosacral ligaments (USL)) in the pelvis when compared to TVU (35, 36). A combination of physical examination and TVU provides the most accurate assessment for the localization and extension of endometriotic lesions.

Transvaginal ultrasound for the pre-operative diagnosis of endometrioma

TVU is the first-line imaging technique for the diagnosis of endometrioma, with a sensitivity and specificity approaching 90% (37). The quintessential TVU findings of endometriomas are unilocular ovarian cysts with a ground glass appearance of the cyst fluid. Typically, they have no more than four locules, and patients are more likely to experience pain during the ultrasound that when compared to other benign or malignant ovarian masses. The presence of papillations or solid components are uncommon findings, and more often found in other benign or malignant ovarian masses (38, 39).

Up to half of all endometriomas will display ultrasound characteristics other than the typical features mentioned above. Atypical endometriomas can demonstrate the following ultrasound characteristics: multiple locules, hyperechoic wall foci, cystic-solid lesions, or anechoic cysts. The optimal rule for the ultrasound diagnosis of endometrioma has been stated as ‘an adnexal mass in a premenopausal patient with ground glass echogenicity of the cyst fluid, one to four

locules and no papillations with detectable blood flow' (39). However, the most accurate identification of endometrioma remains the subjective impression by an experienced sonologist, which provides a positive predictive value of 86% (39).

Colour doppler can be useful in distinguishing endometriomas from malignant ovarian pathology. The solid locules and hyperechoic wall foci seen in atypical endometriomas are avascular, whereas solid papillations which demonstrate vascularity are more often associated with malignancy (39). The caveat is that the accuracy and interpretation of Doppler findings are dependent upon the sonologist's experience, as well as the quality of the ultrasound equipment and Doppler settings used to perform the examination. The clinician should also be aware of the ultrasound appearance of decidualized endometrioma during pregnancy, as these cysts contain solid vascular projections that can mimic the appearance of a malignant lesion (39).

Specialized transvaginal ultrasound for the prediction of pelvic DIE and adhesions in women with endometrioma

In addition to the standard pelvic ultrasound evaluation of the ovaries and uterus, sonographic assessment of ovarian mobility, POD obliteration, site-specific tenderness and anterior/posterior pelvic compartment DIE should be included in the workup of women with endometrioma.

Women with ovarian endometriosis are likely to have additional deposits elsewhere in the pelvis or bowel (4). Furthermore, the presence of endometrioma has been shown to be significantly associated with POD obliteration (as demonstrated at laparoscopy in Figure 1.) and bowel DIE (as demonstrated on TVU in Figure 2.) (10, 12, 22). The pre-operative TVU finding of endometrioma may therefore be considered a red flag for the presence of complex endometriotic disease, and thus, the requirement for an advanced laparoscopic surgeon and longer surgical times. Figure 3. displays an endometrioma with a co-existing USL nodule at TVU. In a study by Kondo et al., 98% of women with endometriomas had associated posterior compartment DIE, and 57% were found to have bowel DIE (12). In another recent study of 189 women with suspected endometriosis, 49% of women with endometrioma had associated rectal/rectosigmoid DIE (10). However, it should be noted that the absence of endometrioma does not preclude the presence of DIE or POD obliteration.

In a recent systematic review, the pooled sensitivities and specificities of TVU for the diagnosis of rectosigmoid DIE were 91 and 98%, respectively (40). In another systematic review, the pooled sensitivities and specificities for prediction of bladder, USL, vaginal and rectovaginal septum DIE with TVU were reported as 62 and 100%, 53 and 93%, 58 and 96%, and 49 and 98%, respectively (41). A consensus statement on the use of ultrasound for the assessment of women with suspected endometriosis was recently published, and describes the definitions and ultrasound techniques used for the standardised sonographic assessment of women with suspected endometriosis (7).

The use of the uterine "sliding sign", a dynamic TVU technique assessing the mobility of the rectosigmoid/anterior rectum along the posterior uterine fundus/cervix, has been demonstrated to predict POD obliteration with an accuracy, sensitivity, specificity, positive and negative predictive value of 95%, 85%, 98%, 93%, and 95%, respectively, in women with pelvic pain/suspected endometriosis (10). In the same study, 55% of women with a negative TVU "sliding sign" (i.e. POD obliteration) had either unilateral or bilateral endometrioma. As POD obliteration is known to be associated with both endometrioma and rectal endometriosis, the use of the TVU "sliding sign" technique aids in the pre-operative assessment of disease severity and planning of endometriosis surgery for these women.

The use of the TVU 'soft markers' ovarian mobility and site specific tenderness have also been shown to assist in the prediction of pelvic pathology in women with suspected endometriosis. Positive findings of ovarian fixation or site specific tenderness at TVU can improve the prediction of endometriosis and/or adhesions at laparoscopy (42, 43). In addition, a recent study demonstrated that ovarian immobility at TVU was significantly associated with endometrioma, when compared with normal ovaries (11).

The ability to predict endometriosis type, location and extension with TVU allows not only for the prediction of disease severity, but also for the expected level of surgical expertise required to excise the endometriotic disease. Our group recently published a study introducing an ultrasound based endometriosis staging system (UBESS) for the prediction of the level of complexity of laparoscopic surgery for women with suspected endometriosis(15). According to the three stage UBESS, women with endometrioma are classified as either UBESS stage 2 or 3, which corresponds to a laparoscopic complexity level of 2 or 3, respectively (laproscopic complexity as defined by the Royal College of Obstetricians and

Gynecologists (RCOG). In the case of endometrioma in the absence of bowel DIE/POD obliteration at TVU, the UBESS stage is 2, whereas endometrioma in the presence of bowel DIE/POD obliteration at TVU is assigned UBESS stage 3 (i.e. surgery should be performed by an advanced laparoscopic surgeon with level 3 surgical expertise). According to the RCOG, level 3 laparoscopic skills include: extensive pelvic sidewall dissection, dissection of an obliterated POD, bowel surgery, and ureterolysis (44).

It is well known that the results of ultrasound studies are variable, with sonographer experience being a significant factor. This is again true of TVU for the diagnosis of endometriosis, with significant differences between routine and expert guided TVU sensitivities (45). As such, if endometriosis is clinically suspected, and access to sonographers/sonologists with such expertise is feasible, they should be utilised in order to improve the diagnosis of endometriosis location and severity, as well as aid in surgical planning and patient counselling.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) has also been shown to be a useful means of diagnosing endometrioma and DIE, and can be used in combination with or exchange of TVU for mapping and surgical planning. The characteristic findings of endometrioma on MRI include rounded structures with high signal intensity on T1-weighted images and the 'shading sign' – variable low signal intensity on T2-weighted images. The 'shading sign' is specific to endometrioma, and thought to be caused by high iron and protein concentrations seen in endometrioma due to recurrent hemorrhage (46). Like TVU, the MRI has high diagnostic accuracy for endometrioma, with a recent systemic review by Nisenblat et al. revealing a sensitivity of 95% and specificity of 91% (47).

MRI also has high diagnostic accuracy for pelvic DIE, though this varies depending on deposit sites and radiologist experience. In a systematic review by Medeiros et al., the pooled sensitivities and specificities for the diagnosis of bladder, bowel, USL, and vaginal DIE using MRI were: 64 and 98%, 84 and 97%, 85 and 80%, and 82 and 82%, respectively (48). Typically, DIE on MRI is described as nodular or retractile fibrotic-like tissue that is hypointense on T2-weighted images and isointense to muscle on T1-weighted images (49).

The diagnosis and localisation of adhesions on MRI is less successful, with a reported sensitivity of 77% and specificity of 50% for POD obliteration (50). Adhesions are sometimes identifiable as spiculated low signal intensity stranding on T1 and T2 weighted images. However, more often only indirect signs such as angulation of bowel loop, elevation of the posterior vaginal fornix, posterior displacement of the uterus and/or ovaries and loss of fat planes between the structures are noted (38).

MRI has benefits over TVU in that it is less invasive (e.g. for nulliparous women), and less operator dependent. It is however, limited by issues of access and cost, and image acquisition can be impeded by gut peristalsis and patient claustrophobia. MRI is a static imaging modality, whereas TVU allows for a dynamic, real-time assessment of the pelvis for endometriosis related adhesions, such as POD obliteration and ovarian immobility. Given its high diagnostic accuracy, low level of patient discomfort and cost-effectiveness, TVU is currently recommended as the first-line imaging modality for the assessment of women with suspected DIE (8). However, gynaecological ultrasound experience and specialised TVU training is required for the accurate diagnosis of pelvic DIE and POD/ovarian adhesions. If a specialised TVU assessment is not available for women with endometrioma and suspected pelvic DIE, pre-operative MRI may be performed instead. In complex cases of endometriotic disease where TVU is inconclusive, it may be useful to also perform MRI in order to give the surgeon the most accurate pre-operative assessment.

Surgical approach to endometriomas

The surgical management of endometrioma improves patient symptoms such as pain (51, 52); but researchers have reported conflicting results regarding the benefit of ovarian cystectomy and reproductive outcomes, particularly for women undergoing ART.

Studies have demonstrated that approximately 50% of women previously infertile for at least one year are able to conceive within two years of surgery, the majority conceiving without ART (20, 22, 23). Other studies have demonstrated that laparoscopic treatment of endometriomas in infertile women can improve the spontaneous pregnancy rates to between 20-60% (19-21).

There remains concern that ovarian surgery for endometriomas impairs ovarian reserve by way of damaging healthy ovarian tissue, thus resulting in poorer fertility outcomes. There also remains some dispute over whether ovarian cystectomy actually improves fertility outcomes. A recent systematic review by Hamdan et al. found that among women undergoing IVF/ICSI with endometrioma, there was no significant difference in reproductive outcome if ovarian cystectomy was performed (27).

A number of older studies have shown combined (spontaneous and assisted) pregnancy rates of approximately 40 to 50% in infertile patients following surgical management of endometriomas (51-55). A large observational study demonstrated an improved combined pregnancy rate in infertile patients with endometriomas following surgical management (65%), when compared to IVF alone (32%) and no treatment (12%) (56). Other IVF studies however, have not been able to demonstrate a difference between pregnancy rates of women with and without surgical management of endometriomas (57, 58). More recently, many studies have found that surgical management of endometriomas has a negative effect on ovarian reserve, as measured by a decreased AMH (17-19, 59-61). This has prompted much research into the different surgical techniques used in the management of endometriomas and their effect on ovarian reserve.

The two most common surgical methods used in the management of endometriomas include ovarian cystectomy via the stripping technique (in which the drained endometrioma and ovarian cortex are pulled apart by atraumatic grasping forceps, and hemostasis applied to the ovarian cyst bed) and ablation (in which the endometrioma is fenestrated, drained, washed out and then the cyst wall destroyed with an energy source). Cystectomy is usually reserved for endometriomas >3cm prior to ART (62). A 2011 systematic review of two RCTs revealed cystectomy to be superior to ablation in terms of endometrioma recurrence, pain symptoms and increased spontaneous conception rate amongst subfertile patients (63). Effect on ovarian reserve however, was not examined. Multiple review articles have shown a significant and sustained reduction in AMH levels following endometrioma excision (20, 64, 65), however follow up AMH levels were only measured so far as to nine months post-operatively.

A single recent study investigating AMH levels following ablation reported a significant decrease in AMH levels post-operatively (66). Interestingly, this study also reported partial recovery of AMH levels eighteen months post-operatively, thus warranting further

investigation of AMH levels long term following endometrioma ablation. Plasma energy has been suggested as a more favourable ablative technique for management of ovarian endometrioma. In a retrospective case-control study by Motte et al, IVF outcomes for 37 women following ablation of endometrioma with plasma energy demonstrated that although a lower number of oocytes were retrieved, the women who underwent plasma energy ablative therapy had a higher implantation, pregnancy and delivery rates per cycle than the matched controls. The researchers concluded that endometrioma ablation with plasma energy may be a viable alternative to ovarian cystectomy for women with infertility secondary to endometrioma (67). In another study, Mircea et al. performed a multicentre case-control study that compared plasma energy ablation to ovarian cystectomy in infertile women with endometrioma and found no significant difference in post-operative pregnancy rates between the two techniques (68).

Ovarian stripping was compared to the combined excision/ablation technique in women with bilateral endometrioma in a multi-centre randomized controlled trial by Muzii et al. The study included 51 women with endometriomas > 3cm. In each patient, one endometrioma was treated with stripping and the contralateral endometrioma was treated with the combined excisional/ablative technique used bipolar coagulation. Recurrence rates for endometrioma were higher in the ovaries that had stripping vs. the combined technique (5.9% vs. 2.0%). However, the AFC did not differ significantly between the two techniques at the 1, 3, and 6 month follow up visits. The authors concluded that ovarian stripping should be considered the gold standard for surgical treatment of endometrioma, however, this was a small study with short follow up duration (69). Larger studies with longer follow up times, that also assess AMH and spontaneous/ART pregnancy outcomes, are required to confirm these findings.

The effect of hemostatic method following endometrioma cystectomy on AMH levels has also been reviewed. A recent systematic review and meta-analysis has revealed that application of a hemostatic sealant to be the least detrimental to ovarian reserve as measured by post-operative AMH levels (21). Suturing appears to be an acceptable hemostatic method, whereas bipolar desiccation appears to cause the largest fall in post-operative AMH levels (21). One study that compared post-operative AMH levels amongst women with endometriomas managed with harmonic scalpel vs. suturing vs. bipolar hemostasis, found suturing again to be superior, whilst harmonic scalpel and bipolar hemostasis were significantly associated with a reduction in ovarian reserve (70).

Three independent factors have also been identified to effect ovarian reserve following endometrioma cystectomy, and should be taken into account when planning surgery for infertility. Firstly, patients undergoing bilateral endometrioma excision will have lower AMH levels than their age and BMI matched counterparts undergoing unilateral endometrioma excision. Alborzi et al found an average AMH drop from 4.19ng/ml pre-operatively to 2.18ng/ml at 9 months post-operatively for unilateral cystectomies versus 3.29ng/ml to 1.19ng/ml for bilateral cystectomies (16). Secondly, the size of an endometrioma has been shown to be directly proportional to the amount of healthy ovarian parenchyma incidentally removed at cystectomy. Using histological measurements of endometrioma cystectomy specimens, Roman et al. found an average loss of 200 micrometres of ovarian tissue per centimetre increase in endometrioma diameter (71).

In women with recurrent endometrioma planning to undergo ART, repeat cystectomy has been shown to be associated with higher risk of ovarian reserve impairment. Ferrero et al. found significantly lower AMH levels in patients following a second cystectomy for a recurrent endometrioma when compared with patients who did not have a recurrence following a primary endometrioma cystectomy (72). In a recent study by Xing et al., the authors evaluated whether aspiration of recurrent endometriomas before controlled ovarian hyperstimulation improved the outcome of IVF-embryo transfer/ICSI cycles. Transvaginal aspiration of endometriomas ≤3cm did not result in an improvement in retrieved oocyte number, implantation or pregnancy rates when compared to women who did not undergo endometrioma aspiration. This study also demonstrated that the number of metaphase 2 stage oocytes following controlled ovarian hyperstimulation was significantly smaller in women with a history of previous cystectomy for endometrioma compared to women with pelvic endometriosis or recurrent endometrioma (73).

Fertility outcomes for excision of non-ovarian endometriosis in the presence/absence of endometrioma

In mild endometriotic disease, there is good quality evidence that laparoscopic treatment of endometriosis in infertile women almost doubles the post-operative clinical pregnancy rate when compared with diagnostic laparoscopy alone, from 17.7% to 30.7% (53). Regarding DIE and endometriosis with bowel involvement, both spontaneous and ART pregnancy rates have also been shown to be improved following surgery, when compared to non-surgical

management. In women with pelvic DIE without bowel involvement, no data on pre-operative spontaneous pregnancy rates was found, however, post-operative spontaneous pregnancy rates of 50% and combined pregnancy rates of 68% (spontaneous plus ART) were reported. In women with DIE and bowel involvement, a non-surgical approach with only ART resulted in a 29% pregnancy rate, whereas a surgical approach produced a 28% spontaneous pregnancy rate, and a combined pregnancy rate of 46% (54).

Shervin et al., evaluated the reproductive outcome for infertile women with DIE +/- endometrioma following laparoscopic excision of endometriosis. The researchers found that women who underwent excision of DIE + excisional ovarian cystectomy had comparable cumulative pregnancy rates to women who underwent DIE excision in the absence of endometrioma (35.6% vs. 39.5%, respectively). The researchers were unable to demonstrate a significant relationship between ovarian cystectomy and fertility outcome in this cohort study. This study suggests that DIE excision plays a large role with regard to fertility outcome; perhaps even more so than ovarian cystectomy (74).

Conclusion

Although endometrioma is significantly associated with infertility, ovarian reserve status and response to ovarian stimulation appear to be more important predictors of reproductive outcomes than the presence of endometrioma alone. A specialised TVU should be performed in all women with infertility, pelvic pain, and/or suspected endometriosis, in order to aid in the diagnosis and mapping of endometriotic lesions and/or pelvic adhesions. The pre-operative ultrasound work up for women with endometrioma is essential not only for the staging of disease severity, but also for the prediction of surgical complexity at laparoscopy. Using ultrasound staging systems such as UBESS can aid in the appropriate referral of women to an advanced laparoscopic surgeon when surgery is planned, which may improve fertility outcomes for women undergoing endometriosis surgery. When treating endometriomas surgically, the greater a surgeon's knowledge of the location and extension of associated endometriotic lesions, the better the surgeon can prepare the patient, the operating theatre, and the required treating team for surgery.

Surgical management should be individualized for women with endometrioma, and strong consideration should be given to the pre-operative ovarian reserve status prior to performing ovarian cystectomy. The evidence suggests that ovarian cystectomy via stripping is the most

preferable surgical technique for management of endometrioma, compared to other excisional/ablative techniques. However, it is important to remember that all of these techniques cause a reduction in ovarian reserve, as measured by a reduction in AMH. The benefit of endometrioma excision for pain management is clear; on the other hand, surgical excision of endometrioma for the sole purpose of improving fertility/reproductive outcomes is not supported by the currently available research.

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Legends

Figure 1: Pouch of Douglas obliteration at laparoscopy in the presence of left ovarian endometrioma.

Figure 2. Deep infiltrating endometriosis (DIE) nodule (N) within the sigmoid bowel. The sigmoid bowel is adherent to the neighbouring ovarian endometrioma, at the level of the DIE lesion.

Figure 3. Ovarian endometrioma with co-existing uterosacral ligament nodule (N).