

ENDOMETRIOSIS AND ART

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Women infertility therapy

current practice

Shoham ,et al 2023

introduction

- Endometriosis, as a clinical entity, has been recognized and intensely investigated for well over 100 years. Despite the accumulation of an enormous amount of information, uncertainty still exists regarding etiologies, clinical consequences, and treatment efficacy.
- The two most common complaints leading to a diagnosis of endometriosis are pelvic pain and infertility.
- Medical, surgical, or a combination of both approaches have been employed to improve many of the symptoms associated with endometriosis.
- Counseller VS. Endometriosis: A clinical and surgical review. Am J Obstet Gynecol. 1938;36:877–88.

introduction

- Assisted reproduction technology (ART)
 has also become an indispensable asset
 in providing affected couples with viable
 pregnancies.
- There is also a growing body of data demonstrating the effectiveness of GnRH agonists and laparoscopically guided laser ablation in increasing live birth rates.
- Hasson HM. Incidence of endometriosis in diagnostic laparoscopy. J Reprod Med. 1976;16:135–8.

- There is little debate that the extensive anatomical distortion and tubal obstruction frequently attributed to severe endometriosis does impair fertility.
- Less clear is the reported association between minimal or mild endometriosis and infertility in the absence of any mechanical disruption.
- Hughes E, Brown J, Collins JJ, et al. Ovulation suppression for endometriosis for women with subfertility. Cochrane Database Syst Rev. 2007;2007(3):CD000155. DOI: 10.1002/14651858.CD000155.pub2.

- Although there is no conclusive evidence that minimal to moderate endometriosis actually causes infertility, several studies dating back to the 1930s have suggested that there is at least an association between the two
- In the 1970s, three studies retrospectively compared the incidence of endometriosis in women undergoing laparoscopy for infertility or voluntary sterilization
- Counseller VS. Endometriosis: A clinical and surgical review. Am J Obstet Gynecol. 1938;36:877–88.
- Hasson HM. Incidence of endometriosis in diagnostic laparoscopy. J Reprod Med. 1976;16:135–8.

- The incidences of endometriosis ranged from 21% to 48% in infertile women, while endometriosis was noted in only 1.3%–5% of fertile women undergoing tubal ligation.
- Subsequent studies including one prospective investigation, have demonstrated that among women undergoing insemination with donor sperm due to severe male factor infertility, those with coexisting endometriosis had markedly fewer conceptions per exposure than women who did not have the disease.
- Hammond MG, Jordan S, Sloan CS. Factors affecting pregnancy rates in a donor insemination program using frozen semen. Am J Obstet Gynecol. 1986;155:480–5.

 Investigators have suggested that women with mild to moderate endometriosis have a higher incidence of endocrine abnormalities, anovulation, corpus luteum insufficiency, hyperprolactinemia , luteinized unruptured follicle syndrome, and spontaneous abortions.

 Pittaway DE, Maxson W, Daniell J, et al. Luteal phase defects in infertility patients with endometriosis. Fertil Steril. 1983;39:712

- A direct association between these genetic polymorphisms and endometriosis-associated infertility has yet to be shown though.
- More recently, research has focused on microRNA as a tool to aid in the diagnosis of endometriosis. One study utilized next generation sequencing to identify a panel of microRNA associated with endometriosis.
- This panel allowed endometriosis to be diagnosed with a blood sample with comparable sensitivity to laparoscopy.
- De Ziegler D, Borghese B, Chapron C. Endometriosis and infertility: Patho-physiology and management. Lancet. 2010;376:730–8.

- Previous studies using magnetic resonance imaging of the uterus in patients with endometriosis have demonstrated up to a 90% prevalence rate of adenomyotic lesions in those patients with established pelvic endometriosis.
- This association between endometriosis and adenomyosis may also contribute to the infertility seen in these patients, particularly those with severe disease.
- As stated, one argument that has been proposed against a causal relationship between endometriosis and infertility is the outright failure of medical or surgical treatment to significantly improve pregnancy success in these patients
- Kunz G, Beil D, Huppert P, Noe M, et al. Adenomyosis in endometriosis—Prevalence and impact on fertility. Evidence from magnetic resonance imaging. Hum Reprod. 2005;20:2309–16.

Endometriosis and Art

Endometriosis and Art

One randomized study, however, did show an improved rate of pregnancy for women with minimal/mild endometriosis treated with ablation of endometriotic lesions, when compared with a control group receiving diagnostic laparoscopy alone.

Marcoux S, Maheux R, Berube S. The Canadian Collaborative Group on Endometriosis. Laparoscopic surgery in infertile women with minimal or mild endometriosis. N Engl J Med. 1997;336:217–22.

Endometriosis and Art

A Cochrane review of four trials concluded that surgery (aspiration or cystectomy) versus expectant management showed no evidence of a benefit for clinical pregnancy with either technique .

- Another meta-analysis had similar findings, demonstrating that surgical treatment of endometrioma did not alter the outcome of IVF/ICSI treatment.
- Gruppo Italiano per lo Studio dell'Endometriosi. Ablation of lesions or no treatment in minimal–mild endometriosis in infertile women: A randomized trial. Hum Reprod. 1999;14:1332–4

Endometriosis and Art

- However, surgical techniques have again advanced and include endometrioma excision, stripping, plasma energy ablation, and CO2 vaporization.
- A recent review focusing on studies from 2015 to 2019 noted increased pregnancy rates from 20%–60% for patients who underwent surgical intervention of endometriomas.
- In a recent meta-analysis of 553 women with endometriomas, four treatment groups were evaluated: surgery and ART, surgery alone, aspiration plus sclerotherapy and ART, and ART alone.
- ART alone had the lowest pregnancy rate (32%, CI: 15.0– 52.0, p = 0.02), whereas surgery alone had the highest pregnancy rate (43.8%, CI: 22.5–66.4, p = 0.01).
- Alborzi S, Zahiri Sorouri Z, Askari E, et al. The success of various endometrioma treatments in infertility: A systematic review and meta-analysis of prospective studies. Reprod Med Biol. 2019 Jun 19;18(4):312–22.

- Controlled ovarian stimulation (COS), in combination with intrauterine insemination (IUI), has proven to be a cost-effective and appropriate first-line treatment for many infertility diagnoses.
- However, the data does not suggest that this approach may be as effective for patients with endometriosis.
 Deaton et al. demonstrated increased fecundity in patients treated with clomiphene citrate and IUI who had already undergone surgical treatment, but fecundity was still low at 9.2%.
- However, Fedele et al. reported that the increased conception rate with COS and IUI did not lead to a significantly different pregnancy rate at six months.
- Fedele L, Parazzini F, Radici E, et al. Buserelin acetate versus expectant management in the treatment of infertility associated with mild endometriosis: A randomized clinical trial. Fertil Steril. 1992;58:28–31.

- In a meta-analysis, Hughes reported that a diagnosis of endometriosis decreased the percycle COS/IUI conception rate by half. Also, a later prospective, randomized study reported live birth rates of 11% and 2% for endometriosis patients undergoing COS/IUI and no treatment, respectively.
- Failure of COS/IUI has been correlated with advanced endometriosis.
- Tummon IS, Asher LJ, Martin JS, Tulandi T. Randomized controlled trial of superovulation and insemination for infertility associated with minimal or mild endometriosis. Fertil Steril. 1997;68:8–12.

- The advent of aromatase inhibitors added to the armamentarium of therapeutic modalities for the treatment of endometriosis.
- Wu et al. found that a third-generation aromatase inhibitor was able to achieve a reasonable pregnancy rate, with a thicker endometrium but fewer ovulatory follicles, when randomized and compared with clomiphene citrate.

 Capelo F, Kumar A, Steinkampf M, Azziz R. Laparoscopic evaluation following failure to achieve pregnancy after ovulation induction with clomiphene citrate. Fertil Steril. 2003;80:1450–3.

- The use of GnRH antagonists in IUI cycles with COS has also been studied.
- A randomized, double-blinded, placebocontrolled trial showed no difference in live birth rates for women with minimal or mild endometriosis when comparing women who were treated with GnRH antagonist to those who received a placebo.
- Alborzi S, Hamedi B, Omidvar A, et al. A comparison of the effect of short-term aromatase inhibitor (letrozole) and GnRH agonist (triptorelin) versus case control on pregnancy rate and symptom and sign recurrence after laparoscopic treatment of endometriosis. Arch Gynecol Obstet. 2011 Jul;284(1):105–10.

Treatment strategies for the infertile

Couple must be based on the specific situation. For young women with only minimal or mild endometriosis, expectant management may be the most appropriate course.

- However, for women approaching the end of their reproductive age, the chances of conceiving drop precipitously.
- In these women, intervention, in the form of COS/IUI or in vitro fertilization (IVF), may be warranted more expeditiously.
- The lower cost and low complication rate of ovulation induction and IUI make the combination an attractive first step.
- The Practice Committee of the American Society of Reproductive Medicine. Endometriosis and infertility. Fertil Steril. 2006;86:S156–60

- However, for women with severe endometriosis or tubal disease, or when male factor or a combination of aetiologies is involved, assisted reproduction such as IVF may be pursued sooner.
- In addition, IVF offers the added benefit of being able to directly observe key events in the conception process, such as the assessment of gamete quality, the observation of fertilization, and the evaluation of early embryo development.
- Sanchez AM, Vanni VS, Bartiromo L, et al. Is the oocyte quality affected by endometriosis? A review of the literature. J Ovarian Res. 2017 Jul 12;10(1):43.

A review of clinical and biological studies described multiple markers of decreased oocyte quality retrieved from women with endometriosis, including altered morphology, decreased cytoplasmic mitochondrial content, higher failure rate of in vitro maturation, reduced retrieval of mature oocytes, and decreased fertilization rate.

 Chiavari. P, Hippelainen M, Anttila M, Heinonen S. Effect ofendometriosis on IVF/ICSI outcome: Stage III/IV endometriosis worsens cumulative pregnancy and live-born rates. Hum Reprod. 2005;20:3130–5

- In a review article on the treatment of infertility associated with deep endometriosis, the authors looked at six studies that investigated the outcomes of IVF in patients with severe endometriosis.
- They found that the pregnancy rate per patient varied between 29% and 68%, with an aggregated rate per patient of 51% (95% CI 45%–56%)
- Somigliana E, Garcia-Velasco J. Treatment of infertility associated with deep endometriosis: Definition of therapeutic balances. Fertil Steril. 2015;104:764–70.

- The improvement in IVF outcomes brought about by the development of GnRH agonists is largely undisputed.
- Olivennes et al. reported a significantly improved clinical pregnancy rate for patients treated with GnRH agonists when compared with standard, gonadotropinonly ovarian stimulation protocols.
- Other investigations have reported similar results .
 Long-term GnRH agonist suppression has been thought to repress further endometriotic lesions and improve IVF outcome for patients with endometriosis.
- Olivennes F, Feldberg D, Liu HC, et al. Endometriosis: A stage by stage analysis—The role of in vitro fertilization. Fertil Steril. 1995;64:392–8.

- Surrey et al. investigated a three-month course of GnRH agonist therapy prior to IVF-ET and found the agonist therapy to be associated with a significantly higher ongoing pregnancy rate.
- Conversely, Chedid et al. found no difference between long and short GnRH agonist administrations.
- Recently, Kaponis et al. performed a large, multicentre prospective RCT comparing three-month GnRH agonist treatment before IVF attempt compared to no GnRH agonist in women with laparoscopically confirmed and ablated mild endometriosis (ASRM I–II).
- There was no statistically significant clinical pregnancy rate between the two groups.

. Surrey ES, Silverberg KM, Surrey MW, Schoolcraft WB. Effect of prolonged gonadotropin-releasing hormone agonist therapy on the outcome of in vitro fertilization–embryo transfer in patients with endometriosis. Fertil Steril. 2002;78:699–704.

Kaponis A, Chatzopoulos G, Paschopoulos M, et al. Ultralong administration of gonadotropin-releasing hormone agonists before in vitro fertilization improves fertilization rate but not clinical pregnancy rate in women with mild endometriosis: A prospective, randomized, controlled trial. Fertil Steril. 2020 Apr;113(4):828–35.

- The use of continuous oral contraceptive pills prior to assisted reproduction treatment has also been examined.
- De Ziegler et al. found that six to eight weeks of continuous use of combined oral contraceptive pills before IVF-ET for patients with endometriosis had similar outcomes patients treated with three months of GnRH agonist treatment.
- de Ziegler D, Gayet V, Aubriot PF, et al. Use of oral contraceptives in women with endometriosis before assisted reproduction treatment improves outcomes. Fertil Steril. 2010;94:2796–9.

- A non-inferiority RCT compared medroxyprogesterone acetate + hMG (human menopausal gonadotropin); dydrogesterone + hMG; and progesterone + hMG prior to IVF-ET. Their primary outcome, oocytes retrieved, was significantly higher in the medroxyprogesterone acetate + hMG group than the two other groups (9.3 ±5.7 vs 8.0 ±4.5 vs 7.8 ±5.2, P = 0.021).
- Notably, clinical pregnancy and live birth rate were similar amongst all three groups.
- Guo H, Li J, Shen X, et al. Efficacy of different progestins in women with advanced endometriosis undergoing controlled ovarian hyperstimulation for in vitro fertilization-a single-center non-inferiority randomized controlled trial. Front Endocrinol (Lausanne). 2020 Mar 20;11:129.

- Another recent RCT evaluating the progestin
 Dienogest in endometriosis patients for 12 weeks
 prior to IVF-ET showed decreased antral follicle
 count, retrieved oocytes, fertilized oocytes,
 pregnancy rate, and live birth rate.
- Therefore, the type of progestin used prior to IVF– ET should be chosen judiciously with the available evidence.
- Tamura H, Yoshida H, Kikuchi H, et al. The clinical outcome of dienogest treatment followed by in vitro fertilization and embryo transfer in infertile women with endometriosis. J Ovarian Restransfer in infertile women with endometriosis. J Ovarian Res. 2019 Dec 12;12(1):123.

- Recent studies have also analysed the use of GnRH antagonist protocols for IVF in patients with endometriosis.
- A prospective randomized trial compared GnRH agonist and antagonist protocols for women with mild to moderate endometriosis.
- This study showed similar implantation and clinical pregnancy rates for patients treated with both GnRH agonist and antagonist protocols.
- Patients treated with a GnRH agonist, however, had a significantly higher number of additional embryos available for cryopreservation, making the cumulative fecundity rate higher with the agonist protocol.

- For now, it appears that endometriosis patients respond to ovarian stimulation in a manner that is similar to other infertility aetiologies.
- Although standard gonadotropin stimulation protocols work reasonably well, the addition of longer GnRH agonist downregulation or the use of continuous oral contraceptive pills may increase
 IVF success and should be considered on a caseby-case basis

Fertilization and early embryo development

Fertilization and early embryo development

- investigators have reported significantly lower fertilization success for stage III or IV endometriosis when compared with stage I or II endometriosis.
- With regard to early embryo development, researchers have reported fewer embryos reaching the four-cell stage at 48 hours, a reduced number of blastomeres at 72 hours, and lower cleavage rates when endometriosis is compared with tubal factor or unexplained infertility.

Wardle PG, Mitchell JD, McLaughlin EA, et al. Endometriosis and ovulatory disorder: Reduced fertilisation in vitro compared with tubal and unexplained infertility. Lancet. 1985;2:236–9.
Fertilization and early embryo development

- Endometriosis does not show an impact on the euploid blastocyst rate as well.
- More specifically, in a case-controlled study conducted by Alberto Vaiarelli et al., there was no impact on the blastocyst rate per cohort of inseminated metaphase-II oocytes.
- In this study, patients who were diagnosed via surgery were matched to two controls: maternal age during retrieval, number of previous failed IVF treatments and number of metaphase-II oocytes retrieved.
- 103. Vaiarelli A, Venturella R, Cimadomo D, et al. Endometriosis shows no impact on the euploid blastocyst rate per cohort of inseminated metaphase-II oocytes: A case-control study. Eur JObstet Gynecol Reprod Biol. 2021;256:205–10.

- Some early studies have shown a decrease in the implantation rate with a subsequent decrease in the pregnancy rate.
- In a small study, Chillik et al. reported a significantly lower implantation and pregnancy rate for patients with stage III or IV endometriosis when compared to patients with tubal factor or endometriosis of a lesser severity.
- Matson and Yovich demonstrated pregnancy rates of 18%, 13%, 14%, 6%, and 2%, for patients with tubal factor and stage I–IV endometriosis, respectively. In a case-control study of 284 IVF cycles
- 61. Chillik CF, Acosta AA, Garcia JE, et al. The role of in vitro fertilization in infertile patients with endometriosis. Fertil Steril. 1985;44:56–61.

 Errors in implantation may be attributed to the relationship between endometriosis and adenomyosis. Recent studies have suggested that treatment with either prolonged downregulation with GnRH agonists or oral contraceptives may help overcome the effects of adenomyosis on the endometrium

 104. Niu Z, Chen Q, Sun Y, Feng Y. Long-term pituitary downregulation before frozen embryo transfer could improve pregnancy outcomes in women with adenomyosis. Gynecol Endocrinol. 2013;29:1026–30.

A recent systematic review found a fourfold increase in the odds of clinic pregnancy (OR 4.28, 95% CI 2.00–9.15) with administration of GnRH agonists for a period of three to six months prior to IVF in patients with endometriosis ;

 105. Sallam HN, Garcia-Velasco JA, Dias S, Arici A. Long-term pituitary down-regulation before in vitro fertilization (IVF) for women with endometriosis. Cochrane Database Syst Rev. 2006;1:CD004635.

- A competitive vasopressin/oxytocin receptor antagonist, atosiban, is undergoing evaluation for utility in treating endometriosis-associated pain and infertility.
- Endometrial cells express oxytocin receptors (OTRs), that have the capacity to trigger the production of prostaglandin (PG)F2a and E2 when oxytocin binds.

. Simsek Y, Celik O, Karaer A, et al. Therapeutic efficiency of atosi ban, an oxytocin receptor blocking agent in the treatment of experimental endometriosis. Arch Gynecol Obstet. 2012 Sep;286(3):777–83.

. Gunther R, Walker C Adenomyosis. [Updated 2021 jul 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021.

- Both endometriotic and adenomyotic endometrial cells have increased levels of prostaglandins
- Decreased endometrial prostaglandin expression may make a more favourable environment for implantation. Atosiban demonstrated a higher pregnancy rate per cycle (58.3% atosiban vs 38.3% control group) when administered before frozen embryo transfer.

- While Simon et al.also reported lower implantation and pregnancy rates for patients with endometriosis versus tubal infertility, they added a dimension to the data by analysing the outcomes of oocyte donation from donors with and without endometriosis.
- They reported comparable implantation and pregnancy rates for women with and without endometriosis who received oocytes from donors without endometriosis.
- Simon C, Gutierrez A, Vidal A, et al. Outcome of patients with endometriosis in assisted reproduction: Results from in vitro fertilization and oocyte donation. Hum Reprod. 1994;9:725–9.

- However, patients who received oocytes from endometriotic ovaries had significantly lower implantation rates.
- From this, it has been suggested that an endometriosis-associated impairment of implantation results from a compromise to the potential of the oocyte or early embryo, and not to the endometrium itself.
- 56. Bishop LA, Gunn J, Jahandideh S, et al. Endometriosis does not impact live-birth rates in frozen embryo transfers of euploid blastocysts. Fertil Steril. 2021 Feb;115(2):416–22.

This was a multicentre and retrospective cohort study including all patients undergoing euploid frozen blastocyst transfer.

- Analysis of 459 euploid frozen embryo transfer cycles among 328 unique patients showed that there was no difference in clinical pregnancy, pregnancy loss, or live birth rates in patients with endometriosis compared with non-infertile patients who underwent assisted reproduction to screen embryos and couples with isolated male factor infertility.
- Díaz I, Navarro J, Blasco L, et al. Impact of stage III–IV endometriosis on recipients of sibling oocytes: Matched casecontrol study. Fertil Steril. 2000;74:31–4.

- For those who have undergone preimplantation testing, aneuploidy rates
 were lowest, whereas endometriosis
 patients had similar aneuploidy rates
 when compared with male infertility
 factored patients.
- They concluded that by controlling embryo quality using frozen blastocysts, endometriosis compared with male infertility and non-infertile patients resulted in similar pregnancy outcomes.

- higher miscarriage rate following IVF among patients with stage III or IV endometriosis when compared to those with less severe disease.
- Along with a diminished oocyte yield and poor embryo quality, Yanushpolsky et al.
 reported a significantly higher early
 pregnancy loss when endometriomas
 were aspirated at the time of oocyte
 retrieval.

- Endometriosis may also be associated with late pregnancy complications, such as preterm birth.
 Stephansson et al. showed that, compared with women without endometriosis, women with endometriosis had a higher risk of preterm birth, with an adjusted OR of 1.33.
- Stephansson O, Kieler H, Granath F, Falconer H. Endometriosis, assisted reproduction technology, and risk of adverse pregnancy outcome. Hum Reprod. 2009;24:2341–7.

A Cochrane review of two randomized trials comparing the effectiveness of laparoscopic surgery in the treatment of subfertility associated with endometriosis versus other treatment modalities or placebo found that use of laparoscopic surgery may improve the chance of pregnancy by an OR of 1.6.

 Jacobson T, Barlow D, Koninckx P, et al. Laparoscopic surgery for subfertility associated with endometriosis. Cochrane Database Syst Rev. 2002;4:CD001398.

A meta-analysis of five studies agreed with these results by concluding that surgical management of endometriomas has no significant effect on IVF pregnancy rates and ovarian response to stimulation compared with no treatment.

 Tsoumpou I, Kyrgiou M, Gelbaya TA, Nardo LG. The effect of surgical treatment for endometrioma on in vitro fertilization outcomes: A systematic review and meta-analysis. Fertil Steril. 2009;92:75–87.

- Pregnancy rates were reported as 70% over two cycles of IVF, compared with 24% for the nine months following surgery.
- There are no similar randomized studies evaluating the effects of surgery on severe disease.

 However, a study by Bianchi et al. of women with deep infiltrative endometriosis found that extensive laparoscopic excision of endometriotic lesions improved pregnancy outcomes significantly (OR 2.45).

 Bianchi PH, Pereira RM, Zanatta A, et al. Extensive excision of deep infiltrative endometriosis before in vitro fertilization significantly improves pregnancy rates. J Minim Invasive Gynecol. 2009;16:174–80.

Future directions

- Additional successes in pregnancy for patients diagnosed with endometriosis might be attributed to metformin.
- Metformin is originally an insulin sensitizer widely used to treat type 2 diabetes mellitus; however, it could be used as treatment for endometriosis without serious side effects because metformin simply increases the activity of superoxide dismutase and decreases the levels of the vascular endothelial growth factor.
- Stochino-Loi E, Major AL, Gillon TER, et al. Metformin, the rise of a new medical therapy for endometriosis? A systematic review of the literature. Front Med (Lausanne). 2021 May 11;8:581311.

Future directions

 Other frontiers include a non-invasive diagnostic marker for endometriosis. B Cell Lymphoma 6, also known as BCL6, and Sirtuin 1, or SIRT 1, are these potential biomarkers.

 127. Kimber-Trojnar Ż, Dłuski DF, Wierzchowska-Opoka M, et al. Metformin as a potential treatment option for endometriosis. Cancers (Basel). 2022 Jan 24;14(3):577

Future directions

- Although results show that higher levels of SIRT1 were found in advanced stages of endometriosis
 compared to controls and lower stages of endometriosis, there were no significant
 differences between BCL6 and SIRT1 in other
 bodily fluids. BCL6 and SIRT1 have a large
 potential to be non-invasive markers to diagnose
 endometriosis.
- The potential for these two markers should thus be further studied and researched to assess outcomes of treatment after diagnosis with these biomarkers and consequently simplify the diagnosis of endometriosis.

Future directions

- Finally, advances in surgical techniques may allow for improved surgical management of infertility associated endometriosis, and as ease and efficiency improve, increase the feasibility of performing RCTs involving surgical interventions.
- The Laparoscopic versus Robotic Surgery for Endometriosis (LAROSE) trial has already demonstrated similar outcomes between robotic and laparoscopic surgery in terms of operative time, complications, and quality of life at six weeks and six months.
- 129. Soto E, Luu TH, Liu X, et al. Laparoscopy vs. robotic surgery for endometriosis (LAROSE): A multicenter, randomized, controlled trial. Fertil Steril. 2017 Apr;107(4):996– 1002.

A REVIEW TO ESHRE GUIDELINE 2022

A REVIEW TO ESHRE GUIDELINE 2022

American Society for Reproductive Medicine **Revised Classification of Endometriosis**

Patient's Name		Date	
Stage I (Minimal) - 1-5 Stage II (Mild) - 6-15 Stage III (Moderate) - 16-40 Stage IV (Severe) - 340	Laparoscopy Recommended Tr	Laparotomy	Photography.
Total	Prognosis		

MUEN	ENDOMETRIOSIS	<1cm	I-3cm	>3cm	
Ĕ	Superficial	1	2	4	
8	Deep	2		6	
	R Superficial	1	2	4	
N.	Deep	-4	16	20	
NO	L Superficial	L	2	4	
1000	Deep	4	16	20	
	POSTERIOR	Partial		Complete	
	OBLITERATION			40	
OVARY OVARY PERU	ADHESIONS	<1/3 Enclosure	<1/3 Enclosure 1/3-2/3 Enclosure		
2	R Filmy	1	2	4	
N	Dense	- 4	8	16	
•	L Filmy	1	2	4	
	Dense	-4	8	16	
_					
	R Filmy	1	2		
	R Filmy Dense	4*	2 8'	16	
TURE	R Filmy Dense L Filmy	1 4* 1	2 8' 2	16 4	

Associated Pathology ...

"If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.

To Be Used with Normal Tubes and Ovaries

Additional Endometriosis: ____

1	Tubes an	with Ab	arics		
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Scoring endometriosis

ENDOMETRIOSIS FERTILITY INDEX (EFI) SURGERY FORM

LEAST FUNCTION (LF) SCORE AT CONCLUSION OF SURGERY



ENDOMETRIOSIS FERTILITY INDEX (EFI)

	Historical Factors		Surgical Factors		
Factor	Description	Points	nts Factor Description		
Age			LF Score		
	If age is ≤ 35 years	2	2 If LF Score = 7 to 8 (high score)		
	If age is 36 to 39 years	1	1 If LF Score = 4 to 6 (moderate score)		
If age is ≥ 40 years		0	0		
Years Int	fertile		AFS Endometriosis Score		
	If years infertile is ≤ 3	2	If AFS Endometriosis Lesion Score is < 16	1	
	If years infertile is > 3	0	If AFS Endometriosis Lesion Score is ≥ 16		
Prior Pre	egnancy		AFS Total Score		
If there is a history of a prior pregnancy		1	If AFS total score is < 71	1	
	If there is no history of prior pregnancy	0	If AFS total score is ≥ 71	0	
	storical Factors		Total Surgical Factors		

ESTIMATED PERCENT PREGNANT BY EFI SCORE



ARE HORMONE/MEDICAL THERAPIES EFFECTIVE FOR TREATMENT ØF ENDOMETRIOSIS-ASSOCIATED INFERTILITY?

ESHRE 2022

 In infertile women with endometriosis, clinicians should not prescribe ovarian suppression treatment to improve fertility. Hormone or medical therapies as an adjunct to surgical therapy

- Women seeking pregnancy should not be prescribed postoperative hormone suppression with the sole purpose to enhance future pregnancy rates.
- Those women who cannot attempt to or decide not to conceive immediately after surgery may be offered hormone therapy as it does not negatively impact their fertility and improves the immediate outcome of surgery for pain.

ESHRE 2022

Other medical treatments

In infertile women with endometriosis, clinicians should not prescribe pentoxifylline, other anti-inflammatory drugs or letrozole outside ovulation-induction to improve natural pregnancy rates. IN WOMEN WITH ENDOMETRIOSIS, IS SURGERY EFFECTIVE TO INCREASE THE CHANCE OF NATURAL PREGNANCY?

- Operative laparoscopy could be offered as a treatment option for endometriosisassociated infertility in rASRM stage I/II endometriosis as it improves the rate of ongoing pregnancy.
- Clinicians may consider operative laparoscopy for the treatment of endometriomaassociated infertility as it may increase their chance of natural pregnancy, although no data from comparative studies exist.
- Although no compelling evidence exists that operative laparoscopy for DE improves fertility, operative laparoscopy may represent a treatment option in symptomatic patients wishing to conceive.
- The GDG recommends that the decision to perform surgery should be guided by the presence or absence of pain symptoms, patient age and preferences, history of previous surgery, presence of other infertility factors, ovarian reserve, and estimated EFI.
- ESHRE 2022

NARRATIVE QUESTION: WHICH PATIENTS NEED TREATMENT WITH ASSISTED REPRODUCTION TECHNOLOGY AFTER SURGERY[®]

- Women should be counselled of their chances of becoming pregnant after surgery. To identify patients that may benefit from ART after surgery, the Endometriosis Fertility Index (EFI) should be used as it is validated, reproducible and cost-effective. The results of other fertility investigations such as their partner's sperm analysis should be taken into account
- It is suggested that the EFI is used for better patient phenotyping in studies on surgical treatment and/or the place of medically assisted reproduction (MAR) in endometriosis-related infertility. The role of the EFI as a pre-surgical triage tool should be validated.
- ESHRE 2022

PICO QUESTION: IS MEDICALLY ASSISTED REPRODUCTION EFFECTIVE FOR INFERTILITY ASSOCIATED WITH ENDOMETRIOSIS? In infertile women with rASRM stage I/II endometriosis, clinicians may perform intrauterine insemination (IUI) with ovarian stimulation, instead of expectant management or IUI alone, as it increases pregnancy rates.

 Although the value of IUI in infertile women with rASRM stage III/IV endometriosis with tubal patency is uncertain, the use of IUI with ovarian stimulation could be considered

• ESHRE 2022

Assisted reproductive technology in women with endometriosis.

- ART can be performed for infertility associated with endometriosis, especially if tubal function is compromised, if there is male factor infertility, in case of low EFI and/or if other treatments have failed.
- A specific protocol for ART in women with endometriosis cannot be recommended. Both GnRH antagonist and agonist protocols can be offered based on patients' and physicians' preferences as no difference in pregnancy or live birth rate has been demonstrated.
- Women with endometriosis can be reassured regarding the safety of ART since the recurrence rates are not increased compared to those women not undergoing ART.
- In women with endometrioma, clinicians may use antibiotic prophylaxis at the time of oocyte retrieval, although the risk of ovarian abscess formation following follicle aspiration is low
- ESHRE 2022

ARE MEDICAL THERAPIES EFFECTIVE AS AN ADJUNCT TO MAR FOR ENDOMETRIOSIS ASSOCIATED INFERTILITY?

- The extended administration of GnRH agonist prior to ART treatment to improve live birth rate in infertile women with endometriosis is not recommended, as the benefit is uncertain.
- There is insufficient evidence to recommend prolonged administration of the COC/progestogens as a pretreatment to ART to increase live birth rates.

• ESHRE 2022

ARE SURGICAL THERAPIES EFFECTIVE AS AN ADJUNCT PRIOR TO MAR FOR ENDOMETRIOSIS-ASSOCIATED INFERTILITY?

- Clinicians are not recommended to routinely perform surgery prior to ART to improve live birth rates in women with rASRM stage I/II endometriosis, as the potential benefits are unclear.
- Surgery prior to MAR in women with ovarian endometrioma
- Clinicians are not recommended to routinely perform surgery for ovarian endometrioma prior to ART to improve live birth rates, as the current evidence shows no benefit and surgery is likely to have a negative impact on ovarian reserve.
- Surgery for endometrioma prior to ART can be considered to improve endometriosisassociated pain or accessibility of follicles.
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Surgery prior to MAR in women with deep endometriosis

Surgery prior to MAR in women with deep endometriosis The decision to offer surgical excision of deep endometriosis lesions prior to ART should be guided mainly by pain symptoms and patient preference as its effectiveness on reproductive outcome is uncertain due to lack of randomised studies.

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WHAT NON-MEDICAL MANAGEMENT STRATEGIES ARE EFFECTIVE FOR INFERTILITY ASSOCIATED WITH ENDOMETRIOSIS ?

- Regarding non-medical strategies on infertility, there is no clear evidence that any non-medical interventions for women with endometriosis will be of benefit to increase the chance of pregnancy.
- No recommendation can be made to support any nonmedical interventions (nutrition, Chinese medicine, electrotherapy, acupuncture, physiotherapy, exercise, and psychological interventions) to increase fertility in women with endometriosis. The potential benefits and harms are unclear.

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IS ENDOMETRIOSIS AN INDICATION FOR FERTILITY PRESERVATION (OVARIAN TISSUE / OOCYTES)



 In case of extensive ovarian endometriosis, clinicians should discuss the pros and cons of fertility preservation with women with endometriosis. The true benefit of fertility preservation in women with endometriosis remains unknown.

WHAT IS THE IMPACT OF WHAT IS THE IMPACT OF ENDOMETRIOSIS ON PREGNANCY AND OBSTETRIC OUTCOME? ENDOMETRIOSIS ON PREGNANCY AND OBSTETRIC OUTCOME?

- Patients should not be advised to become pregnant with the sole purpose of treating endometriosis, as pregnancy does not always lead to improvement of symptoms or reduction of disease progression.
- Endometriomas may change in appearance during pregnancy. In case of finding an atypical endometrioma during ultrasound in pregnancy, it is recommended to refer the patient to a centre with appropriate expertise.

Im PREGNANCY AND OBSTETRIC OUTCOME? pact of endometriosis on early pregnancy (1st trimester)

- Miscarriage
- Ectopic pregnancy
- Clinicians should be aware that there may be an increased risk of first trimester miscarriage and ectopic pregnancy in women with endometriosis.

Impact Impact of endometriosis on 2nd and 3rd trimester pregnancy and neonatal outcomeof endometriosis on 2nd and 3rd trimester pregnancy and neonatal outcome

- Gestational diabetes (GDM)
- Preterm birth / premature rupture of membranes
- Placenta praevia
- Hypertensive disorders and pre-eclampsia
- Stillbirth
- Caesarean section
- Obstetric haemorrhages (placental abruption, anteand post-partum bleeding)
- Small for gestational age, admission to NICU, neonatal death

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ART and endometriosis recurrence

 Clinicians can perform ART in women with deep endometriosis, as it does not seem to increase endometriosis recurrence per se.

Thank you for your attention