

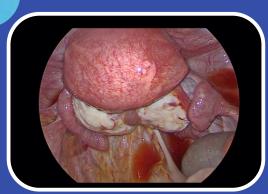




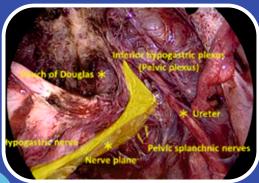


# KSOGA UPDATE ENDOSCOPY COMMITTEE

NOVEMBER - 2024









ENDOSCOPE: "SHEDDING LIGHT ON ENDOMETRIOSIS"

4<sup>™</sup> EDITION











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Dr. M G Hiremath Chief Patron KSOGA & KCOG

### Dear Esteemed Members of the KSOGA Endoscopic Committee,

I am filled with pride and gratitude as I pen this note for the latest edition of the KSOGA UPDATE, Volume 4, focusing on the Complete Management of Endometriosis. This comprehensive review underscores the collaborative excellence and passionate dedication that embodies the spirit of KSOGA.Firstly, I extend my heartfelt appreciation to our remarkable President, Dr. Bharathi Rajashekar. Under her astute guidance and unwavering encouragement, the Endoscopic Committee has reached unprecedented heights. Her vision and leadership have provided a solid foundation for achieving success in all our endeavors.My sincere gratitude also goes to Dr. Rajashree Paladi, our diligent Secretary. Her constant support and dedication have been pivotal in strengthening the Committee and moving our initiatives forward.

It is through her persistence and organizational excellence that we continue to thrive. A special acknowledgment is due to Dr. Suman Gaddi, our esteemed Treasurer. Her unwavering support and meticulous attention to financial matters have ensured the seamless execution of our projects and activities, thus contributing significantly to our shared goals. I would also like to commend Dr. Ramesh B, our Chief Adviser, whose insights and advice have been instrumental in shaping the path for this esteemed publication. His profound expertise continues to inspire us all.Dr. Vidya Bhat, our Master Trainer, has played an invaluable role in sharing her knowledge and skills. Her training and mentorship have been a beacon of excellence, influencing the quality and effectiveness of our initiatives. extend my deepest appreciation to Dr. Ravikanth G O, the Chairperson of the Endoscopic Committee. His leadership has guided the team through various challenges while steering our ambitions towards success with determination and innovation. Finally, I would like to praise all the authors and contributors to the KSOGA UPDATE, Vol. 4. Your creativity, commitment, and active participation have resulted in a publication of outstanding quality. It reflects the collective intelligence and dedication of each of you, showcasing the amalgamation of diverse talents within our organization. Together, we have shaped a cornerstone for excellence in the fields of gynecology and endoscopic advancements. I look forward to witnessing continued success and innovation as we move forward united in our mission.

With deepest regards and warm wishes,

Dr. M G Hiremath
Chief Patron

# PRESIDENTIAL ADDRESS



**Dr. Bharathi Rajashekhar**President,
Karnataka State Obstetrics and
Gynaecologists Association

#### Namaste

It gives me immense delight to know that the ksoga endoscopy committee under the chairmanship of DR Ravikanth is bringing out yet another newsletter, this time the focus is on managing endometriosis.

Endometriosis, a condition affecting an estimated 10% of women and girls of reproductive age worldwide, stays one of the most misunderstood and under-discussed health issues.

Scientific advancements have also made promising strides. Researchers are finding potential biomarkers for earlier diagnosis and exploring less invasive diagnostic methods, which could eventually eliminate the need for diagnostic surgery. Additionally, new treatments and therapeutic approaches are being studied to provide more effective, individualized options for managing pain and enhancing quality of life.

A Call to Stand Together- Let us stand together, united in our commitment to a future where no one must suffer in silence.

We have the power to make a real difference in the lives of millions—by raising our voices, advocating for funding, and fighting for better care and support for those with endometriosis.

This update has been very well composed covering all topics to ensure endoetriossis is managed optimally and effectively, so we can provide the best to these women.

Thank you for your continued support and for standing with us in this journey. Together, we will create a world where endometriosis is understood, treated effectively, and no longer shrouded in stigma.

Dr. Bharathi Rajashekhar

President,

Karnataka State Obstetrics and Gynaecologists Association

### GENERAL SECRETARY ADDRESS



**Dr. Rajshree Paladi** Honorary Secretary KSOGA 2023-2024

### Greeting's to Everyone!

#### **Pranams**

Dear colleagues and esteemed members of KSOGA, As we gather for our state conference, I would like to extend warm \*season's greetings\* to each one of you. This annual event is a time not only for learning and collaboration but also for reflecting on the challenges and advancements within our field. One of the pivotal topics we will be addressing is Endometriosis- a condition that remains an ever challenging question in our medical community. Despite ongoing research and clinical efforts, the answers are few, and the challenges are plenty. Each encounter with a patient facing this condition reminds us of the complexities involved in diagnosis and treatment. The modalities of treatment and solutions keep us, as clinicians, at a crossroads each time we strive to provide the best care possible.In light of this challenging landscape, I would like to take a moment to spotlight the incredible work carried out by the \*KSOGA Endoscopy Committee\*.

Their relentless efforts in exploring and presenting relevant topics related to endometriosis are not only commendable but also essential for our collective growth as healthcare professionals.

The committee's dedication to education and guidance plays an invaluable role in equipping us with the knowledge needed to navigate this complex issue, ultimately benefiting our patients. As we dive into discussions and learn from one another at the conference, I encourage everyone to actively participate, share insights, and engage with the material presented. Continuous learning is crucial in our field, especially when tackling topics that are as multifaceted as endometriosis. I would like to extend my Best wishes to the committee and all team members involved in preparing this informative session. Your hard work does not go unnoticed, and I am confident that the knowledge shared will have a lasting impact on our practices. In conclusion, let us join hands to celebrate the achievements of the past year, acknowledge the ongoing challenges we face, and commit ourselves to continual learning and improvement in the care we provide.

Together, we can make significant strides in understanding and managing endometriosis.\*Congratulations\* to the entire team for your dedication and commitment to this important work. I look forward to seeing you all at the conference and learning alongside you.

Best regards, **Dr. Rajshree Paladi**Honorary Secretary, KSOGA 2023-2025





"Success is not final, failure is not fatal: it is the courage to continue that counts."

The Endoscopy Committee of KSOGA is diligently working to bring endoscopic awareness across Karnataka. This is our fourth bulletin, and I extend my heartfelt gratitude to all committee members for their dedication and commendable contributions.

Our bulletin has always focused on challenging topics in endoscopy that demand careful decision-making. In our previous discussions, we have explored hysteroscopy, electrosurgery, and mullerian anomalies. This issue addresses endometriosis, a prevalent and often complex condition that affects many women. The management of endometriosis requires a balanced approach, combining surgical precision with conservative strategies to optimize patient outcomes. This bulletin sheds light on conservative management techniques for endometriosis and emphasizes the importance of tailoring treatment to each patient, avoiding overtreatment that may lead to unnecessary complications. Our goal is to provide insight into the nuances of managing endometriosis to empower practitioners with the latest knowledge and best practices for their patients.

I would like to thank all the faculty who contributed to this bulletin for their unwavering efforts. I congratulate and thank Dr. Ravikanth for all his efforts. My heartfelt gratitude also goes to Dr. Bharathi Rajashekar, M.G. Hiremath Sir, Dr. Vidya Thobbi, Dr. Rajashree Palladi, Dr. Hema Divakar, Dr. Muralidhar Pai, Dr. Nagaraj, Dr. Bellad and Dr. Durgadas for their constant support and encouragement.

"Together, we can achieve greatness beyond measure."

Regards,
Dr. Vidya V Bhat
"Team work makes the dream work"
Bang Gae

# CHAIRPERSON'S ADDRESS



Dr. Ravikanth G. O
Chairperson, Endoscopic Committee,
Karnataka State Obstetrics and
Gynaecologists Association

### Dear Esteemed Members of the KSOGA Community,

It is with immense pleasure and pride that I address you as the Chairperson of the Endoscopy Committee for the highly anticipated KSOGA UPDATE Volume 4. This edition focuses on the powerful theme of "Endoscopy: Shedding Light on Endometriosis," a topic that continues to advance both our knowledge and our practice.

I would like to extend our heartfelt gratitude to our chief patrons, Dr. M. G. Hiremath and Dr. H. N. Naagraj, for their unwavering support and belief in our mission. Their commitment is a driving force behind our successful endeavors.

Our deepest appreciation goes to the President of KSOGA, Dr. Bharathi Rajashekar, whose encouragement fuels our passion and dedication. Her leadership continues to inspire the Endoscopy Committee to push forward with innovation and excellence.

A special thank you to Dr. Vidya Thobbi, the immediate past president, for laying a strong foundation upon which we continue to grow. Her legacy is one we proudly carry forward.

I am equally grateful to our Secretary, Dr. Rajashree Paladi, for her guidance and insight which has been pivotal in steering our committee towards

success. Her strategic vision has enriched our approaches and outcomes.

We are also indebted to Dr. Durgadas Asaranna, our President Elect, and Dr. Suman Gaddi, our Treasurer, for their outstanding contributions and constant support which strengthens our initiatives.

Our profound gratitude goes to our Chief Advisor, Dr. Ramesh B, whose inspiration and guidance serve as a beacon for us all. Additionally, a heartfelt thanks to our Master Trainer, Dr. Vidya Bhatt, whose expertise and dedication are the main guiding force driving our committee's goals to fruition.

The invaluable contributions of our esteemed advisors, Dr. Sandesh Kade, Dr. Subhash Mallya, and Dr. Jayaprakash Patil, enhance the depth and impact of our work. Their input helps us reach and often exceed our objectives.

Our diligent Secretary of the Endoscopy Committee, Dr. Sonia Batra, deserves commendation for her tireless efforts and exceptional organizational skills that keep the wheels of our committee turning smoothly.

Finally, a huge thank you to all the committee members and contributors who have worked diligently behind the scenes to bring KSOGA UPDATE Volume 4 to life. Your dedication and hard work are evident in every page of this bulletin.

Together, we celebrate these collective achievements and look forward to further innovations and breakthroughs that continue to benefit our practice and patient care.

With warm regards, **Dr. Ravikanth G.O** 

### EDITORIAL TEAM



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**Dr Vidya Bhat**Advisor, Endoscopic Committee
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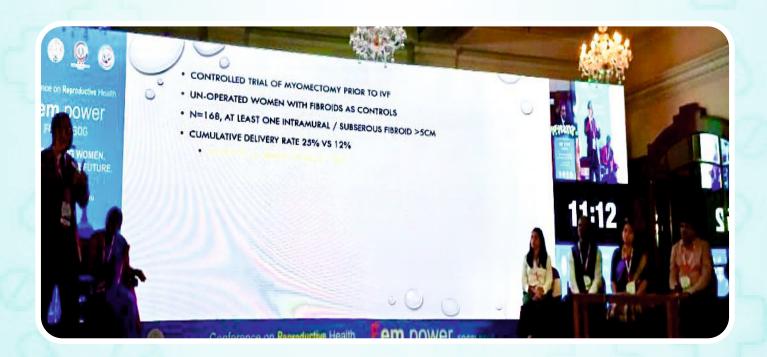




CME ON FERTILITY ENHANCING SURGERY IN ASSOCIATION WITH KOIMS KODAGU AND NOVA IVF MYSORE ON 22/6/2024 CLUB MAHENDRA KODAGU

### PANEL DISCUSSION ON FERTILITY ENHANCING SURGERY AT FEM POWER











Endovision, Webinar from
FOGSI Dr Ravikanth, Chairperson
for the Video Presentation
on 26/01/24



Dr Prabha Desai contributed to FOGSI activity webinar



Yuva KSOGA 2024 MANIPAL & Live Surgery conducted by: Dr. Vidya Bhat, Dr. Ramesh B & Dr. Rajesh Bhakta

### EVE ENDOSCOPY AT ITC GARDENIA, BANGALORE ON OCTOBER 3









### ENDOSCOPE: "SHEDDING LIGHT ON ENDOMETRIOSIS"

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# COMPREHENSIVE OVERVIEW: PATHOPHYSIOLOGY AND PATHOGENESIS OF ENDOMETRIOSIS



Dr. Prema D. Cunha Prof & Unit Head FMMC Mangaluru

Endometriosis is the presence of functional endometrial tissue in the peritoneal cavity and other sites, classically defined by the presence of endometrial glands and stroma in extrauterine locations. It is a complex reproductive disorder affecting between 6% and 10% of reproductive-age women worldwide. Women in the reproductive-age experiencing chronic pelvic pain or infertility, the prevalence of endometriosis amounts to around 45% and 35%, respectively.

#### PATHOPHYSIOLOGY OF ENDOMETRIOSIS

Endometriosis is a complex, multifactorial disease with still undetermined cause. Several theories have been put forward to the disease development but no exact cause has been established. These theories may be classified as implants a) of uterine origin b) of extra uterine origin

### Of Uterine Origin

a)Sampson's theory of retrograde menstruation states that the endometrial cells which are found at ectopic locations are the result of menstrual blood, through fallopian tubes is pushed into the peritoneal cavity during the menstrual cycle. Three conditions must be fulfilled for endometriosis to occur: retrograde menstruation must happen, the menstrual efflux must contain viable endometrial cells, and these cells must adhere to the peritoneum and continue their proliferation there following this successful implantation.

b) The theory of benign metastasis holds that ectopic endometrial implants are the result of lymphatic or hematogenous dissemination of endometrial cells. Microvascular studies demonstrated flow of lymph from the uterine body into the ovary, rendering possible a role for the lymphatic system in the etiology of ovarian endometriosis.

### Of Extra Uterine Origin

a) Coelomic metaplasia theory proposed by Iwanoff and Meyer in 1942, states that there is a species of cells, located in the mesothelial lining of the ovary and the peritoneum, that is able to differentiate into endometrial cells under certain conditions.

b)Embryonic rest theory also referred as mulleraniosis postulates that embryonic cell rests of müllerian origin are present in both men and women, and are capable of differentiating into ectopic endometrium under specific conditions, possibly the influence of estrogen.

c)Extra-uterine stem/progenitor cells originating from bone marrow may differentiate into endometriotic tissue.

#### PATHOGENESIS OF ENDOMETRIOSIS

No single theory can completely explain the pathogenesis of endometriosis. It is the result of complex interaction between the expression of genes involved in endometriosis, inflammatory reactions, and the disrupted hormone response. A theory linking endocrine disrupting chemicals (EDCs) with endometriosis suggest these, and endogenous/exogenous estrogens, as potential transforming/inductive/ stimulant candidates in theories of endometriosis pathogenesis. The developmental timing of action of such agents and their roles in influencing other systems that predispose to endometriosis (endocrine, immune, stem/progenitor cells, epigenetic

modifications) must be considered in the context of genetic background as well as stimulusdriven reprogramming of the female reproductive tract.

The endometriotic disease theory (EDT) considered genetic incidents as necessary for the development of the disease. The genetic-epigenetic theory developed from the basis of EDT, states that both genetic incidents and epigenetic factors of the peritoneal cavity are central to the development of endometriosis. A genetic alteration of the endometrial cells influencing their tendency to implant may be hereditary, since it is seen higher in families. Acquired genomic alterations represent a potential source for a conferred survival advantage. The occurrence of genomic alteration in eutopic endometrium is well documented, and may be consequent to epigenetic factors or oxidative stress (increasing evidence supports epigenetic regulation of steroid hormone action in the endometrium and dysregulation in women with endometriosis. Induction theory holds that an endogenous inductive stimulus, such as a hormonal or immunologic factor, promotes the differentiation of cells in the peritoneal lining to endometrial cells.While the source of endometriotic lesions remains disputed, research into the mechanisms behind their survival and activity in peritoneum has found that dysfunctions in the immune system facilitate the uninterrupted growth of these lesions. Normally, refluxed endometrial tissue is cleared from the peritoneum by the immune system, and the dysregulation of this clearance mechanism has been implicated in the predisposition to implantation and growth of endometrial cells.

Hormonal alterations may influence the ability of endometrial cells to proliferate, attach to the mesothelium and/or evade immune mediated clearance. In addition to estrogen dependence, there is increasing evidence to support a profile of progesterone resistance in the pathophysiology of endometriosis.

These theories are put forward to explain changes seen in endometriosis such as:

a)Endometrial cell survival

b)Endometrial cell attachment and invasion

c)Lesional neuroangiogenesis and growth

d)Inflammation

### **ENDOMETRIOSIS AND INFERTILITY**

One of the symptoms which has the most significant effect on the quality of life in patients with endometriosis is infertility. Women with a more advanced stage of the disease due to severe endometriotic growths usually alter the shape of the reproductive structures and reduce oocyte and sperm motility within the organs. However, infertility affects women with mild endometriosis as well. The increased levels of pro-inflammatory factors within the PF of diseased individuals inhibit sperm motility, and damage oocytes and even the embryo itself. Endometrioma presence on either ovary significantly alter the fertility of the individual by interfering with ovulation and oocyte production of the affected ovary. Follicular fluid from patients with endometriosis causes DNA damage in oocytes through increased reactive oxidative species (ROS) production.

### **ENDOMETRIOSIS AND PELVIC PAIN**

The development of a new blood supply and associated nerves (neuroangiogenesis) is considered key to the establishment of endometriotic lesions and the activation of peripheral pain pathways Sensory C, sensory Ad, cholinergic, and adrenergic nerve fibres have all been detected in lesions.

Estrogens can promote crosstalk between immune cells and nerves within lesions, increasing expression of nociceptive ion channels. There is a central pain process where patients experience reduced pain thresholds, increased responsiveness and duration of after effects to noxious stimuli, so that input from non-injured tissue may elicit pain.

Endometriosis is an inflammatory, estrogen dependent condition associated with pelvic pain and infertility. Understanding its pathogenesis and pathophysiology will help towards its prevention and the development of sensitive non-surgical diagnostic assays and effective treatments.

### **REFERENCES**

1.Burney, R.O. and Giudice, L.C. (2012) 'Pathogenesis and pathophysiology of endometriosis', Fertility and Sterility, 98(3), pp. 511–519. doi:10.1016/j.fertnstert.2012.06.029.

2. Pašalić, E., Tambuwala, M.M. and Hromić-Jahjefendić, A. (2023) 'Endometriosis: Classification, pathophysiology, and treatment options', *Pathology - Research and Practice*, 251, p. 154847. doi:10.1016/j.prp.2023.154847.

### "PRECISION IN PRACTICE: CLINICAL DIAGNOSIS OF ENDOMETRIOSIS"



**Dr. UMAMAHESHWAR SINDUR** Sindur hospital, vijayapur

Endometriosis is a chronic condition defined by the presence of endometrial-like tissue outside of the uterus, which can lead to estrogen-driven inflammation. Prevalence of endometriosis is reported to be about 10% of reproductive age women, about 20–30% of infertility women, and

### Clinical Diagnosis of Endometriosis:

The diagnosis of endometriosis is challenging. There are no pathognomonic features or biomarkers sufficient to define endometriosis. The diagnostic paradigm is now shifting to a multi-modal approach. History: Menstrual, medical, surgical, family, medication, lifestyle, and environmental, physical examination, and imaging prior to initiating medical therapies for pain and/or infertility. Several professional organizations across the globe endorse this approach, including the American College of Obstetricians and Gynecologists (ACOG), WES, the Society

One large retrospective analysis (Ballard et al., 2008)<sup>7</sup>described symptoms that are predictive of the diagnosis of endometriosis, including severe dysmenorrhoea in infertile women, abdominopelvic pain, dysmenorrheoa, heavy menstrual bleeding, infertility, dyspareunia, postcoital bleeding and/or previous diagnosis of ovarian cyst, irritable bowel syndrome or pelvic inflammatory disease

The GDG (<u>Guideline development group (GDG)</u> recommends that clinicians should consider the diagnosis of endometriosis in the presence of gynaecological symptoms such as dysmenorrhoea, non-cyclical pelvic pain, deep dyspareunia, infertility and fatigue. and in women of reproductive age with non-gynaecological cyclical symptoms such as dyschezia, dysuria, haematuria and rectal bleeding, shoulder pain.

### Clinical Examination:

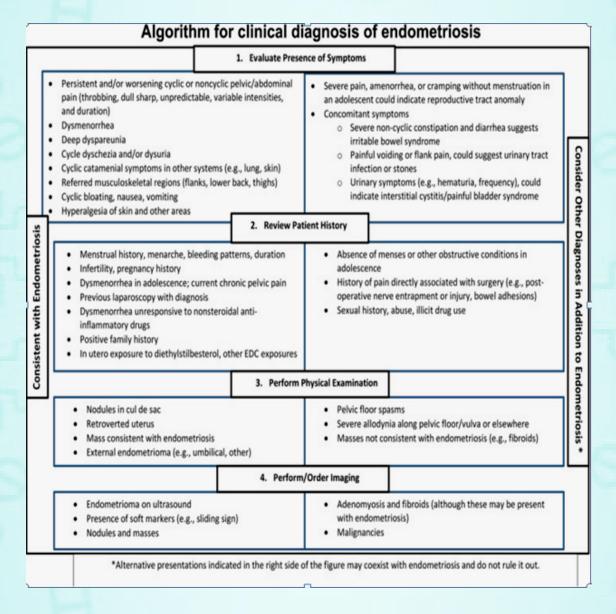
- Cervical Motion Tenderness
- 2. Fullness or induration in fornices
- 3. Induration/Nodularity in posterior fornices (uterosacrals)
- 4. Painful Rectovaginal examination with Induration Clinicians may consider the diagnosis of deep endometriosis in women with induration and nodules of the rectovaginal wall found during clinical examination or visible vaginal nodules in the posterior vaginal fornix (Bazot et al., 2009).

Data from comparative studies suggest that findings on physical examination can identify endometriosis with high accuracy.<sup>15-16</sup> On bimanual examination palpable nodularity, Induration of the uterosacral ligaments, vagina, rectovaginal space, pouch of Douglas, adnexa, rectosigmoid, or posterior wall of the urinary bladder), endometriosis diagnosis accuracy of 86to99%,(Hudelist et al) <sup>17</sup>.

Anterior vaginal wall tenderness has low sensitivity for detecting endometriosis in women with chronic pelvic pain,<sup>17</sup> but demonstrates prognostic value for endometriosis among women with unexplained infertility.<sup>18</sup>.

The clinical assessment of endometriosis is enhanced when multiple factors are combined. Diagnosis of endometriosis is increased with the number of symptoms present, from an odds ratio of 5.0 with one symptom to 84.7 for seven or more symptoms. (Ballard et al<sup>7</sup>).

Using data from a prospective, multinational study, An Algorithm for a clinical diagnosis of endometriosis is developed. This algorithm reduces diagnostic delay, high investigation costs, and personal suffering associated with endometriosis. It also provides unified practical approach to clinically diagnosing endometriosis.



The algorithm shows sequence of clinical diagnosis beginning with evaluation of symptoms (section 1), review patient history (section 2), perform physical examination (section 3), and performing/order imaging (section 4). Items on the left side of the figure are informative about possible endometriosis diagnosis. Items on the right side may co-exist with endometriosis but do not rule it out.

Ref.: Agarwal SK, Chapron C, Giudice LC, et al. Clinical diagnosis of endometriosis: a call to action. Am J Obstet Gynecol. 2019;220(4):354.e1-354.

### Various studies on clinical assessment of Endometriosis

Study design and population	Method of diagnosis	Assessment or parameter	Results
Marasinghe 2014 <sup>49</sup> Prospective, observational study comprising women evaluated for	Laparoscopically visualized endometriosis	Dyspareunia	Sensitivity, 46%; specificity, 77%; PPV, 52%; NPV, 73%; accuracy, 47%
infertility and/or chronic pelvic pain (N = 110)		Dysmenorrhea	Sensitivity, 76%; specificity, 70%; PPV, 57%; NPV, 84%; accuracy, 71%
		Dyspareunia and dysmenorrhea	Sensitivity, 78%; specificity, 64%; PPV, 54%; NPV, 85%; accuracy, 68%
		P	Sensitivity, 73%; specificity, 88%; PPV, 77%; NPV, 86%; accuracy, 83%
		Dyspareunia, dysmenorrhea, and vaginal examination	Sensitivity, 84%; specificity, 62%; PPV, 54%; NPV, 88%; accuracy, 69%
		Fixed ovaries on TVS	Sensitivity, 78%; specificity, 94%; PPV, 88%; NPV, 89%; accuracy, 88%
		Dyspareunia, dysmenorrhea, vaginal examination and fixed ovaries	Sensitivity, 92%; specificity, 61%; PPV, 56%; NPV, 93%; accuracy, 71%
Deep endometriosis			
Perello 2017 <sup>56</sup> Retrospective analysis of consecutive women with ovarian endometrioma who underwent surgery (N = 178)	Histologically verified endometriosis	Model including previous pregnancy, history of surgery for endometriosis, endometriosis- associated pelvic pain score	Sensitivity, 80%; specificity, 84%
Lafay Pillet 2014 650 Prospective, single-center study of		Infertility (primary or secondary)	Sensitivity, 51%; specificity, 73%; 0R, 1.5; $\rho=0.003$
women with a histological diagnosis of endometriosis (N = 211)		Duration of pain >24 mo	Sensitivity, 62%; specificity, 81%; 0R, 7.1; $\rho < 0.001$
	VAS GI syr	VAS deep dyspareunia >5	Sensitivity, 69%; specificity, 59%; 0R, 3.2; $\rho=0.007$
		VAS GI symptoms ≥5	Sensitivity, 75%; specificity, 76%; 0R, 9.3; $\rho < 0.001$
		Severe dysmenorrhea	Sensitivity, 55%; specificity, 75%; OR, 3.5; $\rho < 0.001$
Hudelist 2011 <sup>52c</sup> Prospective study of premenopausal women with	Histologically verified endometriosis	Vaginal examination	Sensitivity, 25–78%; specificity, 80–100%; PPV, 43–100%; NPV, 84–98%; accuracy, 73–98%
suspected endometriosis (N = 129)		TVS	Sensitivity, 50-96%; specificity, 96-100%; PPV, 50-100%; NPV, 90-99%; accuracy, 90-99%

Study design and population	Method of diagnosis	Assessment or parameter	Results
Peterson 2013 <sup>41b</sup> ENDO Study—Prospective, matched-exposure cohort study	Surgically visualized endometriosis (operative cohort) Pelvic MRI-diagnosed endometriosis (matched cohort)	History of infertility	OR, 2.43 (95% Cl, 1.57—3.76) [operative]; 7.91 (1.69—37.2) [matched]
comprising women undergoing pelvic surgery (n = 495) and a matched cohort (n = 131)		Dysmenorrhea	OR, 2.46 (95% Cl, 1.28-4.72) [operative]; 1.41 (0.28-7.14) [matched]
		Petvic pain	OR, 1.39 (95% Cl, 0.95—2.04) [operative]; 0.76 (0.09—6.54) [matched]
		Pelvic pain (surgical indication)	OR, 3.67 (95% CI, 2.44-5.50) [operative]
Nnoaham 2012 <sup>43</sup> Prospective, observational study of symptomatic women with scheduled laparoscopy	Laparoscopically visualized endometriosis	Model comprising multiple factors (eg, dysmenorrhea, dyschezia, nonmenstrual pelvic pain, ovarian cyst, family history, race, etc)	Sensitivity, 85%; specificity, 44%
(N = 1396)		Model and ultrasound	Sensitivity, 58%; specificity, 89%
Paulson 2011 <sup>54</sup> Prospective cohort of women	Laparoscopically or histologically confirmed endometricsis	Anterior vaginal wall tendemess (endometriosis and other pathology)	Sensitivity, 93%
with chronic pelvic pain (N = 284)		Anterior vaginal wall tendemess (endometriosis only)	Sensitivity, 17%
Droz 2011 <sup>65</sup>	Histologically verified	Short-form MPQ pain descriptor:	
Retrospective cohort of women evaluated for chronic pelvic pain N = 331)		Cramping	Sensitivity, 92%; specificity, 33% PPV, 40%, NPV, 89%
,,, = 331,		Sickening	Sensitivity, 73%; specificity, 46%; PPV, 40%; NPV, 78%
		Tiring/exhausting	Sensitivity, 77%; specificity, 38%; PPV, 38%; NPV, 77%
		Shooting	Sensitivity, 70%; specificity, 43%; PPV, 37%; NPV, 75%
		Punishing/cruel	Sensitivity, 49%; specificity, 65%; PPV, 40%; NPV, 72%
		Splitting	Sensitivity, 36%; specificity, 77%; PPV, 43%; NPV, 71%
Paulson 2009 <sup>15</sup> Prospective study of consecutive women with unexplained infertility N = 55)	Laparoscopically or histologically confirmed endometriosis	Anterior vaginal wall tendemess	Sensitivity, 84%; specificity, 75%; PPV, 86%; NPV, 69%
Meuleman 2009 <sup>79</sup> Retrospective case series	Histologically verified endometriosis	Pelvic pain	Sensitivity, 59%; specificity, 56% PPV, 54%; NPV, 57%
comprising infertile women with regular cycles and no prior endometriosis diagnosis (N = 221)		Pelvic pain and type of infertility, age, and duration of infertility	Sensitivity, 65%; specificity, 73%
Hudelist 2009 <sup>51c</sup> Prospective study of consecutive women with symptoms of	Histologically verified endometriosis	Vaginal examination	Sensitivity, 23-88%; specificity, 89-100%; PPV, 65-100%; NPV, 85-99%; accuracy, 86-99%
endometriosis (N = 200)		Vaginal examination and TVS	Sensitivity, 67-100%; specificity 86-100%; PPV, 50-100%; NPV, 93-100%; accuracy, 86-100%

Study design and population	Method of diagnosis	Assessment or parameter	Results
Peterson 2013 <sup>41b</sup> ENDO Study—Prospective, matched-exposure cohort study	Surgically visualized endometriosis (operative cohort) Pelvic MRI-diagnosed endometriosis (matched cohort)	History of infertility	OR, 2.43 (95% Cl, 1.57—3.76) [operative]; 7.91 (1.69—37.2) [matched]
comprising women undergoing pelvic surgery (n = 495) and a matched cohort (n = 131)		Dysmenorrhea	OR, 2.46 (95% CI, 1.28-4.72) [operative]; 1.41 (0.28-7.14) [matched]
		Pelvic pain	OR, 1.39 (95% CI, 0.95—2.04) [operative]; 0.76 (0.09—6.54) [matched]
		Pelvic pain (surgical indication)	OR, 3.67 (95% Cl, 2.44-5.50) [operative]
Nnoaham 2012 <sup>(3)</sup> Prospective, observational study of symptomatic women with scheduled laparoscopy	Laparoscopically visualized endometriosis	Model comprising multiple factors (eg, dysmenorrhea, dyschezia, nonmenstrual pelvic pain, ovarian cyst, family history, race, etc)	Sensitivity, 85%; specificity, 44%
(N = 1396)		Model and ultrasound	Sensitivity, 58%; specificity, 89%
Paulson 2011 <sup>54</sup> Prospective cohort of women	Laparoscopically or histologically confirmed endometriosis	Anterior vaginal wall tendemess (endometriosis and other pathology)	Sensitivity, 93%
with chronic pelvic pain (N = 284)		Anterior vaginal wall tendemess (endometriosis only)	Sensitivity, 17%
Droz 2011 <sup>65</sup>	Histologically verified endometriosis	Short-form MPQ pain descriptor:	
Retrospective cohort of women evaluated for chronic pelvic pain (N = 331)		Cramping	Sensitivity, 92%; specificity, 33% PPV, 40%, NPV, 89%
,,,		Sickening	Sensitivity, 73%; specificity, 46% PPV, 40%; NPV, 78%
		Tiring/exhausting	Sensitivity, 77%; specificity, 38% PPV, 38%; NPV, 77%
		Shooting	Sensitivity, 70%; specificity, 43% PPV, 37%; NPV, 75%
		Punishing/cruel	Sensitivity, 49%; specificity, 65% PPV, 40%; NPV, 72%
		Splitting	Sensitivity, 36%; specificity, 77% PPV, 43%; NPV, 71%
Paulson 2009 <sup>55</sup> Prospective study of consecutive women with unexplained infertility (N = 55)	Laparoscopically or histologically confirmed endometriosis	Anterior vaginal wall tendemess	Sensitivity, 84%; specificity, 75% PPV, 86%; NPV, 69%
Meuleman 2009 <sup>33</sup> Retrospective case series		Pelvic pain	Sensitivity, 59%; specificity, 56% PPV, 54%; NPV, 57%
comprising infertile women with regular cycles and no prior endometriosis diagnosis (N = 221)		Pelvic pain and type of infertility, age, and duration of infertility	Sensitivity, 65%; specificity, 73%
Hudelist 2009 <sup>31c</sup> Prospective study of consecutive women with symptoms of	Histologically verified endometriosis	Vaginal examination	Sensitivity, 23-88%; specificity, 89-100%; PPV, 65-100%; NPV, 85-99%; accuracy, 86-99%
endometriosis (N = 200)		Vaginal examination and TVS	Sensitivity, 67-100%; specificity 86-100%; PPV, 50-100%; NPV, 93-100%; accuracy, 86-100%

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### IMAGING ADVANCES IN ENDOMETRIOSIS: ENHANCING DIAGNOSTIC ACCURACY



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Endometriosis is a chronic disorder characterized by the presence of endometrial-like tissue outside the uterine cavity, causing significant pain, infertility, and diminished quality of life. It affects 247 million women globally and 42 million women in India 2 It is a leading cause of infertility, affecting up to 50% of women who struggle to conceive. For decades, the gold standard for diagnosing



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endometriosis had been laparoscopy, which delays definitive diagnosis by an average of 6-10 years after symptom onset.'4 However, radio-imaging advances are rapidly shifting the diagnostic paradigm in favour of a non-invasive diagnostic gold standard.

Ultrasonography has become an investigation of choice due to its wide availability, non-invasive nature, affordability, and high sensitivity 5 This article will discuss the advancements in radio-diagnosis of endometriosis, emphasizing its evolving role in improving diagnostic accuracy, the modalities available, and potential challenges.

### 1.2D-Transvaginal Sonography (TVS)

Transvaginal ultrasound TVS) is usually initial modality for evaluation of patients with pelvic pathologies including suspected endometriosis, and is a primary diagnostic tool. TVS allows high-resolution visualisation by placing the transducer in close proximity to the area of interest. A systematic 4-step approach as proposed by International Deep Endometriosis Analysis (IDEA) consensus enables a thorough evaluation (Table 1)

Table 1. IDEA consensus for endometriosis evaluation

Step	Assessment performed	Pathology detected
1	Uterus and ovaries	<ul><li>Adenomyosis</li><li>Ovarian endometriomas</li></ul>
2	Ovarian mobility and site-specific tenderness	<ul><li>Ovarian adhesions</li><li>Sites of tenderness which may indicate endometriosis</li></ul>
3	Uterine sliding sign	<ul> <li>Obliteration of the pouch of Douglas</li> </ul>
4a	<ul><li>Anterior compartment</li><li>Bladder</li><li>Ureters</li><li>Vesicouterine space</li></ul>	<ul> <li>Nodules of deep endometriosis within the anterior compartment</li> </ul>
4b	<ul> <li>Posterior compartment</li> <li>Posterior vaginal wall</li> <li>Uterosacral Ligaments</li> <li>Rectosigmoid colon</li> <li>Pouch of Douglas</li> <li>Rectovaginal septum</li> </ul>	<ul> <li>Nodules of deep endometriosis within the posterior compartment</li> </ul>

### Ovarian Endometrioma (OMA)

Also known as "chocolate cysts" of the ovary, OMAs are present in 17–44% of patients with endometriosis. It has been demonstrated that OMAs can be reliably diagnosed by TVS. They should be carefully measured in three orthogonal planes. They typically appear as unilocular or multi-locular (less than five locules) ovarian cysts with low-level echoes giving a ground-glass appearance, with no vascularisation on colour Doppler (Fig 1). However, in about 5–10% of cases, they might appear as unilocular cysts with ground-glass echogenicity and papillary projections with little or no vascularity (atypical OMA). These are not true papillary projections, but fibrin and blood clots. OMAs should be described using the International Ovarian Tumor Analysis (IOTA) terminology.

including the characteristic question mark sign (Fig 2).

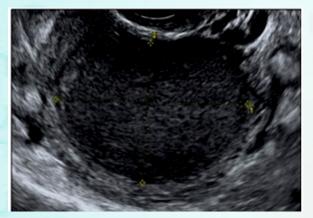


Fig 1. Typical endometrioma on gray-scale imaging with ground-glass appearance



Fig 2. Question mark sign in adenomyotic uterus

"Kissing ovaries" sign (Fig 3), where the ovaries adhere to each other behind the uterus, may be seen. Probe tenderness may also indicate site of involvement. TVS is highly sensitive for detection of ovarian endometriomas, with a reported sensitivity of up to 90-95%, making it one of the primary diagnostic tools for this type of lesion.7



Fig 3. Kissing ovaries sign

### **Atypical ovarian Endometriosis**

Atypical features in ovarian endometriosis may be seen in <1% - 5.8%. These include larger cysts of size  $10 \pm 1$  cm, multi-cystic appearance, presence of any solid component or papillae (Fig 4), or detection of blood flow.

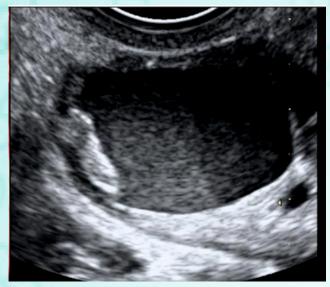


Fig 4. Large atypical endometrioma with solid component

These require a more detailed evaluation to rule out malignancy. The International Ovarian Tumor Analysis (IOTA) ADNEX (Assessment of Different Neoplasias in the adnexa) model is widely used for distinguishing between benign, borderline, and malignant tumors8. A 2020 validation study reported a sensitivity of 96% and specificity of 82-83% for detecting ovarian malignancies, demonstrating its clinical utility in reducing unnecessary surgeries while accurately identifying malignancies.9

### Deep Infiltrating Endometriosis (DIE)10

Key ultrasonographic findings of DIE include hypoechoic lesions seen as bands, nodules, thickening of involved tissue.

Anterior Compartment: Hypoechoic nodules or thickening of the bladder wall may be seen. Ureteral and vesicouterine space involvement should also be assessed.

<u>Posterior Compartment:</u> On ultrasound, endometriotic lesions involving the rectum may have variable appearance, either as wall deposits of anechoic cystic lesions with variable possible hyperechoic blood components (endometriomas) or hypoechoic (echogenicity is compared to the myometrium) irregular thickening, nodules or masses adhered to or infiltrating the deep layers of the bowel wall. TVS can also help to identify depth of bowel layer involvement, especially for small lesions of uterosacral ligament, but these are better characterized on MRI.

*Moose Antler' or 'Indian Headdress' sign:* Sometimes, the normal muscularis propria of the rectum can be replaced by hypoechoic retractile and adhesive endometriotic deposit, giving an irregular shape structure resembling a 'Moose Antler' or 'Indian Headdress' sign.

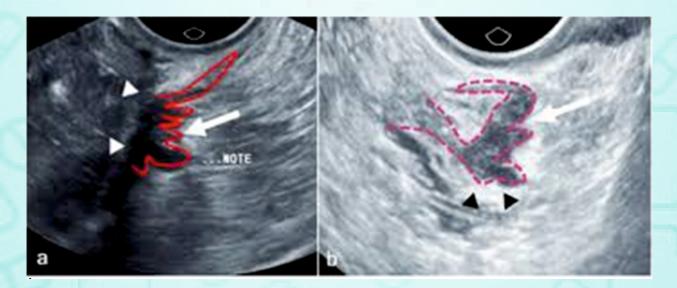


Fig 5: Typical 'Indian Headdress sign', with the deposit shape irregular in shape (outlined in red) and resembling the Indian headdress (arrow), adherent to the rectum with non-visualization of the muscularis propria (white arrowhead)

Sliding sign: On TVUS ultrasound, this sign can be used as a routine screening test for DIE, and one of the components of the standardized systematic approach developed by the IDEA (International Deep Endometriosis Analysis) Consensus Group for sonographic evaluation in patients with suspected endometriosis. It involves manually putting pressure on the anterior pelvis, and evaluating the normal gliding movement of the uterus over the rectum. A negative sliding sign suggests Pouch of Douglas involvement by endometriosis, which increases likelihood of posterior compartment DIE and rectal involvement by almost 3 times.<sup>10</sup> A recent study by Young et al. incorporating routine sliding sign evaluation in all patients with suspected DIE for chronic pelvic pain, found a rise in detection rate (from 2% to 6%), sensitivity (36%–94%) and specificity (68%–98%).<sup>11</sup>

### Peritoneal Endometriosis and Soft Markers

Superficial peritoneal endometriosis is perhaps the most common form of the disease but also the most difficult to detect via ultrasonography due to the small size and flat nature of the lesions. MRI or direct visualization via laparoscopy is often required.12

Some soft markers include a negative sliding sign and point specific tenderness.13 The presence of a hydrosalpinx or adenomyosis or a retroverted uterus may also hint towards the possibility of concomitant endometriosis. Even MRI demonstrates a somewhat low specificity and low sensitivity (72% and 79%, respectively) in diagnosing peritoneal endometriosis.14

### 1. Transabdominal Ultrasonography (TAS)

Transabdominal ultrasonography (TAS) provides a wider field of view, which can be beneficial for examining structures beyond the pelvic cavity. However, TAS is generally less effective than TVS in diagnosing endometriosis but can be useful in cases where the transvaginal route is not feasible, such as in unmarried women or those with extreme pelvic

pain.15

#### 2. MRI

TVS and MRI have similar diagnostic accuracies for ovarian endometriomas and posterior DIE. However, MRI generally outperforms TVS for detecting small peritoneal lesions (Fig 6) and anterior compartment DIE, owing to superior tissue contrast. As such, MRI is often considered a second-line imaging modality when TVS findings are inconclusive or when anterior compartment disease is suspected. 16

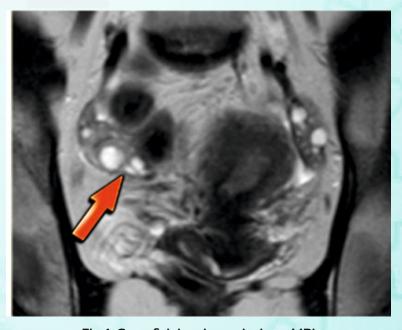


Fig 6. Superficial endometriosis on MRI

### 1. Gel Sonovaginography

Sonovaginography involves instillation of saline solution or gel in the vaginal cavity to enhance the visualization of deep infiltrating endometriosis, particularly in the rectovaginal septum and uterosacral ligaments. By creating a separation between the vaginal wall and surrounding structures, sonovaginography improves the detection of subtle nodular lesions that may be missed on conventional TVS.–17 This principle is useful in both MRI and TVS. Although not widely used due to its invasive nature, it may further optimise 3D-USG findings.

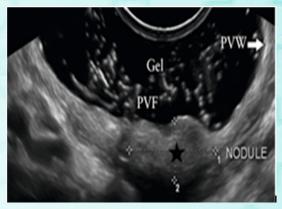


Fig 7. Gel vaginosonography to improve detection of DIE. (PVW- posterior vaginal wall, PVF- posterior vaginal fornix)

### 1. Three-Dimensional (3D) Ultrasonography and Enhancements in Techniques

3-D USG represents an advanced technique that offers more detailed views of the pelvic anatomy by reconstructing images in multiple planes (Fig 8). This method can improve the detection of subtle lesions and enhance the evaluation of the extent of disease in complex DIE lesions, particularly in the rectosigmoid and bladder.18

While the routine use of 3D ultrasonography in endometriosis diagnosis is still limited due to the need for specialized equipment and training, its diagnostic potential is promising.–19

### 6. Future Directions and Emerging Technologies in 3D-USG

### 6.1. Elastography

Elastography may help to differentiate endometriomas from other ovarian cysts20 as endometriotic cysts tend to be stiffer due to fibrosis. While still largely experimental, elastography holds promise as a tool in distinguishing endometriosis from other pelvic pathologies. 21

### 6.2. Contrast-Enhanced Ultrasonography (CEUS)

Contrast-enhanced ultrasonography (CEUS) uses intravenous contrast agents to improve the visualization of blood vessels and tissue perfusion. This highlights areas of neovascularization, which are common in endometriotic implants 22 lt represents an exciting area of research with potential to improve diagnostic accuracy 23

### 6.3. Artificial Intelligence (AI) and Machine Learning

Al and machine learning algorithms can be trained to recognize patterns in ultrasonographic images that may be too subtle for the human eye to detect. This could help reduce operator dependency, improve diagnostic accuracy, and potentially reduce the time to diagnosis for patients with endometriosis.24

Al could also assist in standardizing ultrasonographic evaluations by providing real-time feedback to sonographers and ensuring that all relevant anatomical structures are adequately assessed, and is a promising avenue for future research 25

### **Challenges and Limitations**

Despite significant advancements, several challenges remain:

- Operator Dependency: The accuracy of the diagnosis is closely tied to the experience and skill of the sonographer, especially in case of deep infiltrating endometriosis. This underscores the importance of adequate training and need of standardized scanning protocols.
- Limited Visualization of Peritoneal Endometriosis: Superficial peritoneal endometriosis is often difficult to visualise on sonography-necessitating MRI or laparoscopy in such cases.
- Variability in Ultrasonographic Findings: Endometriotic lesions have varied presentations, from typical ovarian endometriomas to more atypical lesions that are difficult to differentiate from other pathologies.
- Involvement of Atypical Locations: Endometriosis can involve extra-pelvic locations. In such cases, ultrasonography may have limited utility, and other imaging modalities, such as MRI or CT, are required.

#### Conclusion

Radio-imaging has emerged as a powerful tool in the diagnosis of endometriosis offering high sensitivity and specificity. TVS, both 2D and 3D, can serve as an effective non-invasive diagnostic alternative or adjunct to surgical exploration. However, it requires specific skills, expertise, and experience that can be obtained through appropriate training. Modifications to the traditional TVS technique may further facilitate the accurate assessment of certain locations of endometriosis. The IDEA structured ultrasound approach is systematic and quite useful.

MRI should, generally, be considered a second-line investigation due to potential discomfort, bowel movements generating artefacts, higher cost, and the need for expert radiologists, with no overall clear benefit over TVS.

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### MEDICAL MANAGEMENT OF ENDOMETRIOSIS: CURRENT THERAPIES AND FUTURE DIRECTIONS



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Biochemical abnormalities in endometriosis – Continuous estrogen supply, resistance to progesterone and exaggerated inflammatory response are critical underlying mechanisms leading to symptoms in endometriosis. Endometriotic implants have shown impaired molecular and immunologic functions leading to increased production of estrogen, pro-inflammatory cytokines, prostaglandins and metalloproteinases and a failure of immune cells to suppress and clear the inflammatory response.

### Sources of constant estrogen supply –

- 1. Estrogen from ovaries and peripheral fat
- 2. Endometrium with rich PG-E2 receptors and activation of PG receptor subtype EP-2 leads to signalling the key steroidogenic activity and aromatase activity eventually leading to estradiol production.
- 3. Endometrial implants have intrinsic aromatase activity leads to conversion of cholesterol to estradiol.

### Progesterone resistance -

Studies have shown that the endometriotic lesions have a low progesterone receptor level. Progesterone is important for the activation of key enzyme 17-betahydroxy-steroid-dehydrogenase 2, which helps in converting estradiol to estrone, which is less biologically active. Thus, increased production of estradiol and decreased clearance leads to the growth of the endometriotic tissue.

### Increased concentrations of Prostaglandins (PG)-

Pelvic pain in endometriosis is secondary to increased concentrations of PGs, especially of the subtype E2 and F2 $\alpha$ .Cyclooxygenase catalyzes the conversion of arachidonic acid to PGH2 which is converted to PGE2 and F2 $\alpha$  via the action of PG synthetase. COX 2 is expressed in higher concentrations in the endometrial implants as compared to the normal endometrial cells. Again, as discussed previously, the increased concentration of PGE2 also provides a stimulus for estrogen production. Along with estradiol and PGE2, studies have shown a role of cytokines, especially IL-1 $\beta$  and angiogenic factors like vascular endothelial growth factor (VEGF) in inducing COX-2 expression and increased PG production in endometriotic implants.

Medical management of endometriosis is targeted towards correcting these biochemical abnormalities in turn controlling pain and suppression of the hormonally active endometriotic tissue.

#### **ENDOMETRIOSIS AND MEDICATIONS**

Over years, several therapeutic options have been developed and successfully used to achieve these aims and newer targets are being developed at a fast pace. A trial of non-steroidal anti-inflammatory drugs (NSAIDs) initially can be helpful in controlling the pain associated with dysmenorrhea. Hormonal therapies that rely on suppression of the endometriotic tissues include combined oral contraceptives, progesterone only contraceptives, gonadotropin releasing hormone (GnRH) agonists, aromatase inhibitors and danazol. Although quite successful, they have unwanted side effects secondary to hormonal suppression and need to be closely monitored.

HORMONAL	NON-HORMONAL
<ul> <li>Combined oral contraceptives</li> <li>Progesterone containing contraceptives</li> </ul>	NSAIDS     Aromatase inhibitors     Danazol
<ul> <li>➢ Oral or injectable</li> <li>➢ Implant</li> <li>➢ Levonorgestrel containing intrauterine system (LNG- IUS)</li> <li>• Selective progesterone receptor modulators</li> <li>➢ Mifepristone</li> <li>➢ Ulipristal acetate</li> <li>➢ Onapristone</li> </ul>	FUTURE THERAPIES  Anti- angiogenesis factors  • Statins  • TNF-α blockers  • Peroxisome proliferator activated-receptor gamma ligand (PPAR-γ)
<ul> <li>Gonadotrophin releasing hormone agonists</li> <li>➤ Leuprolide acetate</li> <li>➤ Nafarelin</li> <li>➤ Goserelin</li> <li>• Gonadotrophin releasing hormone antagonists</li> <li>➤ Elagolix, Relugolix, Cetrorelix and Ganirelix</li> </ul>	• Pentoxifylline

#### NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

NSAIDs are the most commonly used first line agents in the management of endometriosis related pain and dysmenorrhea. NSAIDs work by blocking the enzyme COX that is crucial for the production of the inflammatory mediators. Although, both COX1 and COX2 receptors are present, studies have shown that the ectopic endometrial tissues have a higher concentration of COX2 receptors. Both selective and non-selective COX inhibitors are widely used for symptomatic relief. Along with pain control, new studies have shown that selective COX 2 inhibitors like rofecoxib can also inhibit the growth of the endometrial tissue. The safety profile with prolonged use of NSAIDs, negative gastrointestinal side effects, inconclusive evidence regarding effectiveness in controlling endometriosis related pain limits their prolonged use.

#### COMBINED HORMONAL CONTRACEPTIVES

Estrogen and progesterone combinations or progesterone only contraceptive pills are most commonly used first line hormonal therapy that acts by suppressing the HPO axis and ovaries thus halting the disease activity. Decreased levels of hormones lead to decidualization of the endometriotic tissue and is proposed to slow the progression of the disease. Availability, cost, ease of administration and tolerability makes them popular when compared to injectable drugs. The continuous administration of OCP's has shown better pain control than compared to cyclic administration.

The limiting factors include long-term administration, risk of thromboembolism, high rates of recurrence after discontinuation and impaired fertility due to contraceptive action. Combinations containing lower dose of ethinyl estradiol (20 micrograms) as compared to high dose (30 micrograms) have a lower risk of venous thromboembolism and are currently recommended.

#### GONADOTROPIN RELEASING HORMONE AGONISTS (GnRH AGONISTS)

These are a great option for women who have failed initial therapy with OCP's or are not candidates for OCPs due to medical history. GnRH agonists acts by suppressing the hypothalamic pituitary ovarian axis leading to anovulation and hypoestrogenism, thus depriving implants of estrogen which is crucial for their growth. Due to agonist action there is initial rise in FSH and LH levels, however, chronic administration leads to downregulation of pituitary GnRH receptors.

Leuprolide acetate 3.75 mg monthly injection or 11.25 mg used three monthly, Goserelin and Nafarelin are the most commonly used preparation. GnRH agonists are available in both nasal and injectable forms and studies have shown a significant reduction in pelvic pain in patients with endometriosis.

GnRH agonists are approved for continuous use for only up to six months due to concerns of side effects secondary to hypoestrogenism like bone loss, vaginal atrophy and dryness, hot flashes and abnormalities in lipid profile. The addition of add- back therapy provides symptomatic relief and decreases the rate of bone loss. Norethindrone acetate, a progestin is the only FDA approved add-back therapy, but low dose estrogen and a combination of estrogen and progesterone have also been used. The combination of GnRH agonists and norethindrone acetate are only approved for use for duration of 12 months, as the data beyond that duration is not available. Another limitation of the use of GnRH agonists is that they suppress ovulation and cannot be used in women desiring fertility.

#### GONADOTROPIN RELEASING HORMONE ANTAGONISTS (GnRH ANTAGONISTS)

Compared to GnRH agonists they do not cause the initial flare and have lower degree of hypoestrogenism and a better side effect profile with equivalent symptomatic improvement. Elagolix, Relugolix, Cetrorelix and Ganirelix are some of the FDA approved GnRH antagonists. Studies have shown a significant symptomatic relief and regression of the endometriotic implants as visualized on laparoscopy. With a lower degree of hypoestrogenemia and better

tolerance than the GnRH agonists they offer a great potential in the treatment of endometriosis. Common side effects of the GnRH antagonists include symptoms of hypogonadism such as hot flashes, gynecomastia, fatigue, weight gain, fluid retention, erectile dysfunction and decreased libido. Long term therapy can result in metabolic abnormalities, weight gain, worsening of diabetes and osteoporosis.

The FDA has approved two gonadotropin-releasing hormone (GnRH) antagonist drugs for treating endometriosis:

**Elagolix (Orilissa)** - The first oral GnRH antagonist approved by the FDA to treat endometriosis and pelvic pain. Elagolix can help with dysmenorrhea, non-menstrual pelvic pain, and dyspareunia.

**Relugolix** - An oral combination therapy that contains estradiol and progestin. It's approved to treat moderate to severe endometriosis-associated pain.

#### PROGESTERONE CONTAINING CONTRACEPTIVES

Progesterone has multiple mechanisms of action that form the pathophysiologic basis of its use in endometriosis. It induces decidualization of the endometrium, inhibits estrogen induced mitosis, alters estrogen receptors, inhibits angiogenesis and expression of matrix metalloproteinase needed for the growth of the endometriotic implants. Available in different forms oral, injectable or intra-uterine device, they have gained popularity and are a great option for women with contraindications to estrogens. Some of the progestins that have been studied and used in the treatment of endometriosis include medroxyprogesterone acetate, dienogest, dydrogesterone, gestrinone, lynesterole, megesterol acetate, and norethindrone acetate.

Medroxyprogesterone is available as oral and injectable preparation and can be administered 150 mg intramuscularly every three months. Although there is no standardized oral dose, studies using different doses of oral medroxyprogesterone from 10 to 100 mg per day for 3-6 months have reported varying degree of improvement in endometriosis related pain. Injectable progesterone offers the added advantage of better compliance by avoiding daily administration and erratic gastrointestinal absorption.

Norethisterone acetate is a 19-nortesterone derivative and has been proven effective in control of dyspareunia, dysmenorrhea, pelvic pain and dyschezia with better tolerability and less side effects in lower doses. Used at a dose of 2.5mg per day for 12months has achieved similar control when compared to combined oral contraceptive.

Dienogest, a 19-nortestosterone derivative is another progestin that has been studied in the treatment of endometriosis. It has high specificity for progesterone receptors and less anti-androgenic side effects. Continuous administration leads to decidualization and atrophy of the endometrial lesions. It also has anti-inflammatory, anti-angiogenic and anti-proliferative effects. In a dose of 2mg or 4mg per day, dienogest has been shown to have a favorable profile for safety and efficacy, patients reported improvement in the endometriosis related symptoms and an overall improvement in quality of life. It is in general well tolerated and side effects included irregular bleeding, which improves with time.

#### LEVONORGESTREL CONTAINING INTRA-UTERINE DEVICE (LNG-IUD)

LNG-IUD is a T shaped device that contains 52 mg of Levonorgestrel, which releases 20 micrograms of hormone per day over a five-year period. They suppress endometriosis by local action causing atropy of endometrium, decreased retrograde menstruation due to hypomenhorrea and local high concentration of progesterone causing anti-inflammatory and immunomodulatory effect. Studies have reported good control of pelvic pain in endometriosis and are also successfully used in patients with adenomyosis and deep rectovaginal endometriosis.

LNG-IUD have proven to be similarly effective with better compliance when compared to depot administration of GnRH analogues, with lower incidence of hypo estrogenic side effects in women using the intrauterine device. It has also been shown to decrease the rates of recurrence of dysmenorrhea in women after laparoscopic surgery for symptomatic dysmenorrhea. With its longterm use and better side effect profile LNG-IUS offers a great option in women who are desirous of fertility.

#### **ETONOGESTREL IMPLANT**

Intradermal implants containing etonogestrel used for contraception have shown some benefits and pain relief in patients with endometriosis. It's efficacy is comparable with depot medroxyprogestrone acetate with similar side effect profile. In carefully selected patients who do not desire fertility Etonogestrel implants could be another option.

#### SELECTIVE PROGESTERONE RECEPTOR MODULATORS (SPRMs)

SPRMs are a relatively new class of agents that have tissue effect ranging from pure agonists to agonist/antagonist to antagonist. They have shown a significant suppression of estrogen dependent endometrial growth. Mifepristone and ulipristal acetate are the two SPRMs that are commonly used. Selective inhibition of endometrial growth without the side effects of hypoestrogenism, decreased menstrual bleeding via effect on the endometrial blood supply and suppression of endometrial blood supply are some of the mechanisms that have provoked interest in their use in endometriosis.

#### AROMATASE INHIBITORS

Studies have shown that aromatase activity is absent in normal endometrium, but is over expressed in endometriosis. Aromatase enzyme helps in the conversion of the steroid precursors into estrogen. Aromatase induced estrogen synthesis leads to the growth of the endometrial implants, COX expression, prostaglandin secretion, which further induces aromatase activity. Anastrazole, letrozole and exemestane are aromatase inhibitors that can be administered orally. Used in combination with combined oral contraceptives, GnRH agonists or progesterone, they significantly decrease the endometriosis-associated pain, improve quality of life and have shown to decrease the size of the lesion. However, their side effects including ovarian follicular cyst and bone loss with long-term use can be decreased by combining them with OCPs and progestins.

#### DANAZOL

Danazol, a derivative of 17 alpha-ethinyl-testosterone, is an androgenic agent that inhibits LH surge and decreases ovarian steroidogenesis by direct inhibition of the ovarian enzymes. Usually given in divided doses of 400–800 mg per day for six months. Although it has been effective in controlling endometriosis-associated pain, its use is limited due to its side effects like acne, hirsutism, deepening of voice, weight gain, muscle cramps, liver dysfunction and an abnormal lipid profile.

#### **NEWER THERAPIES**

The limitations of currently available treatment options like long term use, prolonged hypoestrogenism and its consequences and high recurrence of symptoms after discontinuing of treatment call for future research for a novel drug to treat endometriosis. Several newer therapies are under trial. Some of them being mentioned here

#### ANTI-ANGIOGENESIS FACTORS

Endometriotic lesions secrete angiogenic growth factors like vascular endothelial growth factor (VEGF) this is evident by raised levels in peritoneal fluid in patients with endometriosis. In theory, halting the growth of new blood vessels could stop the growth of new lesions and regress older ones. These agents are still in early development with most of the research on animal models. Agents like TNP-470 (an analog of antibiotic fumagilin), endostatin (a proteolytic fragment of collagen with endogenous anti-angiogenic activity), anginex (a synthetic peptide that stops the growth of blood vessels and induces apoptosis) and anti-VEGF antibody (Avastin) have been successful in decreasing the size of endometriotic lesions in animal models, however, no data is available in humans.

Dopamine receptor 2 agonists, cabergoline and quinagolide have been shown to reduce angiogenesis by dephosphorylation of VEGF2. In mouse model, treatment with ergot derived dopamine agonist (cabergoline) and non-ergot dopamine agonist (quinagolide) were effective in inhibiting angiogenesis and reducing the size of endometriotic lesions. In limited human studies with less cases, results are promising but still further studies with larger population and sample size are required.

#### **STATINS**

Typically used in the treatment of hypercholesterolemia, statins are a group of drugs that lower cholesterol levels by blocking the conversion of 3-hydroxy-3 methylglutaryl - coenzyme A into mevalonate, which is a precursor for cholesterol. Their anti-inflammatory, antiangiogenic and antioxidant properties have provoked interest in their use in endometriosis. Atorvastatin, simvastatin, mevastatin and lovastatin have been tested in invitro tissue cultures and animal models of endometriosis. An increased inhibition of inflammatory and angiogenic genes (COX-2, VEGF, RAGE and EN-RAGE) in atorvastatin treated endometrial- endometriotic cells is reported. They also reported increased expression of anti-inflammatory genes (PPAR- $\gamma$  and LXR $\alpha$  and IGFBP-1). In another study, simvastatin induced a dose dependent decrease in MMP-3 (matrix metalloproteinase) and the number and size of the endometriotic lesions in a mouse model.

#### **TNFα BLOCKERS**

TNF $\alpha$  is a pro-inflammatory cytokine and its levels have been found to be elevated in the peritoneal fluid of women with endometriosis with a direct correlation with the stage of the disease. Agents targeting TNF $\alpha$  have been successfully used in the treatment of inflammatory conditions like rheumatoid arthritis and Crohn's disease. Infliximab, a monoclonal antibody against TNF $\alpha$  and Etanercept, a fusion protein with the ability to neutralize TNF $\alpha$  are being actively studied in the treatment of endometriosis. In animal models, treatment with these agents has shown to reduce the size and number of the endometriotic implants along with a decrease in the levels of inflammatory cytokines. However, there is paucity of evidence in humans regarding the efficacy of these agents.

## PEROXISOME PROLIFERATOR- ACTIVATED RECEPTOR GAMMA LIGANDS (PPAR-γ)

PPARs are ligand activated nuclear receptors with a suggested role in inflammation and lipid and glucose metabolism. PPAR-  $\gamma$  ligands have anti-inflammatory properties and reduce estrogen biosynthesis by inhibiting aromatase enzyme. In experimental models they have been shown to inhibit cell proliferation, increase apoptosis and inhibit the growth of the endometriotic lesions by an affect on the angiogenic factor VEGF. In animal models Rosiglitazone and Pioglitazone reduce the volume, weight and size of the endometriotic lesions. Human studies are underway.

#### CONCLUSION

In summary, endometriosis is a chronic medical condition that not only negatively affects a woman's quality of life but has a huge economic impact often due to delay in diagnosis, need for ongoing treatment and high recurrence rates. Currently, several therapeutic options both hormonal and non-hormonal are available to provide symptomatic relief and control the progression of the disease. All the options discussed above have been fairly successful in controlling pelvic pain in women with endometriosis. In carefully selected women these medications can be used either alone or in combination with surgery. However, they are limited by their side effects and negative impact on fertility. Currently there is no evidence that the medical therapy alone or a combination of medical therapy with surgery improves fertility. Management of infertility in women with endometriosis is a complex issue and needs to take into account the age, duration of infertility, severity of symptoms and stage of the disease. With more understanding of the pathophysiology of endometriosis, newer targets are being developed with the hope of avoiding unwanted side effects and specifically targeting the lesions without affecting the ovarian function.

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## OPTIMISING OUTCOMES: CONSERVATIVE SURGICAL MANAGEMENT FOR ENDOMETRIOSIS

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Endometriosis is a chronic gynecological disorder characterized by the ectopic implantation of endometrial-like tissue outside the uterine cavity, leading to a spectrum of symptoms including dysmenorrhea, chronic pelvic pain, dyspareunia, and infertility. While definitive surgical interventions such as hysterectomy and bowel resection are often considered in severe cases, conservative surgical management has gained recognition as an effective alternative. This approach emphasizes the excision of endometriotic lesions while preserving reproductive anatomy, thereby optimizing patient outcomes.

#### Advantages of Conservative Surgery in Endometriosis

centre

The primary advantage of conservative surgery lies in its focus on preserving reproductive potential. By excising ectopic endometrial tissue, surgeons aim to alleviate pain and restore normal anatomy, thereby enhancing fertility. This is particularly significant for women of reproductive age, as studies indicate that those undergoing conservative surgical techniques demonstrate higher rates of spontaneous conception compared to those who undergo radical procedures. The preservation of the uterus and ovaries allows for the maintenance of hormonal function and fertility, which are critical considerations in managing endometriosis.

Furthermore, conservative surgical techniques are frequently performed laparoscopically, allowing for minimally invasive access to the pelvic cavity. This approach minimizes postoperative morbidity, reduces scarring, and shortens recovery times compared to open laparotomy. The advantages of laparoscopy include decreased intraoperative blood loss, lower infection rates, and faster return to normal activities, all of which contribute to enhanced patient satisfaction.

Additionally, conservative surgery offers a personalized approach to treatment. Surgeons can tailor their techniques based on the patient's unique disease presentation and reproductive goals. This flexibility enables the selection of the most appropriate surgical strategies, such as peritoneal excision or ovarian cystectomy, thereby optimizing surgical outcomes.

#### **Peritoneal Excision**

Peritoneal excision is a critical component of conservative surgical management for endometriosis. This technique involves the meticulous resection of endometrial implants from the peritoneum and surrounding tissues. Comprehensive peritoneal excision has been associated with a significant reduction in disease recurrence rates and provides effective symptomatic relief. The complete removal of these ectopic lesions helps to alleviate chronic pelvic pain and restore normal anatomy, thereby enhancing the overall quality of life for patients

Studies indicate that patients who undergo thorough peritoneal excision report lower levels of dysmenorrhea and pelvic pain postoperatively. This procedure is particularly advantageous for patients with deep infiltrating endometriosis, where excision can also relieve pressure on adjacent structures, further mitigating pain.



Fig.1 – Peritoneal endometriosis

#### Sclerotherapy

Sclerotherapy is an emerging therapeutic modality for the management of endometriosis, involving the percutaneous injection of sclerosing agents, such as sodium tetradecyl sulfate or polidocanol, into endometriotic lesions.

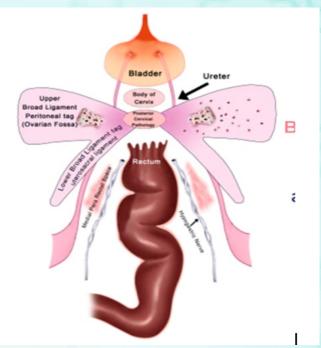


Fig- 2- Butterfly Peritonectomy in Deep Infiltrating Endometriosis

This procedure induces localized fibrosis and vascular occlusion, leading to the shrinkage of lesions and alleviation of associated pelvic pain. The primary advantages of sclerotherapy include its minimally invasive nature, allowing it to be performed in an outpatient setting under local anesthesia, which significantly reduces the patient's recovery time compared to traditional laparoscopic excision. Furthermore, sclerotherapy offers a lower risk of complications, such as infection or significant postoperative pain, making it an appealing option for patients who may not be ideal candidates for more invasive surgeries.

Despite these benefits, there are notable disadvantages. One concern is the potential for incomplete lesion ablation, which may necessitate multiple treatment sessions and lead to variable outcomes among patients. Additionally, the efficacy of sclerotherapy can be influenced by factors such as the size, type, and location of the endometriotic lesions, as well as the individual patient's response to the sclerosing agent. There is also limited long-term data on the durability of the treatment effects and potential recurrence rates.

Looking ahead, the future of sclerotherapy in endometriosis management holds promise for refinement and innovation. Research is needed to identify optimal sclerosing agents and delivery techniques, including ultrasound-guided injections for improved precision. Furthermore, exploring combination therapies—such as integrating sclerotherapy with hormonal treatments or laparoscopic interventions—could enhance therapeutic outcomes and provide a more

Fig 3- Sclerotherapy for endometrioma

comprehensive approach to managing endometriosis. By focusing on these advancements, sclerotherapy may evolve into a more effective tool in the multidisciplinary treatment landscape for endometriosis, offering patients relief while minimizing the risks associated with conventional surgical approaches

#### **Ovarian Cystectomy**

Ovarian cystectomy is another vital aspect of conservative surgical management, particularly in the treatment of endometriomas—cysts resulting from endometriosis that can develop on the ovaries. The removal of these cysts is essential not only for alleviating associated pain but also for preserving ovarian reserve. Unlike more radical options such as oophorectomy, which entails the complete removal of an ovary, cystectomy allows for the retention of ovarian function, thereby maintaining hormonal balance and fertility potential.



Fig. 4- Ovarian Endometrioma

The procedure involves the careful excision of the endometrioma while preserving healthy ovarian tissue. This is critical, as studies have shown that preserving ovarian function can lead to better reproductive outcomes and lower rates of premature ovarian in sufficiency. Additionally, addressing endometriomas can prevent complications such as cyst rupture or torsion, which can lead to

#### **Nerve-Sparing Techniques**

In cases where endometriosis invades neural structures, employing nerve-sparing techniques becomes paramount. Endometriosis can infiltrate the pelvic autonomic nerves, leading to significant postoperative pain and chronic pain syndromes. Nerve-sparing surgical techniques aim to preserve these critical structures during excision, thereby minimizing the risk of neuropathic pain postoperatively.

These techniques involve careful dissection and resection strategies that avoid damaging the surrounding nerves. By preserving nerve function, patients can experience a smoother recovery, with a reduced incidence of chronic pain and enhanced functional outcomes. This focus on nerve preservation is an important aspect of modern surgical practice, highlighting the need for specialized surgical expertise in the management of endometriosis.

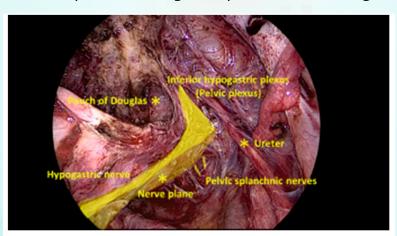


Fig. 5- Fertility- and Nerve-sparing Laparoscopic
Eradication of Deep Endometriosis with Total Posterior Compartment
Peritonectomy: The Kurashiki Method

#### **Ureteric Dissection**

Endometriosis can also involve the ureters, necessitating careful ureteric dissection during surgical management. This technique is critical in preventing ureteral injury, which can lead to severe complications such as urinary obstruction, hydronephrosis, and urinary tract infections.

During surgery, meticulous identification and preservation of the ureters are essential to avoid these complications. Proper ureteric dissection not only ensures the maintenance of urinary function but also contributes to a lower risk of intraoperative and postoperative complications.

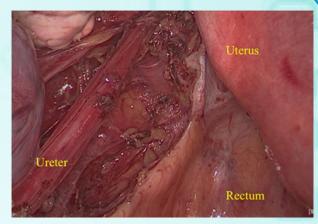


Fig. 6 – Ureteric dissection in DIE

This technique underscores the importance of a comprehensive surgical approach in managing endometriosis, where the preservation of all affected structures is prioritized.



Fig. 7- Rectal Shaving for Bowel Endometriosis by Laparoscopic Reverse Submucosal Dissection

#### **Rectal Shaving**

For patients with deep infiltrating endometriosis affecting the rectum, rectal shaving can be employed as a conservative surgical technique. This method involves the careful excision of endometrial tissue infiltrating the rectal wall without necessitating bowel resection. By preserving bowel continuity and function, rectal shaving offers a less invasive alternative to more radical surgical options.

This technique allows for effective removal of endometriotic lesions while minimizing the risks associated with bowel resection, such as anastomotic leakage or changes in bowel function. Additionally, rectal shaving can significantly reduce pain and improve the quality of life for patients suffering from rectal endometriosis, providing a targeted and effective treatment option.

#### Disadvantages of Radical surgeries

While definitive surgical options such as hysterectomy and bowel resection may be necessary in certain severe cases of endometriosis, they come with significant drawbacks. Hysterectomy eliminates the uterus, precluding any possibility of future pregnancies. For many women, particularly those seeking to conceive, this loss can be devastating.

Moreover, these radical surgeries are associated with higher risks of intraoperative and postoperative complications, including infection, excessive hemorrhage, and longer recovery times. In addition, hysterectomy, especially when performed alongside oophorectomy, can lead to premature menopause and associated hormonal imbalances, negatively impacting overall health and quality of life.

Bowel resection can alter bowel function, leading to complications such as diarrhea or constipation, and may necessitate lifelong dietary modifications. The long-term effects of these surgeries can be profound, underscoring the importance of considering conservative options whenever possible.

Conservative surgery presents numerous advantages over definitive surgical options. By preserving reproductive function, these techniques maintain a woman's ability to conceive in the future, which is a critical consideration for many patients. Furthermore, conservative surgical approaches generally carry a lower risk of complications due to their minimally invasive nature.

Shorter recovery times are another significant benefit, enabling patients to resume their daily activities and quality of life more quickly. Additionally, conservative techniques provide effective symptom relief without the extensive physiological alterations associated with radical surgeries, allowing for a more holistic approach to managing endometriosis.

#### Disadvantages of Conservative Surgery

Despite its many benefits, conservative surgery is not without challenges. One of the primary concerns is the risk of recurrence; endometriosis can reappear after surgical intervention, necessitating further treatment. The complexity of some cases may pose intraoperative challenges, requiring a surgeon with specialized expertise to navigate the intricacies of the disease.

The success of conservative surgery often relies on the surgeon's skill and experience in managing endometriosis. Thus, ensuring access to specialized care is essential in optimizing surgical outcomes for patients.

#### Conclusion

Conservative surgical management of endometriosis represents a significant advancement in the treatment of this complex condition. By focusing on the preservation of reproductive function, minimizing invasiveness, and effectively addressing symptoms, conservative approaches offer a promising alternative to radical surgical options. Techniques such as peritoneal excision, ovarian cystectomy, nerve-sparing methods, ureteric dissection, and rectal shaving collectively enhance patient outcomes and quality of life. As the understanding of endometriosis continues to evolve, the role of conservative surgical management remains crucial in providing comprehensive care for those affected by this chronic illness.

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# ACHIEVING COMPLETE SURGICAL CURE IN ENDOMETRIOSIS: TECHNIQUES AND OUTCOMES



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Most difficult question to answer in endometriosis is whether the surgery was complete? Will it recur is always a question. The most important goal, is reduction of recurrence of pathology and symptoms.

The **recurrence** of endometriosis symptoms and pelvic pain are **directly proportional to the surgical precision and removal of peritoneal and deeply infiltrated disease**. Surgical effort should always aim to eradicate the endometriotic lesions completely to keep the risk of recurrence as low as possible.

The uncomfortable and inconvenient truth is that we don't even know the etiology for sure. Review of the most current guidelines from the major societies reveal that there is no clear consensus regarding the recommendations for diagnosis, preoperative evaluation, surgical indication, and treatment approaches for patients with different types of endometriosis.

According to the **2022 ESHRE** guidelines, **Laparoscopy** is usually associated with less pain, shorter hospital stay, quicker recovery ,better cosmesis and hence it is usually preferred to open surgery. If the relevant experience with laparoscopy is not available, the patient should be referred to a centre of expertise.

#### **OPTIMAL SURGICAL EXCISION**

Since the symptoms do not proportionately correlate to the surgical findings in endometriosis, hence, for attaining optimal surgical excision in endometriosis, it is important to have:

- \* a centre of expertise, and the patient should be informed on potential risks, benefits, and long-term effects.
- \* a structured approach with *proper multidisciplinary team* involving experts in different specialities, such as a gynaecologist, radiologist, anesthetist, urologist, and colorectal surgeon if required depending on the severity of disease,
- \* A thorough knowledge and *understanding of the anatomy* of the various structures involved and retroperitoneal structures as well.
- \* Adhering to *sound surgical principles* facilitates safe and effective operating in endometriosis surgery, as well as any other surgical intervention.

#### PRINCIPLES OF DISSECTION:

- The most effective approach is to start the dissection from *virgin area towards the endometriotic nodule*.
- The use of tissue traction and counter-traction facilitates opening spaces and often guides the surgeon to the best tissue plane to explore.

Pushing the instrument gently into the plane and opening the jaws of the laparoscopic instrument can help develop these spaces, while minimising blood loss.

Till date, no single classification system adequately classifies endometriosis. However in the recently introduced **#ENZIAN CLASSIFICATION** (figure1) Endometriosis can be mapped with one single classification system applicable by pre-invasive (TVS, MRI) and invasive methods thereby enabling the use of one common language for describing



So surgical strategy for endometrioisis can be discussed according to the structures involved, whether superficial or deep and deep infiltrating endometrioisis can further be delt with according to the compartment involved.

#### **SUPERFICIAL PERITONEAL ENDOMETRIOSIS:**

According to ESHRE 2022, when surgery is performed, clinicians may consider *excision instead of ablation* of endometriosis to reduce endometriosis-associated pain and the quality of as it is impossible to know if the entire lesion is destroyed with ablation.

#### **OVARIAN ENDOMETRIOMA:**

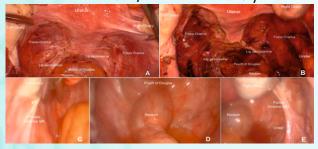
Options available - cystectomy, ablation by laser or by plasma energy, or electrocoagulation. According to ESHRE guidelines 2022 cystectomy in endometrioma (≥3cm) should be preferred instead of drainage and coagulation, as



cystectomy reduces recurrence of endometrioma and endometriosis-associated pain. Specific caution should be used to *minimise ovarian damage*.

#### **DEEPINFILTRATING ENDOMETRIOSIS (DIE):**

Apart from significant improvement of pain and improves quality of life, radical treatment of deep endometriosis also positively impacts fertility outcomes. Many studies have claimed that more than fifty percent of the patients have conceived after surgery for deep endometriosis and the majority did so without the need for assisted reproductive therapy (Daraï, et al., 2017, A M Dückelmann 2021, Elene et al 2019.).



**Fig. 6** Surgical site before complete peritonectomy surgery (a), after surgery (b) and at re-operation (c-e). Completely fresh peritoneum (without disease) after complete peritonectmy on relook operation.

#### DECODING FROZEN PELVIS (the middle compartment):

various techniques have been demonstrated for peritonectomy: **10-step en bloc peritonectomy** (Chiminacio, i et al), **SOSURE** technique(Dr Shaheen Khazali et al), **Butterfly peritonectomy** (Dr Sanjay Patel et al) etc.



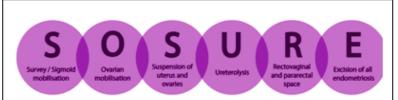


Figure 2. SOSURE steps. Graphic indicating the steps of SOSURE.

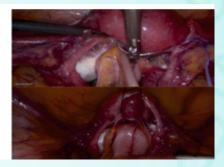
<u>DR SHAHEEN KHAZALI</u> conceptualised the SOSURE mnemonic (2021 Royal College of Obstetricians and gynaecologists)



SIGMOID MOBILISATION



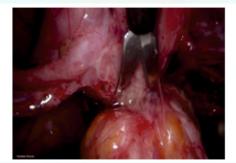
**OVARIAN MOBILISATION** 



**SUSPENSION** 



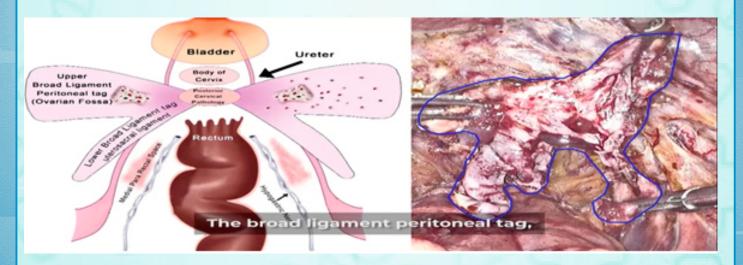
**URETEROLYSIS** 



**RECTOVAG SPACE DISSECTION** 



E: Excision of disease



MAYFLOWER BUTTERFLY PERITONECTOMY

**Ultimately**, **the entire peritoneum**, starting from the broad ligament on the top, going through the posterior cervix to end with the uterosacaral ligament at the bottom has to be **removed** which forms a shape that resembles a butterfly. Clinicians can consider hysterectomy (with or without removal of the ovaries) with removal all visible endometriosis lesions, in those women who no longer wish to conceive and failed to respond to more conservative treatments.

When a decision is made whether to remove the ovaries, the long-term consequences of early menopause and possible need for hormone replacement therapy should be considered. **ENDOMETRIOSIS OF THE BLADDER AND URETERS (ant compartment and ureters)** 

Surgical treatment of bladder endometriosis is usually excision of the lesion and primary closure of the bladder wall. Ureteral lesions may be excised after stenting the ureter; however, in the presence of intrinsic lesions or significant obstruction, segmental excision with end-to-end anastomosis or reimplantation may be necessary.

#### BOWEL ENDOMETRIOSIS (posterior compartment endometriosis)-

Split the nodule and then try **shaving**, **discoid excision** followed by **resection anastomosis as the last resort**.

To summarize, En bloc *peritonectomy* of the pelvis appears to be an effective and safe way to completely remove endometriosis at all stages of the disease, both as an isolated technique in mild to moderate cases, as well as a step in the technique of removing intestinal disease or deeper infiltration in the lateral pelvic wall. With this technique *the ideal removal of endometriosis is possible, with complete preservation of the anatomy and function* of the pelvic organs. long-term follow-up demonstrated *a recurrence rate in 1.8% of patients*.(Chiminacio, I et al.2023, Misal et al 2020, Patel S et al 2022.)

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### SCAR ENDOMETRIOSIS-TIP OF ICEBERG TO BE EXPLORED



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Endometriosis is a sex hormone-dependent gynaecological disease that is characterized by the growth of endometrial tissue outside the uterine cavity. It usually occurs in the pelvis, at sites such as the ovaries and the pelvic peritoneum. However, ectopic endometrial tissue can also be found outside the pelvis, at sites such as the lung, brain, bowel, and abdominal wall. The presence of ectopic endometrial tissue embedded in the subcutaneous adipose layer and the muscles of the abdominal wall is called abdominal wall endometriosis (AWE) and around surgical scar, viz -caesarean scar, laparoscopic portal scars and episiotomy is called surgical scar endometriosis (SSE). AWE can occur spontaneously, but usually develops in association with a previous surgical procedure, such as a caesarean section (CS), hysterectomy, or appendectomy.

Caesarean scar endometriosis (CSE) is the most commonly reported type of AWE. Nominato et al. suggested that CS greatly increased the risk of developing AWE. The pathophysiology of CSE may be due to the direct

implantation of endometrial tissue in the caesarean incision (the implantation theory). During caesarean de livery, the endometrial tissue is inoculated directly in the caesarean incision. With an appropriate supply of nutrients and hormonal stimuli, these endometrial cells survive and proliferate, which finally leads to CSE. Although it is an unusual disease, with a reported incidence of 0.03–0.45%, CSE may cause long-term discomfort involving cyclic lower abdominal pain. Case reports of malignant transformation of CSE have also been sporadically reported.

#### **EPIDEMIOLOGY**

The reported incidence of abdominal scar endometriosis following caesarean section is 0.03-0.6% but this can be a tip of an iceberg as many patients may not consult because of mild symptoms. As caesarean section rate is increasing and also many laparoscopic surgeries are being carried out in recent days the incidence of scar endometriosis is also increasing.

#### **CLINICAL PRESENTATION**

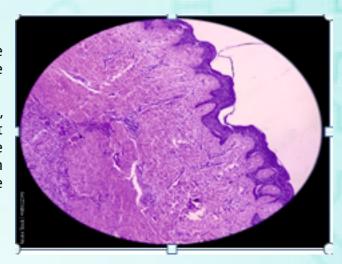
Patients may complain of tenderness to palpation and a raised hypertrophic scar. Most patients have cyclical pain (up to 70%). The pain is usually intermittent and associated with the patient's menstrual cycle but it may be constant. Some reports state that only as low as 20% of the patients exhibited cyclical symptoms. The overlying skin may be hyperpigmented due to the deposition of haemosiderin. Some patients may be asymptomatic.



#### Pathology

It is thought to be caused by the implantation of endometrial stem cells at the surgical site at the time of uterine surgery.

To achieve a definitive diagnosis, histopathology is mandatory. It may detect endometrial-type glands, endometrial-type stroma, and/or haemosiderin-laden macrophages and must display two of the aforementioned three components.



#### Radiographic features

Imaging studies should ideally be carried out during the menstrual cycle.

In general, lesions found along the visible abdominal wall scar and along the predicted path of a previous caesarean section scar should initially raise concern for this diagnosis in imaging studies.

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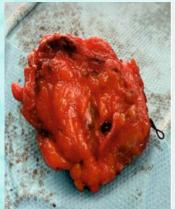
Because of its larger field of view and reproducibility, MRI is better than ultrasound and can help identify more areas of endometriosis development. Furthermore, because of its greater tissue property characterisation and lack of ionising radiation, it is advantageous to CT.

#### Ultrasound

Ultrasound may be of limited value if lesions have developed deeply within the abdominal cavity and are not superficially situated within the abdominal wall. Additionally, sonographic features are not specific. A subcutaneous nodule having relatively irregular borders, a heterogeneous, but predominantly



hypoechoic echotexture with internal scattered hyperechoic echoes surrounded by a hyperechoic ring of variable width, and vascularity may be present. Occasionally cystic changes may be present.



Due to the nonspecific and frequently inconclusive sonography findings, ultrasound is primarily useful for image-guided tissue biopsy of suspected lesions and for confirming or ruling out other conditions included in the differential diagnosis. Those may include lipomas, suture granulomas, incisional or other types of abdominal wall hernias, etc. In most other situations, further imaging will be necessary.

Resected abdominal wall mass showing tiny hemorrhagic foci and chocolate colored cystic lesions with a faint white background.

General characteristics	Frequency	Percent
Age (in years)	Mean – 34.47 standard deviation	n – 8.39
BMI (kg/m <sup>2</sup> )	Mean – 29.15 standard deviation	n – 4.72
Underweight (18)	0	0
Normal (18.5 – 24.9)	7	21.8
Overweight (25 – 29.9)	11	34.4
Obese >30	14	43.8
Parity		
Nullipara	3	9.4
Multipara	29	90.6
Mode of delivery		
Normal vaginal delivery	4	12.5
1 LSCS	8	25.0
2 LSCS	17	52.5

#### TABLE 1: General characteristics of the study participants (n=32)

BMI - Body Mass Index, LSCS - Lower Segment Cesarean Section

Refrence:2023 Durairaj et al. <u>Cureus</u> 15(2): e35089. DOI 10.7759/cureus.35089

Lesion characteristics	Frequency	Percent	
Index surgery			
Episiotomy	3	9.4	
LSCS	25	78.0	
Hysterectomy	2	6.3	
Laparoscopic cyst excision for endometriosis	2	6.3	
Duration between index surgery and onset of symptoms (in years)	Mean - 6.19 Standar	Mean – 6.19 Standard deviation – 4.25	
Symptoms			
Cyclical pain at scar	29	90.4	
Swelling or lump	26	81.25	
Cyclical bleeding from lump	4	12.5	
Dysmenorrhea	21	65.6	
Ultrasound diagnosis of scar endometriosis			
Correct	31	96.8	
Wrong	1	3.2	
Preoperative medical management	11	34.4	

Refrence: 2023 Durairaj et al. Cureus 15(2): e35089. DOI 10.7759/cureus.35089

#### CONCLUSION

Scar endometriosis incidence is increasing, USG and MRI are best imaging modalities to diagnose and surgical excision is currently the best treatment.

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- 2023 Durairaj et al. Cureus 15(2): e35089. DOI 10.7759/cureus.35089

## URINARY ENDOMETRIOSIS: EFFECTIVE MANAGEMENT ANDTREATMENT APPROCHES



Proprietor, LYDM Sparsh Multi Speciality Hospital, Gadag

#### Introduction:

The prevalence of UTE in the general female-born population remains unclear, since around 50% of women with UTE may be asymptomatic. UTE most commonly affects the bladder. The prevalence of UTE, from studies done in Europe, is estimated to range from 0.3 to 12% of all people affected by endometriosis and about 20–52.6% of women with deep endometriosis (DE). The urinary system is the second most common site of extrapelvic endometriosis after the gastrointestinal tract.

The prevalence of disease at specific sites among women with UTE is as follows: bladder, 85%; ureter, 10%; kidney, 4%; and urethra, 2%.

#### Pathogenesis of UTE

The two phenotypes of UTE are superficial endometriosis (SE) and deep endometriosis (DE). SE can be recognized with a laparoscopy as black, white, or red implants, depending on the degree of fibrosis, scarring, and hemorrhage

within the tissue. DE is defined by the invasion of endometrial-like glands and stroma at least 5 mm beneath the peritoneal surface. Deep implants are often associated with fibrosis and/or smooth muscle proliferation and are most frequently associated with pelvic pain and infertility. Apart from others theiories of endometriosis in some women UTE appears to be iatrogenic; bladder endometriosis may be more prevalent amongst women with previous Caesarean section(s).

#### **Bladder Endometriosis**

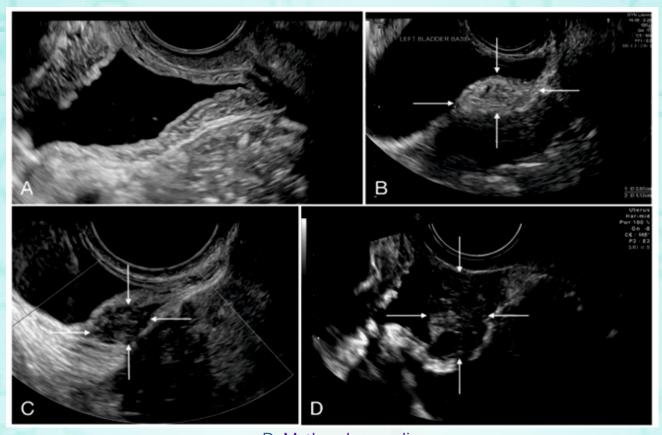
The presence of endometriotic tissue invading the detrusor muscle of the bladder. The invasion of detrusor muscle can be either full thickness or partial thickness. Bladder DE most commonly develops in the bladder base and bladder dome, rather than in the extra-abdominal bladder.

Pt presents with dysuria but may also have urinary frequency, recurrent urinary tract infections and hematuria, and, more atypically, urinary incontinence. Rarely it may be asymptomatic and incidentally diagnosed at the time of a cystoscopic or intra-abdominal procedure for a different indication.

**Evaluation** -Per speculum examination (looking for lesions on the posterior cervix or vaginal mucosa), tenderness on vaginal examination, nodules in the posterior vaginal fornix, adnexal masses, and immobility or lateral displacement of the uterus.

Urinalysis test to exclude infection or hematuria should be conducted. If infection -urinary culture. Women with hematuria and suspected bladder endometriosis should receive further testing.

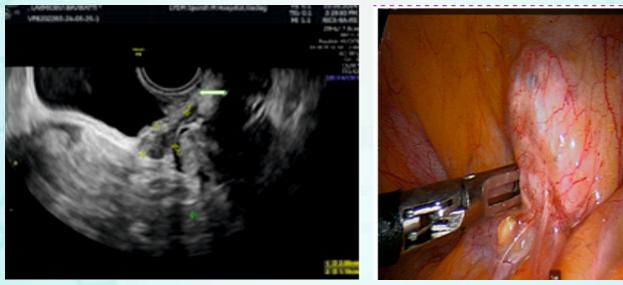
**Ultrasound** is the first-line imaging modality for diagnosing or excluding BE and should be performed transvaginally. Transabdominal ultrasound is also important for renal assessments. The International Deep Endometriosis Analysis (IDEA) group recommends a focused assessment of the bladder and ureters (in addition to a thorough examination for other sites of DE, ovarian endometriomas, and pelvic adhesions, as depicted by the immobility of pelvic organs). It is important to note that the components of this ultrasound examination exceed those of the traditional, basic pelvic ultrasound, which does not include a direct evaluation of DE or dynamic pelvic organ mobility as a soft marker for DE. Patients should be sent to the closest radiologist or sonologist with expertise in endometriosis, with a requisition that specifies the need to evaluate the bladder wall and ureteral size and position. helpful in order to better identify the different portions of the bladder wall. It is recommended to place the TVS probe in the anterior vaginal fornix and gently swinging it side-to-side, visualizing the mucosa and muscularis for focal thickening and for hypoechoic linear or nodular lesions (either spherical or comma-shaped). Bladder nodules must be measured in three orthogonal planes. Measuring the distance between the lesion and ureteral orifices may assist in surgical planning.



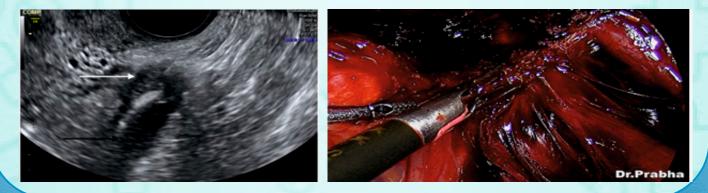
Dr <u>Mathew Leonardi</u>.

Transvaginal ultrasound depiction of the bladder. (**A**) Normal bladder and (**B**-**D**) three bladder deep

endometriosis nodules, identified with white arrows.



Dr Prabha Desai , LYDM Sparsh



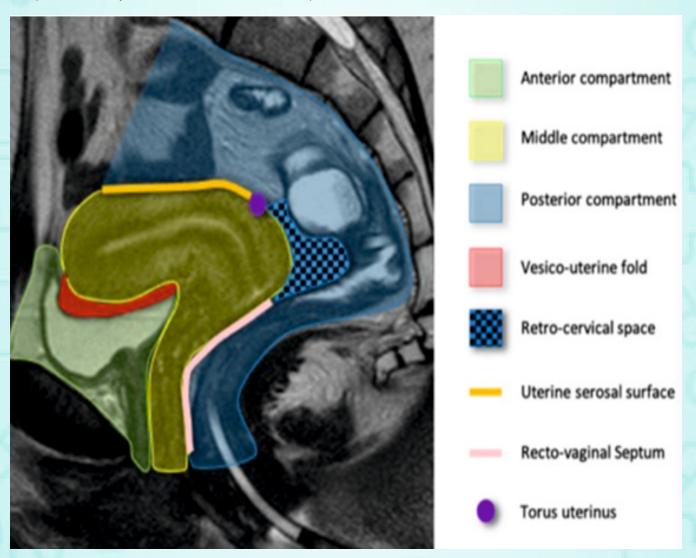
Transvaginal depiction of ureteral deep endometriosis nodule (white arrow) and hydroureter (black arrow). The nodule originates from the uterosacral ligament but infiltrates the parametrium and extrinsically compresses the ureter.

#### Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is an adjunct imaging tool that can be considered as completing or supplementing TVS for an accurate presurgical staging of UTE .As such, MRI may be most appropriate in centers where advanced TVS for UTE is not yet available or where TVS is negative and there is a high clinical suspicion of bladder DE.

The diagnosis of bladder DE is based on a hypointense signal of nodules on T2-weighted images with a frequent hyperintense signal on fatty saturation T1-weighted images.

#### Mayflower hospital, endometriosis weekly



This image helps to understand the location of nodules in pelvis on MRI A transabdominal scan (TAS) of the kidneys is recommended in all women with concerns for UTE in order to exclude the presence of hydronephrosis, as this is usually asymptomatic in cases of ureteral DE. For women with bladder lesions on TVS and asymmetrical ureteral caliber or hydronephrosis, a computed tomography (CT) urogram, which utilizes contrast, may be useful in completing the evaluation because CT best depicts the course of the ureters. CT is not used as a supplement to diagnose bladder DE.

#### CYSTOSCOPY-

When there is proven hematuria or a bladder nodule visible on TVS orMRI,cystoscopy will be helpful to confirm the diagnosis. Cystoscopically, BE can have a spectrum of possible appearances from normal-appearing mucosa that is noticeably raised due to a nodule beneath the mucosa to infiltration through the mucosa. In the latter scenario, lesions can appear to be multiloculated with a combination of colors (from the same color as the bladder mucosa to a blue/violet color). Cystourethroscopy can also aid in excluding malignancies and in measuring the distance from the lesion to the ureteral openings to help urologists and gynecologists anticipate the type of urologic procedure necessary (particularly if the removal of the lesion will also require ureteral resection and reimplantation with ureteroneocystostomy). If the distance between the edge of the endometriotic lesion and the interureteric ridge is less than 2 cm, ureteroneocystostomy is typically performed in order to reduce the risk of ureteral obstruction and fistula formation and in order to optimally restore a normal anatomy.

#### Treatment of Bladder DE

The aim of the treatment of bladder DE is to resolve symptoms and avoid possible renal damage. Treatment can be expectant, medical, or surgical. A conservative management with a sonographic follow-up can be chosen for asymptomatic women without hydronephrosis, while surgery should always be performed in women with ureteral obstruction and hydronephrosis. Pain symptoms can be managed medically or surgically.

**Medical Management**: For patients with pain symptoms due to bladder DE, continuous progesterone-based regimens (pills, intrauterine device, implant, injection), combined estrogen-progesterone therapy (continuous or sequential regimens), and GnRH analogues (with or without add-back therapy) have all been associated with an improvement of symptoms from bladder DE. Women who respond to medical management can continue the treatment until menopause or until the desire to conceive from pregnancy or to achieve an optimal quality of life and reduce the risk of progression, unless there is superimposed hydronephrosis, in which instance surgery would be the first treatment choice to prevent irreversible renal failure from ureteral obstruction.

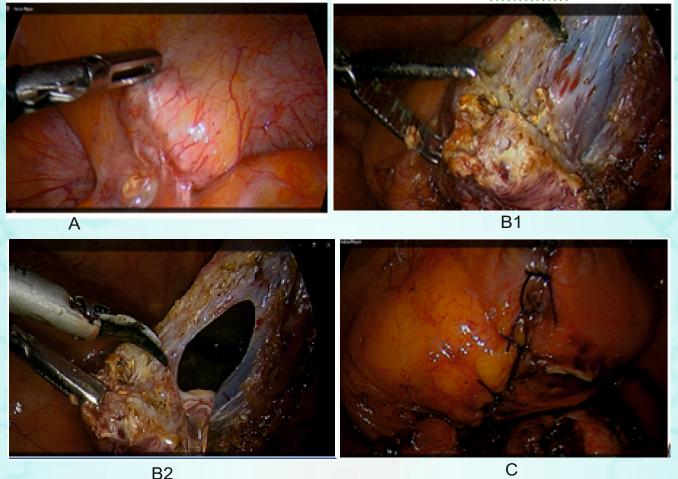
**Surgical Management**: Procedures to surgically address bladder DE include the shaving of serosal lesions and full thickness resection of DE lesions. Most surgeries can be performed laparoscopically or robotically

#### Surgical Approach

**Cystourethroscopy**: to evaluate the size of the lesion(s) and measure the distance between the lesion and the ureteral ridge. The use of ureteral catheters is not supported by strong evidence-based data; however, their use might be helpful when the distance between the lesion and the ureteral ridge is less than 2 cm or when the anatomy is distorted from previous surgeries or extensive disease, in order to reduce the risk of inadvertent ureteral damage at surgery.

Diagnostic laparoscopy, followed by the shaving of superficial serosal lesions off the bladder or partial cystectomy when there is infiltration of the detrusor muscle, in order to restore a normal anatomy and prevent hydronephrosis and recurrence of the disease. If the nodule affects the vesical base, it can either be approached laparoscopically (starting with the dissection of the vesicouterine pouch to facilitate a complete resection) or through an operative cystoscope, followed by reconstruction of the bladder either laparoscopically or robotically. Resecting the underlying myometrium has been proven to prevent a recurrence of the symptoms when it comes to bladder DE affecting the vesical base.

## Laparoscopic depiction of bladder deep endometriosis (A) before (B1,B2) during full-thickness



resection(C) after closure of bladder. Dr Prabha Desai, LYDM Sparsh

Bladder closure: It is recommanded to close the bladder with two layers of transverse sutures 3-0 or 2-0 vicryl. First layer continuous submucosomuscularies and second layer intermittent sutures musculoserosal burring the first layer. At the end of the operation, the bladder is filled with methylene blue to confirm the integrity of the bladder, and a bladder catheter should be left in place for 7 to 10 days to prevent fistula formation. Abdominal drain to be kept for early diagnosis of bladder repair leak. Surgical resection of bladder endometriosis is a risk factor for fistula formation (up to 15% of patients).

Medical versus Surgical Treatment: There are limited data comparing the surgical and medical approach to bladder DE. On this basis, we would recommend to start on a trial of COCP, progesterone, or GnRH analogues (with or without add-back therapy) for six months for women with symptomatic bladder DE who do not have associated hydronephrosis, and to reserve the surgical approach to patients who either do not respond to medical treatment or who have hydronephrosis

#### **Ureteral Endometriosis**

Ureteral endometriosis (UE) is defined by the presence of endometriotic tissue involving the ureter. UE can be further subclassified as intrinsic, consisting of 40% of lesions when endometriosis develops within the ureteral wall, resulting in fibrosis and hypertrophy of the muscularis propria, and extrinsic, consisting of 60% of the lesions when the endometriosis develops primarily out of the ureteral wall and causes compression from the outside. Though the parametrium is the main site of endometriosis that leads to extrinsic ureteral compression, it is thought that many of these nodules originate from the anterior rectal wall or uterosacral ligaments (USLs) DE.

Clinical Symptoms of UE:Patients with UE generally have nonspecific symptoms. It is estimated that 50% of women with UE are asymptomatic, 25% present with flank pain, and 15% have associated gross hematuria .Other concomitant symptoms associated with UE include dysmenorrhea and deep dyspareunia.

Diagnosis of UE: Tissue biopsy and histologic confirmation is the gold standard for diagnosing UE. The initial evaluation of suspected UE includes a detailed medical history, physical examination, and complementary tests (laboratory testing, cystourethroscopy, and imaging techniques)

Medical History and Physical Examination: UE is often associated with extensive pelvic disease, and therefore the initial history and physical assessment are key and should include a speculum examination (looking for lesions on the posterior cervix or vaginal mucosa), tenderness on vaginal examination, nodules in the posterior vaginal fornix, adnexal masses, and immobility or lateral placement of the uterus

Laboratory Testing: It is important to exclude impaired renal function when there is suspected UE. Renal function tests and urinalysis, to include infection, should be conducted in patients with flank pain or hematuria.

Imaging Techniques :TAS can help to detect ureteral obstruction and evaluate the thickness of the renal parenchyma. TVS can only assess the pelvic ureter, but it is very useful for evaluating other sites of implants of endometriosis in the pelvis. Combined TAS/TVS should be performed as a first-line exam when suspecting UE. By doing combined TAS/TVS, the ureters can be visualized from the anterior parametrium to the renal pelvis.

When there is associated hydroureter or hydronephrosis, additional radiologic studies such as MRI, CT and intravenous pyelography can help identify the sites of stenosis and assist with surgical planning. Women with suspected ureteral endometriosis should also be evaluated for bladder DE.

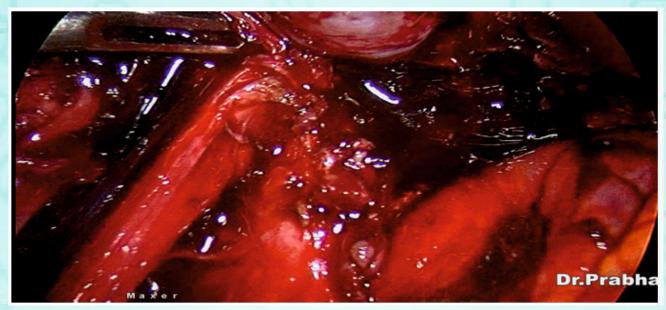
#### Treatment of UE

Since medical treatment does not necessarily revert the fibrotic component of UE yielding ureteral obstruction, surgical treatment of both extrinsic and intrinsic UE is generally necessary. However, in the absence of obstruction, medical management can be considered, if desired by the patients, to reduce the risks associated with surgery.

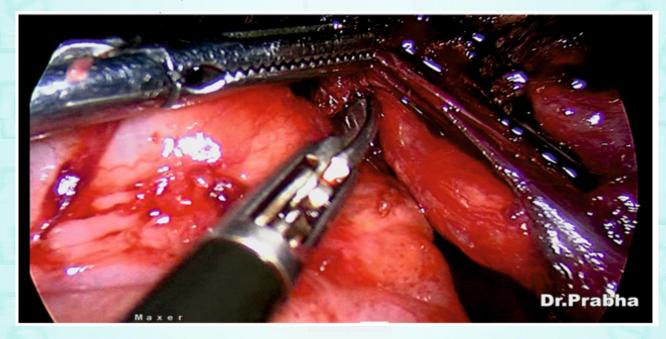
The surgical treatment of UE aims at relieving ureteral obstruction and avoiding recurrence and re obstruction. The surgical approach depends on the symptoms, types of eventual previous surgery for UE, location of DE, the extent of compression, and the kidney function. Regardless of the planned procedure, ureteral catheters or stents can be used before surgically managing UE. In women with severe stenosis, they may have a preoperative placement of a ureteral pigtail stent to limit the ongoing loss of kidney function. For those where there is no concern of a kidney function loss, ureteral catheters or stents may be placed intraoperatively.

The surgical management of UE includes conservative ureterolysis with the removal of the adjacent DE, or radical approaches such as ureterectomy with end-to-end anastomosis, ureteroneocystostomy, or nephroureterectomy. There is a lack of prospective randomized trials, given the low incidence of UE, and most of the studies regarding the surgical management of UE are retrospective. In general terms, the surgical choice depends on the renal function and the extension of the ureteral segment (or segments) involved.

**Ureterolysis**: Any ureter affected by DE (USL/parametrial or peritoneal) will first require a ureterolysis. Coexisting DE in the posterior compartment may involve the bowel, torus uterinus, posterior vaginal fornix, or rectovaginal septum. In many cases, rectouterine pouch obliteration will exist, and the normalization of the anatomy must be an early surgical priority with the identification of the hypogastric nerves. As the approach to normalizing the distorted anatomy should start retroperitoneally, ureterolysis is often one of the first steps of the procedure. This is also important because the identification of the ureter course, which is often altered with posterior compartment DE, should lead to a reduction in the rate of ureteral injury. Identification of the hypogastric nerves, as they branch from the superior hypogastric nerve plexus, allows for a nerve-sparing procedure to preserve the patient's bladder, bowel, and sexual functions.



Laparoscopic depiction of left ureteric extrinsic entrapment by rectal and uterosacral endometriotic tissue

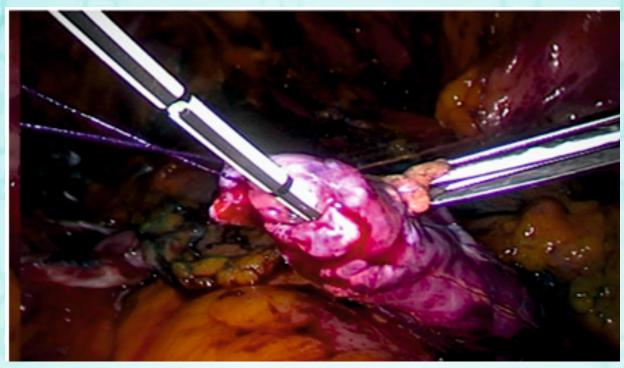


Laparoscopic depiction of right ureteral deep endometriosis leading to hydroureter. Ureterolysis alone is indicated for minimal, extrinsic, and nonobstructive UE and is contraindicated in patients who have a complete ureteral obstruction. Excision of surrounding endometriosis is recommended over ablation because ablation increases the risks of ureteral thermal injury, further obstruction, and fistula. In case of intrinsic disease or cases in which ureterolysis fails or is unlikely to work, distal ureterectomy with reimplantation is reported to have excellent long-term results with regard to renal preservation.[22]

**Ureterolysis, Ureterectomy with Ureteroureteral Anastomosis**: The procedure of choice for middle or upper third UE.

#### Ureterolysis, Ureterectomy, and Ureteroneocystostomy:

The procedure of choice for distal third UE. After transection of the ureter proximal to the stricture, it is generally reimplanted in the bladder dome, with or without a bladder-psoas hitch, in order to achieve a tension-free anastomosis with antireflux plasty of the bladder valve



Dr Mathew Leonardi Laparoscopic depiction of a transected ureter with stent

**Renal endometriosis**: Renal endometriosis should be considered when the patient is in the reproductive age group and symptoms of cyclical flank pain correlating with menses with cystic lesion in kidney on usg. Treatment options vary from active surveillance to thermal ablation, partial or radical nephrectomy depending upon the complexity of the tumour.

Nephrectomy in ureteric endometriosis with gross hydronephrosis- Donnez et al. reported the risk of loss of renal function with 11.5% of ureteral endometriosis patients. Up to 47% of the patients will require nephrectomy at the time of diagnosis for nonfunctioning kidney or ureteral endometrial lesion mimicking transitional cell carcinoma. The best diagnostic test is IVP, which can be confirmed by a filling defect of contrast within the lumen of the ureter. IVP is necessary in patients with rectovaginal endometriotic nodules of more than 3 cm in size, if they have no typical symptoms of hydroureteronephrosis. When hydroureteronephrosis is confirmed by IVP, renal scintigraphy should be performed to test the renal function. Complete loss of renal function is an indication of nephrectomy, as a nonfunctioning kidney associated hydronephrosis can lead to vascular hypertension, recurrent pyelonephritis, or kidney stones. On DTPA scan the normal GFR for an adult male is 90 to 120 mL/min. However, this number varies significantly by age. GFR less than 15 mL/min/1.73 m² is end-stage renal disease and Nephroureterectomy is a successful treatment in such cases with refractory pain

**Complications**:Complication rate amongst those who undergo a combined gynecologic-urologic surgery for endometriosis with a thorough interdisciplinary evaluation, including preoperative imaging. It is currently thought that the cumulative surgical complication rate for patients surgically treated for UE is estimated to be 9%. Major complications included the recurrence of ureteral obstruction (7.4%), ureteral or ureterovaginal fistula (1.6%), and hemoperitoneum (0.4%)

#### Conclusion:

Early diagnosis and treatment of urinary tract endometriosis are necessary to avoid the loss of kidney function. Urinalysis with cytology examination is nonspecific for the diagnosis of urinary tract endometriosis. Ultrasonography, especially endovaginal sonography, is more sensitive for diagnosis than CT or magnetic resonance imaging (MRI).

In view of the frequently prolonged diagnostic delay with related morbidity and erroneous treatments, its better to have a high index of suspicion of vesical endometriosis in all premenopausal women complaining of irritative urinary symptoms with negative urine cultures. Imaging and cystoscopy should be scheduled during or near a menstrual period to allow for the best chance of diagnosis. Open or laparoscopic partial cystectomy is a better alternative option in comparison with transurethral resection in vesical endometriosis. Ureteral endometriosis needs individualised treatment to maximise the preservation of renal function.

Although surgical complications remain a reality due to the infiltrative and anatomic-distorting nature of endometriosis, these can be mitigated by an earlier recognition of UTE symptoms, comprehensive noninvasive imaging diagnoses, and a strong collaboration between minimally invasive gynecologists and urologists

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### "LAPAROSCOPIC MANAGEMENT OF BOWEL ENDOMETRIOSIS: A COMPREHENSIVE GUIDE"



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#### Introduction

Endometriosis is a disease that can seriously affect quality of life. We are still coming to understand and acquire skills and knowledge to optimally treat it. It has three main phenotypes that may coexist- peritoneal disease, ovarian endometriomas and the deep endometriosis (DIE). DIE is most commonly seen in rectovaginal septum, involving the POD, uterosacral ligaments and rectosigmoid. In 15% cases it may involve appendix, caecum, vagina, genitourinary tract, pelvic side wall, diaphragm and scar tissue.

Digestive lesions are single in around two-third of the cases and multifocal in around one-third. they may involve the superficial layer or sometimes also involve the muscularis and mucosa.

Endometriosis is a chronic, oestrogen dependent inflammatory condition affecting approximately 10% of all reproductive-aged women and approximately 35-50% of women with pelvic pain and infertility.

Endometriosis can be genital or extragenital. One of these extra-genital locations is the bowel. Affecting 3.8-37% of patients with known endometriosis, bowel endometriosis is the most common "non-gynaecological" location for endometriosis. In the bowel the most common site is the rectosigmoid colon, followed by the rectum, ileum, appendix, and cecum.

In the vast majority of cases, it occurs in the rectum and sigmoid colon. In less than 10% of cases, endometriosis lesions are also found in the appendix, the terminal part of the small intestine (the last 30-40 cm), or the most proximal part of the colon (caecum). In contrast, endometriosis lesions are very rare or absent in the stomach, duodenum, proximal and intermediate small intestine, or on the surface of the liver and spleen.

#### **Pathogenesis**

Bowel endometriosis probably has a multifactorial pathogenesis. Multiple theories have been suggested for its genesis.

## TABLE1 Theories surrounding pathogenesis of bowel endometriosis Theory and Explanation

- Retrograde menstruation; Most commonly cited theory involving retrograde flow during menses
- Coelomic Metaplasia; Metaplastic extrauterine cells aberrantly differentiate into endometrial cells along visceral or abdominal peritoneum
- Benign metastasis Where endometrial tissue spread through lymphatic or hematologic system to ectopic anatomic sites
- Genetic and immune dysfunction Includes possible apoptosis suppression, greater expression of invasive mechanisms, greater expression neuro angiogenesis factors, genetic alterations of endometrial cellular function, and oxidative stress and inflammation

- latrogenic Causes; For Example, endometrial cells can be spread after surgical procedures that involve endometriosis or endometrium itself, with lesions presenting along scars such as laparoscopic port sites and caesarean delivery hysterotomies
- Anatomical Shelter Theory; Rectosigmoid colon may act as anatomic barrier that prevents retrograde menstrual flow from spreading cephalad from pelvis, so that more endometriotic implants imbed along pelvis and rectosigmoid than along upper abdominal structures.

The pathogenesis of pain related to endometriosis is complex and multifactorial, with evidence suggesting that there may be an autonomic component explaining why.

#### Clinical features

Main symptom is pain which includes dysmenorrhea, deep dyspareunia, chronic pain, and/or dyschezia. Other symptoms which suggest the involvement of the bowel include catamenial diarrhea, blood in the stool, constipation, bloating, pain with sitting, and radiation of pain to the perineum. many patients are misdiagnosed as irritable bowel syndrome because of similar complaints and never treated for their condition which can lead to further aggravation of complaints and no relief despite treatment. Therefore, it is important to keep in mind bowel endometriosis as a differential when dealing with similar complaints. Other differential may include inflammatory or ischemic colitis, radiation colitis, diverticulitis, malignancy, or pelvic inflammatory disease. histologically the nodule is made up of muscular or fibrous tissue while endometrial like cells account for 15 to 20 %which explains relative ineffectiveness to medical line of treatment hormonal treatment may stabilize the nodule but does not cure it totally there is irritation and thickening of the digestive wall around the nodule due to cyclical inflammation during periods due to retrograde menstruation which explains cramps and diarrhoea adhesions and fixity of bowel leads to constipation there is also reduction in the lumen of rectum causing symptoms of bloating and even nausea and vomiting Diagnosis

#### **Physical examination**

iagnosis begins with a thorough history and physical examination, specifically rectovaginal examination which is often helpful in diagnosis, especially if performed at the time of menstruation, during which time lesions may be more inflamed, tender, and palpable. Findings may include a palpable nodule or a thickened area along the uterosacral ligaments, uterus, vagina, or rectovaginal septum. Visualization of the vagina may reveal a laterally displaced cervix or a blackish-blue lesion.

During gynaecological examination, the palpation of a fibrotic nodule in the posterior vaginal fornix will allow the surgeon to suspect deep lesions. During this examination, the mucosal protrusion, the retraction, or the invasion has to be evaluated, as well as the extension of the fibrotic lesion to the pelvic sidewalls.

Regarding the diagnosis of endometriosis, the delay that typically precedes proper diagnosis (6 to 7 years) [54] is probably one of the most challenging aspects of managing this disease. There is a need for non-invasive diagnostic tools. Transvaginal ultrasound and magnetic resonance imaging have good sensibility and specificity in diagnosing OMA and DIE, but the non-invasive diagnosis of SPE remains a challenge.

#### **Biochemical**

Monitoring of CA-125 levels to diagnose and evaluate disease progression in deeply infiltrative endometriosis has been proposed but is of little utility and is not recommended.

#### Laparoscopic visualization

Direct visualization by a laparoscope is the gold standard. Bowel endometriosis may also be diagnosed incidentally at the time of surgery performed for other indications.

#### **Imaging techniques**

Ultrasonography can give us more information about the site, size, depth of invasion and complications which are important in pre-operative planning. Although it has high degree of sensitivity and specificity, the main drawbacks remain that accuracy of diagnosis is correlated with sonographer experience and sigmoid may be out of view leading to inaccuracy of results.

#### Treatment

Medical treatment, which permits the suppression of estrogen synthesis and atrophy of the endometriotic implants, is usually associated with significant side effects. However, if hormonal therapy alleviates symptoms such as dysmenorrhea, there is a high recurrence rate after cessation of the therapy. Histologically, colorectal endometriosis is characterized by hyperplasia of fibroblasts located in the muscularis layer of the bowel wall. This fibrosis is considered as a host tissue reaction to the presence of ectopic endometrial cells [6]. Fibrosis will not be affected by the hormonal therapy explaining the relative ineffectiveness of the medical treatment on other symptoms such as deep dyspareunia and dyschezia. Medical treatment for DE can reduce symptoms but does not cure the disease, and surgical removal of the lesion is required when lesions are symptomatic, impairing bowel, urinary, sexual, andreproductive functions. Medical treatment may not provide long-term improvement in patients who are symptomatic, and consequently most of these patients may require surgical intervention.

#### Surgical approach

Although several surgical techniques such as laparoscopic bowel resection, disc excision, and rectal shaving have been described, there is no consensus regarding the choice of technique or the timing of surgery Benefits of excisional surgery include not only pain relief and a potential increase infertility, but also potential cancer prophylaxis. Bowel resection has been performed to treat bowel endometriosis since the early 1900s The risk of immediate complications after shaving and disc excision is probably lower than after colorectal resection, allowing for better functional outcomes. The presumed higher risk of recurrence related to shaving has not been demonstrated. For these reasons, surgeons should consider rectal shaving as a first-line surgical treatment of rectovaginal DE, regardless of nodule size or association with other digestive localizations.

Segmental resection may ultimately be reserved for advanced lesions responsible for major stenosis or for several cases of multiple nodules infiltrating the rectosigmoid junction or sigmoid colon. Endometriotic infiltration up to the bowel serosa is not considered as deep bowel endometriosis and therefore, should not be treated surgically as such.

History of pain, immediate fertility concerns make surgery the obvious choice. However, in case of asymptomatic nodules and no fertility concerns, surgery in not indicated. It is a high-risk surgery because of altered surgical planes and proximity to rectosigmoid and ureter. However, laparoscopy continues to be the preferred mode of surgery due to the following reasons

- 1. Better visualization of rectovaginal area
- 2. Magnification helps in assessment and surgery both
- 3. Pneumoperitoneum helps in dissection of retroperitoneum

#### Aims

- Excision of all visible disease (Excision of rectum, bladder and ureter may be a part of this excision)
- Restoration of normal anatomy
- Prevent or delay recurrence

A more radical approach is total hysterectomy and bilateral salphingo-oophorectomy. It has four-fold increased risk of complication due to adhesions and infiltrative lesions.

#### Preoperative preparation

We recognize the confusion that surrounds the surgical management of deeply infiltrative endometriosis of the bowel. Whereas one size does not fit all, there are principles and approaches that may guide the surgeon to perform the most effective and least harmful procedure in particular cases. The aim of this expert review is to help clinicians navigate the management of this complex disease.

preoperative bowel preparation has advantages of less surgical field contamination, less

contamination during unplanned bowel injury or resection. two days prior to surgery patient is on liquid diet and polyethylene glycol is given to prepare the bowel the preceding evening.

- Optimize the port placement
- Under anaesthesia patient should be examined
- Before placing the patient in head down deep Trendelenburg position examine and rule out other sites like diaphragm, bowel, mesentery, appendix etc.
- Place the patient in deep Trendelenburg position
- A strong uterine manipulator introduced and rectal probe positioned for suitable traction and counter traction to facilitate delineation of correct plane.

#### **Rectal Shaving**

Management of DIE infiltrating into rectum is more complex. In an overwhelming majority of cases a 'rectal shaving' is sufficient, where the margins instead of being healthy can be fibrotic. The endometriotic nodule is pulled anteriorly while the ventral surface of the rectum is carefully shaved off (Unlike in vagina, we can leave behind fibrotic tissue and not excise till healthy tissue), with rectum falling away with dissection followed by excision at the vaginal margin. A 'reverse approach' has also been used.

#### **Disc Excision**

n case of disease infiltrating till the mucosa or deeper muscularis layer, excision of disease also includes full thickness of rectal wall. If this infiltration involves less than 50% of rectal margin, disc excision with laparoscopic and trans anal approach is the method of choice. Steps of this procedure using the Rouen technique have been explained in the referenced article by Horace et al.

#### Resection Anastomosis

It has been suggested this may be reserved for cases with more extensive infiltration lesions more than 3 cm/ involvement of more than 50% diameter, strictures, multiple nodules higher up around the rectosigmoid junction or the sigmoid colon. Consensus is still elusive.

Factors that decide if and what kind of rectal resection is advisable are depth of invasion into the rectum, presence or absence of bowel symptoms and stricture, distance from the anal margin, extent of circumferential involvement of rectum. While more conservative surgery has less intraoperative, postoperative and medium-term complications, the need for going conservative has to be balanced with long-term complications, possibility of recurrent disease and a very difficult surgery later. This more than anything else warrants a referral to an expert center and multidisciplinary involvement instead of a surgical misadventure.

A thorough peritoneal lavage could be done to avoid re-implantation of any endometriotic tissue. This fluid can also be used to look for any rectal injury by insufflating air through the rectal probe, looking for bubbles laparoscopically and a ureter check. Fluid barriers like 4% icodextrin or leaving 3 litres of Ringer lactate intraperitoneally can help with adhesion prevention.

#### Recurrence and Response

The recurrence of the rectovaginal disease is much less when compared to other forms of endometriosis owing probably to its different pathogenesis, many studies finding it less than 5% compared to 20-40% in other forms of endometriosis. Thus, while the surgery for DIE may be challenging, it is also fruitful. Relief in pain score are unequivocal with about 85% women becoming free of pain. Spontaneous and cumulative pregnancy score have been found to be around 59% and 81% in these patients, 19

#### CONCLUSION

Deep endometriosis is different from the rest with a differing pathogenesis, appearance and natural history. Its surgery in the words of Redwine "is a feast for the surgeon who loves challenges", it is simultaneously challenging and fruitful. Best way to approach it remains by a multidisciplinary team at a specialized center.

It is important to note that shaving and discoid resection techniques are part of the so-called conservative treatment of the rectum, as opposed to segmental resection. Indeed, these two approaches make it possible not to remove an entire rectal segment, and to preserve the mesorectum in its entirety, as well as the volume of the rectal ampulla.

Shaving does not necessarily require digestives suturing. It is a commonly used technique, accounting or 48.1% of digestive procedures in the FRIENDS Study (3). The technique involves peeling" the anterior surface of the rectum, to achieve macroscopically complete excision of the endometriosis nodule, without opening the digestive lumen. It is therefore usually reserved for involvement of the superficial serosa or muscularis propria. For nodules infiltrating the digestive wall deep shaving must be performed with caution, and the exposed submucosa must be covered with sutures, or even resected by discoid excision, to avoid early postoperative digestive fistula. It consists in opening the laterorectal and rectovaginal spaces around the limits of the deep endometriosis nodule. The nodule must first be completely freed and left attached to the rectum before the actual shaving takes place. The nodule is then grasped with claw forceps and progressively detached from the rectal wall. Instruments used depend on surgeons' experience with cold scissors, hook or monopolar scissors, ultrasound scalpel, CO2 laser or plasma energy. A rectal wall tightness test is usually performed at the end of the excision procedure, especially in the case of deep shaving, to ensure that there is no transfixing wound in the rectum. The rectum is examined and palpated using forceps or a rectal feeler, to see that the shaving area is supple, which indicates the completeness of the procedure. Sometimes a "preventive" suture may be performed on the anterior wall of the rectum.

#### **Discoid resection**

The first stage of the operation is identical to "Shaving" with release of the deep endometriosis nodule, opening of the laterorectal spaces, uterosacral ligaments (often resected in their proximal part), torus, posterior vaginal cul-de-sac and vagina, sometimes necessitating partial colpectomy. Uni- or bilateral ureterolysis is also often necessary. The endometriosis nodule is thus "pedicled" onto the rectum. The digestive phase begins with shaving, to reduce the diameter of the lesion and thus limit the size of the resection, and also to reduce the thickness (depth) of the lesion, enabling resection by transanal stapling in the best 168% of conditions. Deep shaving is an absolute prerequisite for discoid excision using trans-anal forceps, as these cannot close around a nodule left in place (fig. 18.6).

#### Manual resection and suturing

This technique involves complete resection of the nodule, with opening of the digestive lumen and direct suturing of the edges. Prior shaving is not necessary. Suturing is usually performed using separate stitches of absorbable thread. Discoid exeresis in the sigmoid colon can be performed by direct suture, through a suprapubic mini-incision. Robotic assistance facilitates suturing of the rectum, thanks to the additional degrees of freedom of the needle holders.

#### Transanal circular stapler disc excision

This technique enables resection of nodules up to 3 to 4 cm in diameter, located no more than 18-20 cm above the anal margin. Prior shaving is essential, and should be performed as deeply as possible to minimize the thickness of the rectal wall to be excised, and thus increase the possible surface area of the disc to be removed. Once the shaving has been performed, the digestive surgeon positions himself between the patient's legs and introduces a transanal forceps with the anvil mounted and lubricated beforehand, into the rectum. The forceps pushed in under endoscopic visual control, until the tip protrudes beyond the shaving zone. In the case of

nodules with intraluminal protrusion, shaving reduces the stenosis and softens the rectal wall, allowing the transanal forceps pass beyond the previously stenotic area. The gynaecological surgeon places a 3/O absorbable thread in e upper and lower limits of the shaving area. The digestive surgeon opens the clamp completely while the gynaecological surgeon ties the thread, cutting the thread 4-5 cm from the knot. Using two needle holders that grip both wires, the knot is pushed downwards, while the transanal forceps are anteroposterior to the maximum, so that the shaving area is completely folded in half between the forceps jaws. The forceps are gradually closed under visual control, until the shaving zone disappears completely between the two jaws. Once closed, the forceps are cocked and the section is released after 10 to 15 seconds (fig. 18.8). The tightness of the suture is tested by insufflating 50-100 mL of air into the rectum. Separate stitches of resorbable thread can be placed on the staple line if required. Examination of the specimen ensures that he surgical procedure is macroscopically complete.

Transanal discoid excision using Contoure Transtar d semicircular forceps: the "Rouen technique". This technique was developed by the Rouen team in 2009. It allows the removal of large nodules of deep endometriosis of the lower and middle rectum, located up to 8 to 10 cm above the anal margin and infiltrating the rectal wall over a length of 5 to 6 cm. This procedure has the advantage of preserving part of the rectum with resection of the anterior wall only, reducing the risk of the dreaded rectal resection syndrome. Prior deep shaving is also necessary in order to benefit from the same advantages described above and to optimize the quality of the stapling. Collaboration between gynecological and digestive surgeons is also essential, as this is a combined procedure with laparoscopic control of the progress of the procedure. The forceps used are the Contour Transtar forceps (Ethicon). After shaving, the digestive surgeon positions himself between the patient's legs. He installs an anal dilator and secures it to the anal margin with 4 sutures placed in the 4 cardinal points. The shaving area is located transanally, under endoscopic visual control. The digestive surgeon places several traction sutures transanally, at the inferior and superior borders, as well as in the center of the shaving zone. He performs traction of the wires downwards, in line with the anal canal, to induce transanal prolapse of the shaving zone. The Contour Transtar forceps are introduced at the 3 o'clock point, with the jaws open, and then rotated counter-clockwise to slide the transanal prolapse into the anal canal. The forceps are closed, the stapler is triggered and the rectal wall is sectioned. The procedure is repeated 3 to 4 times, replacing the staple refills. A leak test is also performed, and a few separate stitches of absorbable thread may be necessary to reinforce the staple line.

The use of anti-adherence barriers is not recommended due to the increased risk of digestive fistula.

#### Radical techniques

Radical techniques such as segmental resection are often presented as opposed to conservative techniques (discoid or shaving). Several studies have compared these two different approaches. Several studies showed overall improvement in pain and recurrence rate, but with a significant difference in terms of dysuria in favour of discoid techniques. The complication rate also appears to favour conservative techniques in Mohr's series. Similarly, functional digestive results appear to be better in patients operated on using a conservative technique.

Parameters guiding the choice of surgical strategy best suited to the clinical situation

- Nodule location (sigmoid, rectosigmoid hinge, upper rectum) hinge, upper rectum, middle rectum, lower rectum),
- size of nodule and digestive infiltration.
- Depth of digestive infiltration (serosal, muscular, mucosal). mucosa).
- Multifocal disease.
- Experience of the surgical team.
- Patient's age, symptoms, desire for pregnancy and surgical history.

#### Laparoscopic rectosigmoid segmental resection

#### Intraoperative preparation

A preoperative assessment is systematically carried out to determine the bowel involvement and damage, the surgical procedure and whether or not a protective stoma is indicated. A residue-free diet is prescribed for 5 days prior to surgery, and a polyethylene glycoltype colonic preparation is administered the day before surgery. In addition to an explanation of the surgical procedure, the risks of complications and an assessment of whether or not a protective stoma should be installed during the digestive surgery consultation, patients meet a stoma therapist preoperatively for information on stoma appliance and for preoperative marking of the future stoma site, to limit appliance difficulties.

#### Operating position

The patient is positioned in the double team position, ideally with both arms alongside the body, with the operator on the patient's left for the gynaecological phase and on the patient's right for the digestive phase. Trendelenburg and right roll positions are checked for ease of exposure.

#### **Trocar arrangement**

In general, 5 trocars are used for this procedure

The 10 mm periumbilical trocar already positioned during the gynecological phase remains the optical trocar; the 5 mm trocars in the left and right iliac fossa, positioned during the gynaecological phase, serve as exposure and operating trocars respectively; -a 5 mm operating trocar is inserted in the right flank or hypochondrium; - a 5 or 10 mm suprapubic trocar is also often positioned during the gynecological phase. It is used to introduce the linear stapling/sectioning forceps if available.

#### Surgical equipment

A 30° optic may be useful and provide additional comfort during rectal dissection, but in our experience, the procedure is performed without difficulty with a 0° optic.

On the other hand, an ultrasonic or thermofusion scalpel should be used for dissection

#### **Exploration**

Exploration of the abdominal cavity is done, in particular the appendix and ileocecal junction, which would require appendectomy or ileocecal resection.

#### **Rectosigmoid resection**

Mobilization of the left colon

The digestive phase begins with detachment of the right Toldt fascia, sagittalizing the left colon and increasing its mobility for extraction of the resection specimen without tension, and for colorectal anastomosis, also without tension. The rectosigmoid hinge is pulled into the right iliac fossa using forceps inserted into the trocar in the left iliac fossa, in the Trendelenburg position and right roll to facilitate tilting of the small intestine into the right hypochondrium. The left colon is pulled to the right by the left hand of the to tension the peritoneum securing the left colon to the left parietocolic gutter. This peritoneal sheet is incised from bottom to top up to the angle, which rarely is needs to be freed. In this way, the left colon is mobilized from the outside in. The left mesocolon is freed in an avascular plane, leaving the left ureter, genital vessels and Gerota's prerenal fascia posteriorly (fig. 18.13).

Sigmoid and rectosigmoid hinge dissection

Key points

Complete segmental resection.

Limitation of functional consequences.

Respect for nerve plexuses.

Preservation of a maximum amount of rectum.

Once the left colon, sigmoid and their mesos are free and mobile, the upper pole of the endometriosis lesion is located and elevated towards the wall. The left mesocolon and mesosigmoid are thus exposed to create a window in the meso-sigmoid just below the mesenteric edge of the sigmoid about 1 cm upstream of the endometriosis lesion, in order to respect the axis of the mesenteric vessels and the bordering arch. Dissection is then carried out along the mesenteric edge of the sigmoid, flush with the gastrointestinal tract, and the mesosigmoid is sectioned using an ultrasound or thermofusion scalpel to progressively hemostasize the small sigmoid branches. This dissection according to the nerve sparing technique preserves the mesocolon, allowing conservation of vascularization and the superior hypogastric plexus. Dissection continues over the rectosigmoid hinge, flush with the digestive tract and away from the ureter, which must be located if left ureterolysis has not already been performed during the gynaecological phase. Lesions of rectosigmoid endometriosis very often form folds of the sigmoid and rectum, which are adherent to the endometriosis nodule. In addition to the nerve sparing technique, sectioning the mesos flush with the digestive tract enables these tract segments to be "unclogged" and resect the lesion without sacrificing a healthy rectum through rectal devascularization if the mesorectum was first approached beneath the lesion.

#### Rectal dissection and section

The major challenges of rectal dissection are to preserve as much of the vascularized native rectum as possible, and to prevent nerve damage to avoid functional sequelae. Dissection should therefore continue, always sectioning the mesorectum as close as possible to the rectum, using ultrasound or thermofusion. The rectosigmoid hinge is drawn upwards with the aid of forceps inserted in the left iliac fossa or suprapubic trocar. Beginning with the posterior mesorectum (usually free, given the location of endometriotic lesions, which are usually anterior), the lateral cheeks of the mesorectum are accessed. In the case of rectal endometriosis lesions, the mesorectum is thickened and more difficult to section, often adhering laterally, where the course of the ureters must be checked and ureterolysis performed if necessary. The hypogastric nerve and inferior hypogastric plexus must be respected as far as possible. An intrarectal phantom head introduced by an assistant between the legs may be useful to expose the rectum and identify the area of rectal section downstream of the lower edge of the lesion. Rectal section is performed using a linear stapler, usually introduced through a 12 mm suprapubic trocar. Ideally, section is performed in a single or double staple-loader, perpendicular to the rectum, over a well-vascularized area to limit the risk of anastomotic fistula.

#### Extraction of the resection part

Extraction of the rectosigmoid resection part is performed through a ort incision (4-5 cm). When a protective stoma is planned, the future stoma orifice is created and the resection piece is extracted through this orifice. A MacBurney scar from a previous appendectomy may also be used as an alternative site. If necessary, and most frequently, the specimen is extracted through a short transverse suprapubic skin incision. The edges of the incision are protected by a circular plastic bag. The freed rectosigmoid is extracted through the incision. The colon is sectioned upstream of the endometriosis lesion. After checking that the colon is well vascularized opposite the window made in the mesosigmoid via the border arch, the colon is sectioned. A bursa is made by hand or with bursa forceps, and the anvil of a circular suture cutter is inserted into the colonic segment

before the bursa is closed. When closing the bursa, care must be taken to loosen the colonic mucosa using small atraumatic forceps hooked electively onto the mucosa.

#### Colorectal anastomosis

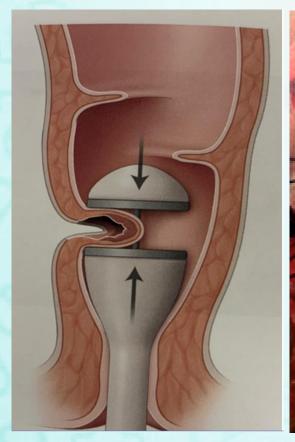
The colon with its anvil is reintroduced intraabdominally, and the incision temporarily closed with the plastic-coated circular cover so that a trocar can be reintroduced if necessary. Via the transanal route, the circular stapling forceps are inserted and, under laparoscopic control, the correct position is checked so that its axis perforates the rectal staple row at its center. The anvil is inserted into the colon and snapped onto the intra-rectal clamp. Before starting clamping, check that the colon is not twisted on its mesocolic axis. Clamping is carried out progressively, while checking for the absence of interposition between the jaws of the posterior vaginal wall, hail or any other structure. The clamp is activated and withdrawn. The rectal and colonic flanges withdrawn from the forceps are examined to check that they are circular, verifying the technical quality of the anastomosis. To check that the anastomosis is watertight, air is injected through the rectum after filling the pelvis with saline. Alternatively, serum stained with methylene blue can be injected transanally via a Foley catheter whose balloon is inflated just above the sphincter.

#### Drainage

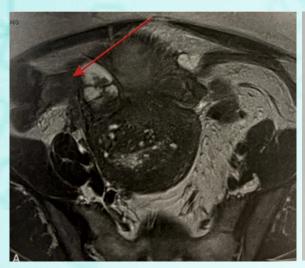
Drainage is not recommended to improve early rehabilitation. We reserve the right to recommend drainage in the event of intraoperative anastomotic technical difficulties or bleeding.

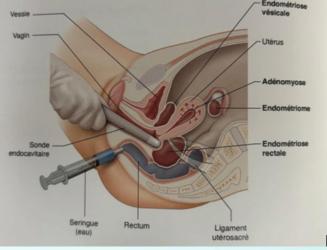
#### **Omentoplasty**

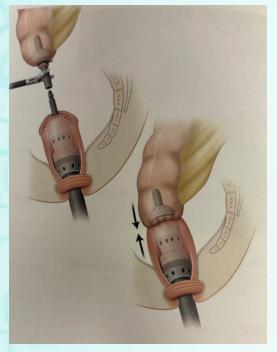
Although widely used in digestive surgery, interposition omentoplasty has shown no benefit in preventing anastomotic fistulas in colorectal surgery. In our team, in view of the possible deleterious effect on fertility due to congestion in the pelvis, it is not performed in case of surgery where pregnancy is planned. On the other hand, in the case of hysterectomy and rectosigmoid resection with colorectal anastomosis or discoid resection, the choice of performing an interposition omentoplasty between the two sutures is left to the surgeon.

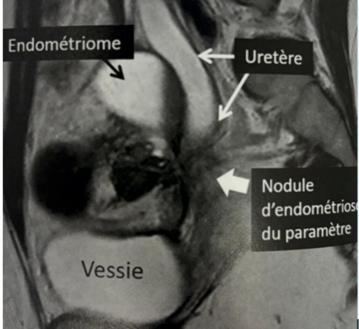






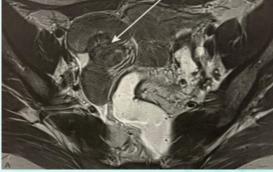


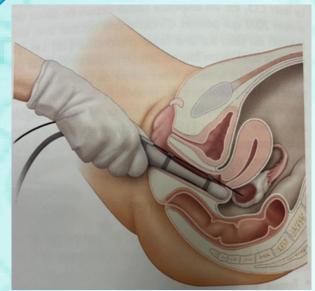


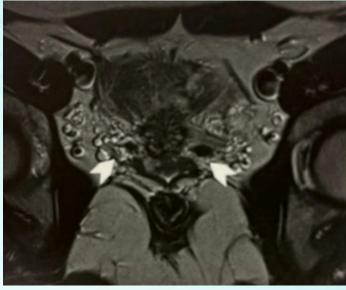


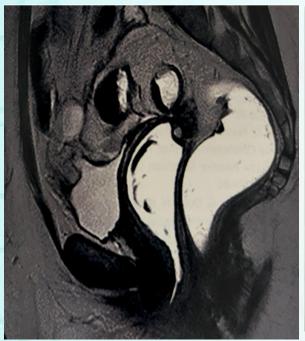


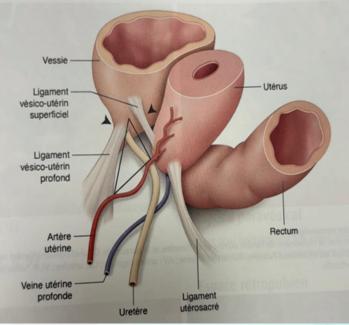




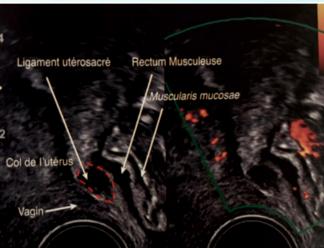


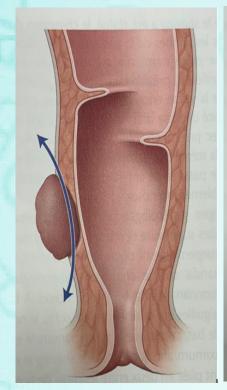


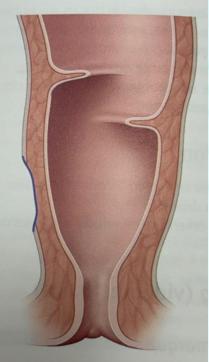


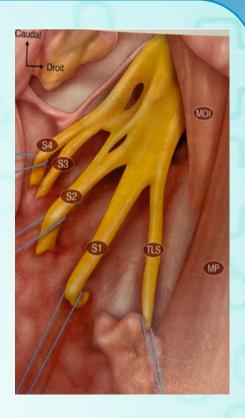


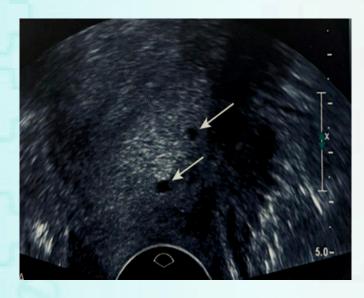


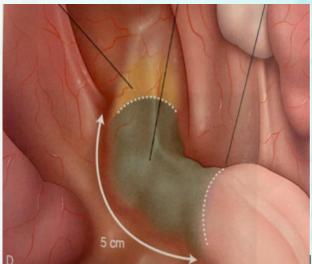


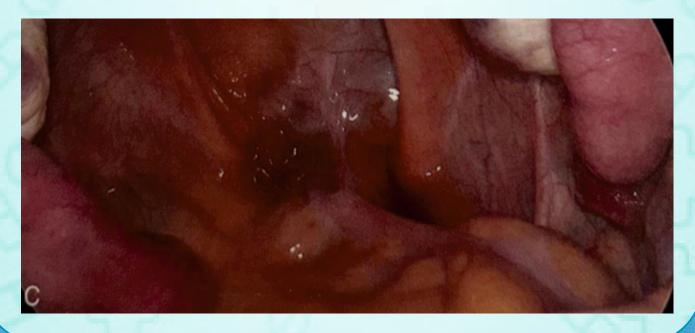




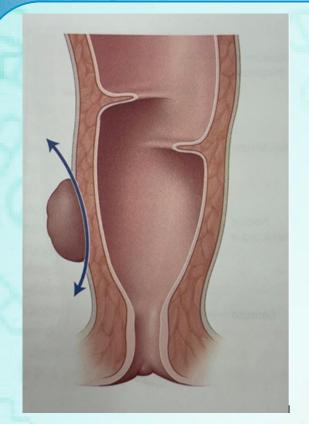


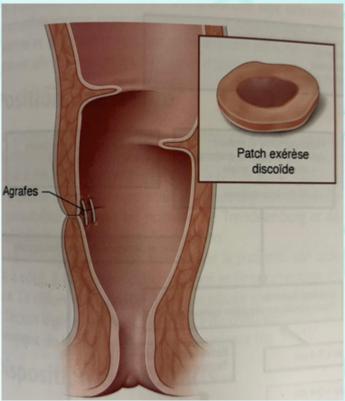






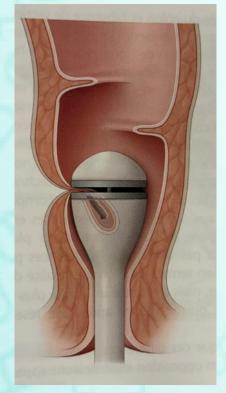
### KSOGA UPDATE



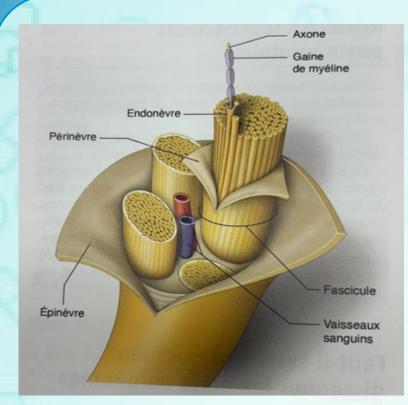


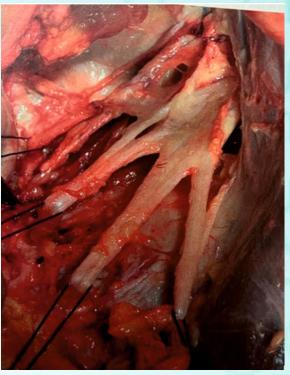






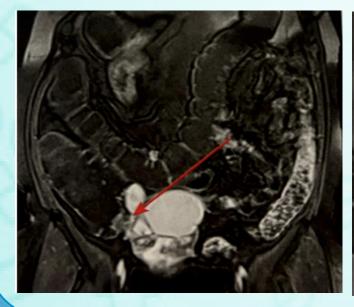


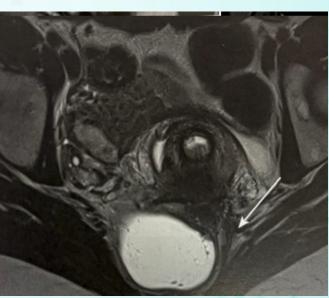




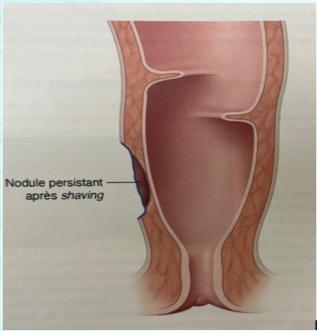


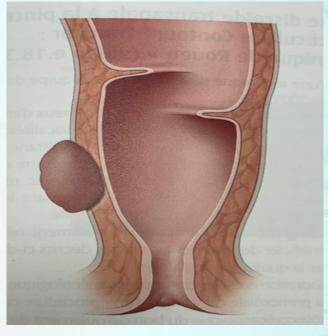


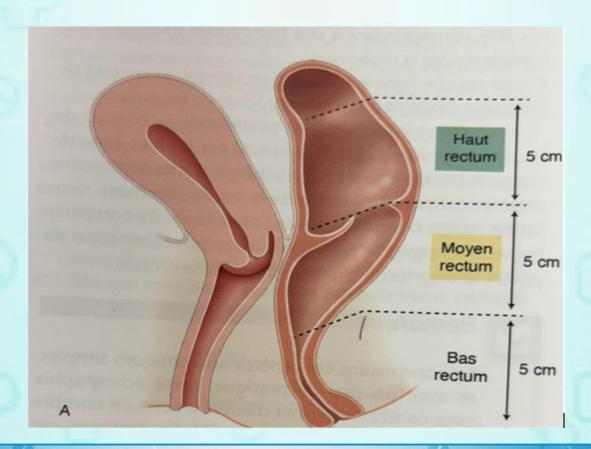


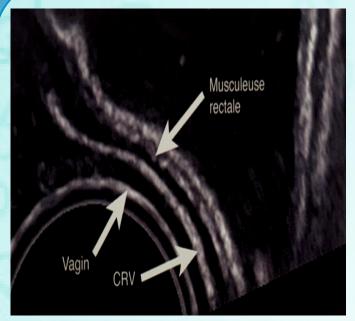


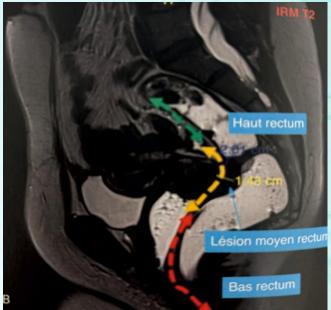


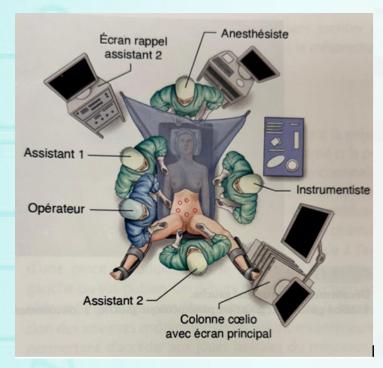


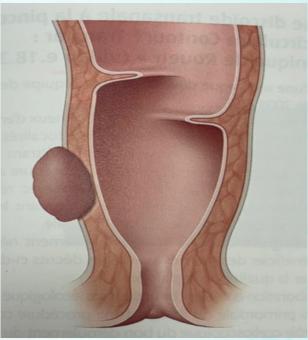


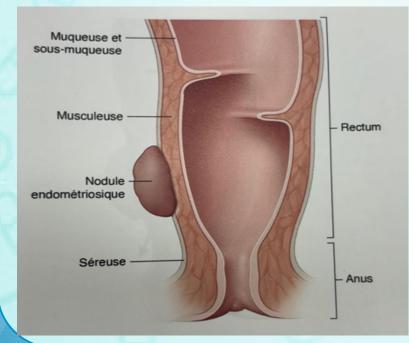


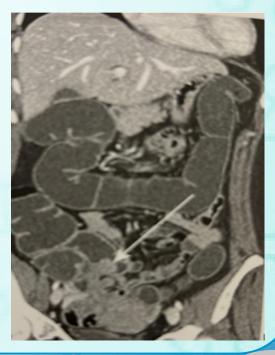












#### ADOLESCENT ENDOMETRIOSIS: EARLY DETECTION AND EFFECTIVE MANAGEMENT STRATEGIES



**Dr Ravikanth G O**Chairperson, Endoscopic Committee,
Karnataka State Obstetrics and
Gynaecologists Association

Dysmenorrhea is a common symptom among adolescent girls, with prevalence ranging from 50% to 90%. One of the common causes of dysmenorrhea in this group is endometriosis. Endometriosis affects 10% to 15% of women of reproductive age. Studies have shown that nearly 70% of women with chronic pelvic pain may have endometriosis. Additionally, it has been demonstrated that 19% to 73% of adolescent women undergoing laparoscopy for menstrual issues are found to have endometriosis.

#### Symptoms of adolescent endometriosis.

Endometriosis is a common cause of secondary dysmenorrhea. Symptoms often include nausea, vomiting, diarrhoea, headache, muscle cramps, and disturbed sleep. It's one of the leading causes of school absenteeism among adolescents. Nearly two-thirds of adolescents undergoing laparoscopy for chronic pelvic pain are found to have endometriosis. A 2015 study highlighted that those with endometriosis can experience cyclical pain, pre-menstrual syndrome, anxiety, depression, and dysphoria before menstruation.

#### Evaluation of dysmenorrhoea among adolescents.

Adolescents are often known for delaying medical care. Early diagnosis of conditions like endometriosis can alleviate pain, prevent further damage to pelvic organs, and improve fertility chances. A pelvic examination should be considered if an infection is suspected, severe dysmenorrhea develops soon after menarche, or progressive dysmenorrhea with heavy menstrual bleeding is present. Endometriosis should be suspected when there's no response to routine medical management, a family history exists, or dysmenorrhea progressively worsens. According to ESHRE guideline, bimanual vagianl and rectal examination should be discussed with the adolescents and her caregiver (Good Practice Point [GPP]) because it is also useful to rule out other causes of secondary dysmenorrhea and pelvic pain. Palpation of adnexal masses and thickening or retraction of uterosacral ligaments (USLs) and nodules in the rectovaginal septum may reveal endometriosis.

#### Imaging in endometriosis of adolescent.

For adolescents who are sexually inactive, transabdominal ultrasound is preferred over transvaginal ultrasound. Alternatively, transperineal or transrectal ultrasound can be considered. Magnetic Resonance Imaging (MRI) might be necessary to rule out obstructive lesions. Ultrasound remains the most preferred diagnostic method, often revealing ovarian endometriotic cysts. However, diagnosing non-ovarian endometriosis can be challenging, especially in adolescents where superficial lesions are common. A negative ultrasound does not rule out endometriosis. Transrectal ultrasound can detect thickening of the uterosacral ligament with endometriotic cysts.

In MRI imaging, endometriomas exhibit high signal intensity in TI-weighted and T2-weighted sequences, remaining noticeable in fat-suppressed TI-weighted images. For endometriotic lesions, MRI features include low signal intensity in TI- and T2-weighted sequences for the fibromuscular component, and hyperintensity in T2-weighted sequences for the glandular component, with alterations in TI-weighted sequences indicating chronic bleeding.

#### Management of adolescent endometriosis.

Endometriosis is a persistent and challenging condition with no definitive cure. Therefore, treatment should focus on alleviating symptoms, halting the disease's progression, and safeguarding future fertility. The recommended approach involves conservative surgery for both diagnosis and initial treatment, followed by suppressive therapy to prevent recurrence.

For managing dysmenorrhea in individuals with endometriosis, non-steroidal anti-inflammatory drugs (NSAIDs) are typically the first line of treatment. Patients with endometriosis tend to have higher levels of prostaglandins and leukotrienes, which can be managed effectively with NSAIDs. While most NSAIDs generally work well for these patients, no specific NSAID is considered superior. They are widely accessible, but it's crucial to ensure proper dosing, as adolescents might take incomplete or infrequent doses, leading to inadequate pain relief.

For optimal results, NSAID treatment should begin one to two days before the onset of menstruation and continue for two to three days into the menstrual period. If one type of NSAID proves ineffective, other options can be tried. However, opioids should be avoided in adolescents due to the risk of developing drug dependence while treating dysmenorrhea.

**Table 1.** Nonsteroidal Antiinflammatory Drugs Used During Menstruation in the Treatment of Primary Dysmenorrhea in Adolescents and Young Adults

mg initially, followed by 400-800 mg every 8 hours as needed
550 mg initially, followed by 220-550 mg every 12 hours as needed
mg initially, followed by 250 mg every 6 hours as needed
mg initially, followed by 200 mg every 12 hours as needed
-

<sup>\*</sup>For females older than 18 years

Reprinted from Harel Z. Dysmenorrhea in adolescents and young adults: an update on pharmacological treatments and management strategies. Expert Opin Pharmacother 2012;13:2157–70.

#### Hormonal agents.

If NSAIDs fail to provide adequate relief from symptoms, hormonal agents can be introduced as part of the treatment strategy. Given that endometriosis is a chronic and progressive disease without a specific cure, continuous hormonal suppression is recommended. Common options include combined oral contraceptives, patches, rings, progestins, Dienogest 2mg injectable progesterone, LNG implants, and intrauterine systems.

Each method has its specific benefits, so it's important to tailor the choice to the patient's individual needs. Hormonal agents work by suppressing the growth of the endometrium or ovulation, leading to reduced production of prostaglandins and leukotrienes. Continuous use tends to offer better early symptom relief compared to cyclical use, although long-term effects are similar. Notably, the continuous use of Norethisterone acetate at 5 mg daily is considered comparable to combined oral contraceptives.

GnRH analogues are potent suppressors of FSH and LH, so they should generally be avoided in patients under 16 to prevent stunted growth. If deemed necessary, they should only be used with add-back therapy to mitigate side effects. Typically, Leuprolide is administered alongside 0.625 mg of ethynyl estradiol and 5 mg of norethisterone for a duration of six months. Routine initial bone scans using Dual X-ray absorptiometry aren't required, although considering one after three months is advisable. During GnRH analogue treatment, it's crucial to ensure the patient maintains adequate Vitamin D and calcium intake, along with engaging in weight-bearing exercises. Continuous suppressive therapy is necessary after discontinuing GnRH analogues.

<sup>†</sup>Cyclooxygenase-2 specific inhibitor

Although CA 125 levels may increase in endometriosis, the American College of Obstetricians and Gynecologists (ACOG) does not recommend its routine monitoring. NSAIDs remain an option for pain relief throughout treatment.

This comprehensive approach, balancing medications and lifestyle changes, can help manage endometriosis effectively, minimizing symptoms and improving quality of life.

#### Complementary and alternative therapy.

For adolescents dealing with discomfort, it's worthwhile to explore alternative methods for relief. Exercise and heat therapy have shown promise in alleviating pain, making them a good option considering their cost-effectiveness and additional health benefits. It's crucial to provide guidance on heat therapy to prevent burn injuries, especially in cases of severe dysmenorrhea.

Regarding supplements, fenugreek, ginger, valerian, zataria, vitamin D, fish oil, and zinc sulfate have been noted for their benefits. Notably, some studies highlight the effectiveness of taking high doses of vitamin D weekly in reducing dysmenorrhea symptoms.

Additional methods like transcutaneous nerve stimulation, acupuncture, yoga, and herbal preparations have also shown promise in some studies for providing relief. Encouraging these practices can offer a holistic approach to managing symptoms and improving overall well-being.

#### Surgical approach for endometriosis in adolescence.

The goal of endometriosis in endometriosis is to, confirm the diagnosis, reduce the bulk of the disease and optimise the fertility outcome. The patient and the family should be aware that there is no cure for endometriosis. Stage I or II endometriosis is more frequently seen than stage III or IV. The preferred treatment is excision of the lesion, fulguration, or remove of the entire cyst. Surgical consent must be obtained from the parent or the guardian in younger than 18 years. The use of Pediatric assent is helpful in the management. Before the surgery, it is necessary to discuss all the available options, possible risks like adhesions, excision, likely injury to ureter, bladder intestine, and even the possibility of suppression of menstruation in the post-operative period.

#### Laparoscopy for endometriosis in adolescence.

Fig 1,Red lesions in the centre the defect in stage two endometriosis

Lesions seen in adolescents differ significantly from those observed in adults. Early lesions in adolescents, such as yellow or red lesions, occur more frequently than the powdered, burned, or white lesions associated with more advanced disease. To better visualize endometriosis, a technique known as the Magnification Technique involves moving the laparoscope closer to the lesions by mere millimeters. Another method, called the Diving In Technique, involves filling the pelvis with water and observing the lesions underwater, which is particularly useful in adolescent cases.

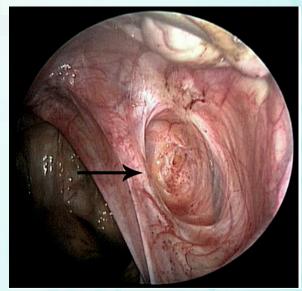


Fig 1,Red lesions in the centre the defect in stage two endometriosis

Suspicious lesions should be excised or ablated; simple drainage is not recommended. The American College of Obstetricians and Gynecologists (ACOG) advises against peritoneal stripping due to the lack of evidence supporting its effectiveness in preventing or alleviating endometriosis-related pain. Concerns exist about potential complications such as adhesions, obstructions, and infertility resulting from peritoneal stripping.

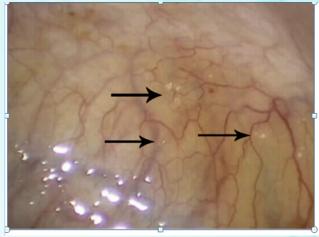


Fig 2: clear vesicular superficial lesions in POD

Fig 2: clear vesicular superficial lesions in PODFig 3: Haemorrhagic, endometriosis, (Single arrow) fibrotic endometriosis (Double arrow)

Adolescents typically present with early-stage endometriosis, though there are instances of advanced disease accompanied by less pain. It is important to note that the location or severity of lesions does not always correlate with the symptoms experienced. Adolescents often experience severe symptoms despite having milder lesions, as these early lesions produce greater amounts of prostaglandins and leukotrienes compared to the healing or fibrotic powder burn lesions common in adults.

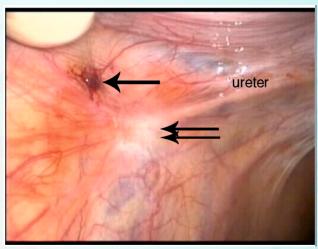


Fig 3: Haemorrhagic, endometriosis, (Single arrow) fibrotic endometriosis (Double

For adolescents whose symptoms are not relieved by oral contraceptives, the levonorgestrel intrauterine system (LNG IUS) can be introduced. This method effectively alleviates endometriosis symptoms and offers long-term relief.

Fig 4: Cortical endometrium

Procedures like presacral neurectomy or uterine nerve ablation have not demonstrated any benefits. Radical surgeries, such as oophorectomy or hysterectomy, should not be considered in adolescents, as the focus should be on preserving fertility and minimizing invasive procedures.

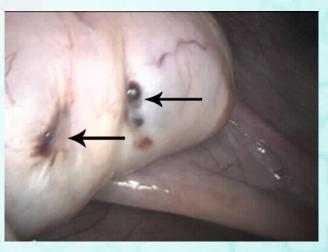


Fig 4: Cortical endometrium

#### Follow up of Endometriosis in adolescence.

It's great that you're emphasizing the importance of follow-up and support for adolescents dealing with endometriosis. Here's a more concise version of your thoughts:

Follow-up care is crucial for adolescents undergoing treatment for endometriosis. This age group often struggles with consistent follow-up and medication adherence due to factors like disorganization, embarrassment, or peer pressure. Studies indicate that adolescents with strong family or peer support tend to have better treatment outcomes.

Symptomatic relief typically requires long-term therapy, so consistent monitoring and adherence to treatment plans are essential. If there's no significant improvement, alternative therapies should be considered. Medication non-adherence can stem from conflicts within the family, and addressing these issues is crucial for successful treatment.

Long-term education and support for both the adolescent and their family are key. Collaborating with pain management teams, or exploring alternative therapies like acupuncture or herbal treatments, can be beneficial. Early diagnosis and continued suppressive treatments are vital for preserving future fertility in adolescents with endometriosis.

This comprehensive approach can significantly alleviate pain and improve the quality of life for these young individuals.

#### Conclusion:

Endometriosis in adolescents is a challenging condition due to its chronic nature and symptom overlap with other conditions. This often leads to delayed diagnosis, especially as adolescents may hesitate to seek help. Early identification and timely intervention are crucial for maintaining their quality of life and ensuring educational opportunities are not disrupted.

A supportive and understanding approach from family members can significantly contribute to effective treatment adherence. It's important for both the adolescent and their family to engage fully with the treatment plan, which should be comprehensive and flexible.

Exploring all treatment options—medical, surgical, and alternative therapies—within a holistic framework ensures that care is personalized and covers all aspects of well-being. This not only addresses physical symptoms but also supports emotional and psychological health, which is vital for young individuals navigating this condition.

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# DECODING DISTINCTIONS- NAVIGATING DEFERENTIAL DIAGNOSIS OF FEMALE REPRODUCTIVE ABNORMALITIES



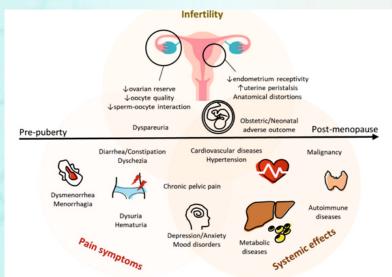
Dr. Sunil Eshwar Lead consultant Aster RV hospital and Aikya fertility and research center

#### Assisted Reproductive Techniques in Endometriosis-Enhancing Fertility & Hope

Endometriosis is an oestrogen-dependent chronic inflammatory fibrotic disease that is characterized by the presence of endometriotic foci outside the uterine cavity. The exact prevalence of endometriosis is unknown, but estimates range from 2% to 10% within the general female population and up to 50% in infertile women (Meuleman et al., 2009; Zondervan et al., 2020).

Endometriosis associated infertility is multifactorial in nature adversely affecting each step of the natural reproductive physiology and thereby processes and outcomes of Assisted Reproductive Technology (ART) cycles. These outcomes are further complicated by the subtype of endometriosis, being peritoneal, deep infiltrating and ovarian, which bear negative effects on ovarian reserve, response to stimulation, accessibility for oocyte retrieval, intraoperative safety and endometrial receptivity.

#### How does endometriosis cause infertility?



The effects of endometriosisassociated infertility are likely to include mechanical, inflammatory, hormonal, genetic and environmental factors. In the pelvic cavity, endometriosis-related inflammation processes amount to causing a toxic pelvic environment susceptible of impairing the chances of natural conception. Oocytes and sperm in the pelvic cavity fluid when meeting in the distal section of the Fallopian tube, are exposed to the toxic effects mediated by the inflammatory processes existing in the pelvic cavity. This is susceptible of altering sperm and oocyte quality as well as sperm-to-oocyte interactions—fertilization.

Consequently, women with endometriomas have reduced ovarian reserve compared to both patients with healthy ovaries and those with other benign ovarian cysts, resulting in lower serum anti-Mullerian Hormone (AMH) levels, and lower antral follicle counts on ultrasound scan (Hamdan, Dunselman et al., <a href="Citation2015">Citation2015</a>). Surgical excision of endometrioma(s) is further associated with a decline in ovarian reserve with up to 38% reduction in AMH after ovarian cystectomy reported (Raffi et al., <a href="Citation2012">Citation2012</a>). The effect of surgery on ovarian decline is greater especially if the pathology is bilateral and after repeat surgery in cases of cyst recurrence (Kwon et al., <a href="Citation2014">Citation2014</a>). The damage inflicted by surgery to the ovarian reserve can occur as healthy ovarian tissue is inadvertently removed during ovarian stripping, as well as through vascular compromise, thermal damage, and local inflammation.

Recent reports indicate that the ART success rates of women with and without endometriomas are similar. Of course, contamination of retrieved oocytes with endometrioma fluid will affect ART outcome. This well-known fact is, however, avoided as much as possible by careful positioning of the aspiration needle.

Endometriosis is known to also affect the uterus itself and disturb endometrial transformations occurring during the luteal phase of natural or stimulated cycles. Globally, this situation stems from inflammatory processes taking place in the eutopic endometrium. The latter causes resistance to the effects of progesterone and results in incomplete decidualization, as studied by Bruce Lessey's team (2) and other investigators. However, recent studies conducted on patients undergoing assisted reproductive technology (ART) cycles consistently demonstrate that oocytes retrieved from patients with endometriosis and endometriomas have a similar potential to be fertilized, develop into blastocysts and yield euploid blastocysts as is seen in various control groups undergoing ART without a diagnosis of endometriosis (Ata and Telek, 2021; Somigliana et al., 2023).

Systematic reviews and meta-analyses concluded that the presence of moderate and severe endometriosis is associated with fewer oocytes retrieved, poorer implantation and lower live birth rates in women undergoing ART (Hamdan, Omar, et al., <u>Citation2015</u>; Harb et al., <u>Citation2013</u>). However, a large analysis of 347,185 fresh and frozen ART cycles from The Society of Assisted Reproductive Technologies (SART) database indicated that women with endometriosis have similar live birth rates to those with other causes of infertility, unless they have a combination of factors for infertility (Senapati et al., <u>Citation2016</u>).

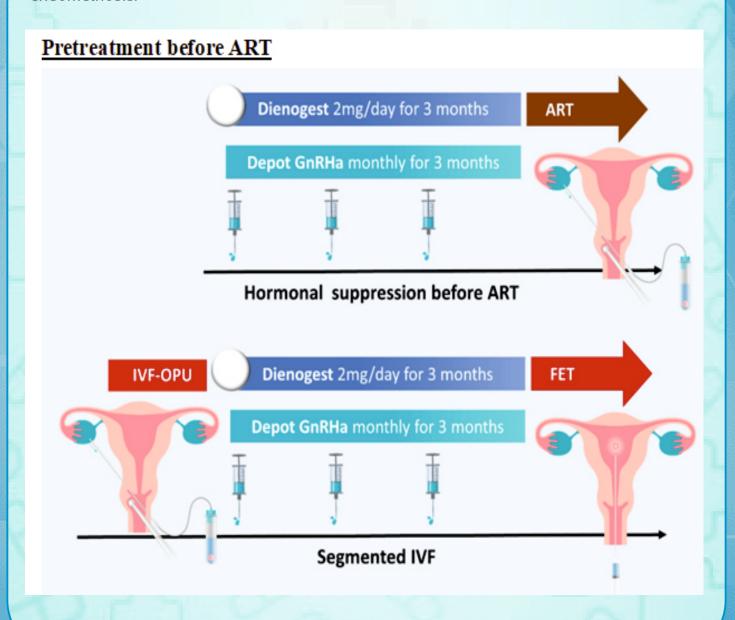
#### **CHALLENGES OF ART WITH ENDOMETRIOSIS**

Numerous publications have reported alterations of the follicular physiology and fluid content in women with endometriosis, with notably increased products of oxidative stress. This has led to suspect possible alterations of oocyte quality in endometriosis (3). In in vivo endometriosis models in mice, oocytes and embryos were found altered and having poorer implantation rates. These findings were used for purporting the mechanism through which endometriosis alters fertility in women, an altered oocyte quality. But contrary to these in vivo findings Bishop et al. (5) observed that euploidy rates were similar in endometriosis and agematched controls in spite of meagre oocytes yields in the former group. In line with these findings of unaltered euploidy rates in endometriosis there are numerous publications reporting similar ART pregnancy rates in age-matched women with or without endometriosis.

The report of similar euploidy rates in women with or without endometriosis leaves open the issue of endometrial receptivity and implantation rates in these women. Bishop et al. (5) report a seminal study documenting implantation rates of frozen euploid blastocyst in women suffering from endometriosis compared with controls affected by male factor infertility or undergoing

preimplantation genetic testing for monogenic/single gene defects. These authors' results show similar implantation rates in women suffering from endometriosis or male factor infertility (controls). The observation is of paramount importance for understanding the proper management of infertile women suffering of endometriosis. The observation of Bishop et al. (5) indicates that endometrial receptivity is normal when the precaution is taken to suppress ovarian function with estradiol ( $E_2$ ) and intramuscular progesterone before embryo transfer. Therefore, the effects of  $E_2$  and intramuscular progesterone treatment are similar to that previously reported after ovarian suppression with the oral contraceptive pill or a gonadotropin-releasing hormone agonist.

The report of normal euploidy rates in women with endometriosis ( $\underline{4}$ ,  $\underline{5}$ ) and now, the unaltered implantation rates of frozen euploid blastocysts ( $\underline{5}$ ) confirm that ART is the treatment of choice for infertility due to endometriosis. Although endometriosis alters natural conception rates—causing infertility—its negative effects—due to a toxic pelvic cavity condition—are bypassed by reverting to ART and deferred blastocyst transfers using  $E_2$  and progesterone preparation cycles. On the contrary, however, treatments based on natural conception, such as r in the free r in the free r in the free r in the r in th



#### Recommendations

- There is insufficient evidence to recommend the use of GnRH agonist therapy or hormonal contraceptives prior to ART to improve live birth rates.
- Suppressive hormonal therapies can be considered after endometriosis surgery to prevent endometriosis associated symptoms and disease recurrence whilst awaiting ART.
- There is insufficient evidence to recommend aromatase inhibitors as pre-treatment prior to ART.
- There is currently no evidence to support the use of GnRH antagonists as pre-treatment prior to ART, but results of ongoing studies will determine further

#### Surgery as an adjuvant/pre-treatment to ART

There is only a single and retrospective cohort study thus far that compared the outcomes in women proceeding with IVF/ICSI who underwent complete surgical excision of disease (n = 399) versus diagnostic laparoscopy only (n = 262) for minimal to mild endometriosis (Opøien et al.,  $\underline{\text{Citation2011}}$ ). This study reported higher implantation, pregnancy, live birth rates, and cumulative pregnancy rates recorded in the group undergoing excision of disease compared to those who just underwent diagnostic laparoscopy, as well as shorter time to first pregnancy (Opøien et al.,  $\underline{\text{Citation2011}}$ ).

#### Recommendations

- Further research is needed to confirm the positive benefits of routine surgery for minimal to mild endometriosis prior to IVF before this can be recommended.
- Further research is needed before surgery prior to IVF for severe endometriosis can be recommended with the sole aim of improving IVF outcomes, given the extent of surgery required and risk of complications to treat severe endometriosis, especially when associated with bowel involvement. Care should be individualised jointly with minimal access surgeons in the multidisciplinary team setting.

## Management of endometriosis during ART Effects of endometriosis on intrauterine insemination Recommendations

- In infertile patients with minimal and mild endometriosis with confirmed tubal patency and normal seminal fluid parameters, IUI with ovarian stimulation using gonadotropins may be performed, especially following surgical management of minimal and mild endometriosis.
- The efficacy of IUI as a treatment option for infertile patients with moderate and severe endometriosis and patent fallopian tubes remains unclear, and if there are additional risk factors, such as advancing maternal age, comparatively IVF appears to have better pregnancy rates.

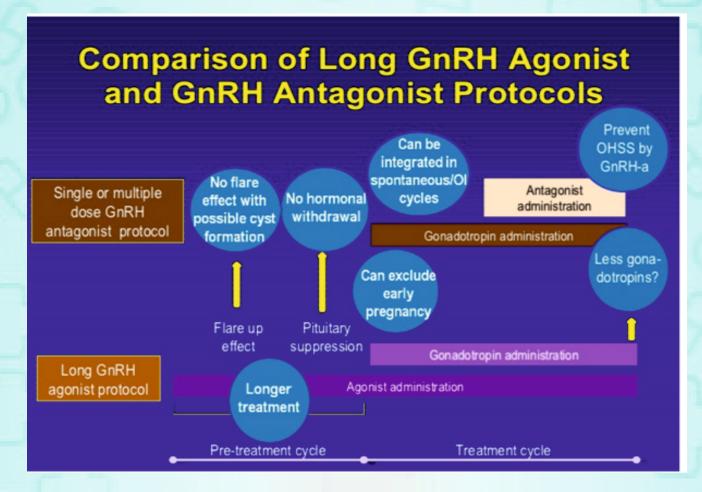
#### Effects of endometrioma on ART

#### Effects of endometrioma on ovarian stimulation

To our knowledge, a publication by Somigliana et al.,  $\underline{\text{Citation2020}}$  is the only study to retrospectively compare the endometrioma sizes of  $20-29\,\text{mm}$  (n = 23),  $30-39\,\text{mm}$  (n = 23) and  $40-49\,\text{mm}$  (n = 21) and ovarian response during controlled ovarian hyperstimulation (Somigliana et al.,  $\underline{\text{Citation2020}}$ ). Women with endometrioma  $40-49\,\text{mm}$  had significantly fewer follicles recruited, and the authors concluded that the threshold to be used to distinguish between endometriomas that could and could not interfere with ovarian response is  $4\,\text{cm}$  in diameter (Somigliana et al.,  $\underline{\text{Citation2020}}$ ). However, there was no difference in the number of oocytes retrieved and the pregnancy rates.

## **Pituitary downregulation protocols during ovarian stimulation**GnRH agonist versus GnRH antagonist protocols

Type of Ovarian stimulation protocol



Several trials and studies evaluated GnRH agonist versus GnRH antagonist ovarian stimulation protocols in women with endometriosis. An RCT including 246 women with stage I/II endometriosis and endometrioma showed that the implantation rate and clinical PR after OS in a GnRH antagonist cycle were not inferior to those for a GnRH agonist protocol (Pabuccu, et al., 2007). An observational retrospective analysis of 1180 cycles with the propensity score matching failed to demonstrate a difference in clinical PR between GnRH agonist and GnRH antagonist protocols in patients with stage IIV endometriosis (Rodriguez-Purata, et al., 2013).

In studies comparing the long GnRH agonist and GnRH antagonist protocols, no difference in ongoing PR was observed between the 2 OS protocols in patients who previously underwent laparoscopic endometrioma resection surgery (Bastu, et al., 2014). Kolanska et al. performed a retrospective analysis of 284 IVF cycles and reported that women with endometriosis experienced higher pregnancy and live birth rates after fresh embryo transfer but not after frozen cycle when long GnRH agonist protocols were compared to GnRH antagonist protocols (Kolanska, et al., 2017). The cumulative live birth rates per cycle were not different between the two groups. Comparison of long GnRH agonist and GnRH antagonist ART protocols was further conducted in an observational retrospective cohort study including 386 women subdivided into two groups (endometriosis stage I/II and endometriosis stage III/IV) (Drakopoulos, et al., 2018). A tendency toward higher biochemical and clinical pregnancy and live birth rates (42.8% vs. 26.7%) was noted in favour of GnRH agonist in patients with stage I/II endometriosis whereas no difference was observed in the endometriosis stage III/IV) group.

Overall, in infertile women, most of the evidence does not demonstrate a negative impact of endometriosis (compared to non-endometriosis patients) on live birth rate after ART, even if the ovarian response and clinical pregnancy rates are lower. Therefore, ART may be effective for endometriosis-associated endometriosis and is recommended (weak recommendation) in women with other infertility factors. The severity of the disease might play a role with stage III-IV endometriosis potentially decreasing the live birth rate. The available evidence failed to demonstrate that a specific ART protocol should be favoured in patients with endometriosis. From a systematic review including moderate quality evidence, ART was not associated with increased endometriosis recurrence rate. A weak recommendation was formulated to inform and/or reassure patients. The use of antibiotic prophylaxis at the time of oocyte retrieval in women with endometriomas seems reasonable and is recommended as a good practice point. There is no evidence on whether IUI or ART is superior in women with endometriosis.

#### Recommendations

- Both GnRH agonist and GnRH antagonist downregulation protocols can be offered in patients with endometriosis undergoing IVF as no difference has been demonstrated in clinical pregnancy and live birth rates.
- There is insufficient data to favour either GnRH agonist or GnRH antagonist protocols in different stages of endometriosis.
- If GnRH agonists are used, a longer protocol may be considered, especially if after surgical management for symptomatic endometriosis, but with caution in those with reduced ovarian reserve.
- There is insufficient evidence to recommend oral progestogens for pituitary suppression during controlled ovarian stimulation in patients with endometriosis.

#### Gonadotrophins

#### Recommendations

- No particular type of gonadotropin is recommended over another for ovarian stimulation in patients with endometriosis. The choice of gonadotropins depends on the clinician's and patient's preferences.
- A higher dose of gonadotropins may be required for ovarian stimulation in patients with stage III-IV endometriosis.
- There is insufficient data to recommend the use of letrozole as an adjunct to gonadotrophins for ovarian stimulation in women with endometriosis.
- There is no evidence for the use of clomiphene citrate in addition to gonadotropins for ovarian stimulation for patients with endometriosis.
- There is no evidence to make recommendations on natural, modified natural cycles or mild stimulation protocols in women with endometriosis undergoing ART.

### Prophylactic antibiotics during oocyte retrieval Recommendations

- There is insufficient evidence to recommend the routine use of prophylactic antibiotics at the time of transvaginal oocyte retrieval in patients with endometriosis, but should be considered in patients with endometrioma.
- There is no evidence to recommend any particular technique for vaginal lavage before performing transvaginal oocyte retrieval.
- Elective aspiration of an ovarian endometrioma is not recommended at the time of transvaginal oocyte retrieval, unless necessary in order to access follicles. If puncture occurs, consider an extended course of antibiotics.
- · Women with endometriosis should be counselled regarding the need to report symptoms suggestive of infection following transvaginal oocyte retrieval.

#### TREATMENT PROTOCOL (8)

#### **ESHRE GUIDELINES 2023 FOR ENDOMETRIOSIS**

Recommendations (49-52)

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.

**600** 

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.

**@000** 

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.

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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.

**GPP** 

#### Outcome of endometriosis on Embryo quality

For women with unilateral endometrioma, pooling of results from the affected ovaries did not show a statistically significantly difference in high-quality embryo rate in comparison to the normal contralateral ovaries.(8)

A study was done which retrospectively analyzed the data from patients with and without endometriosis who underwent oocyte retrieval and/or high-quality embryos transfer between July 2015 and December 2020, including 1312 IVF cycles and 608 IVF or frozenthawed embryo transfer (FET) cycles, respectively. The endometriosis group had a lower percentage of good cleavage-stage embryos and fertilization rates than those in the control group (p = 0.038 and 0.008, respectively). The number of retrieved oocytes, MII oocytes, cleavage, blastocysts, and blastulation rates was comparable between two groups. No significant difference in clinical pregnancy, implantation, live birth, miscarriage, or multiple pregnancy rates between the two groups among patients who transferred high-quality embryos. Stratification analysis showed that patients with stage III-IV endometriosis had fewer retrieved oocytes than those with stage I-II endometriosis (p = 0.012) and marginally fewer retrieved oocytes than the control group (p = 0.051). The stage I-II group had the lowest percentage of good cleavage-stage embryos, which was significantly lower than that of the control group (p = 0.043). In FET cycles, patients with stage III-IV endometriosis had a higher miscarriage rate than those in the control group (p = 0.023). The results suggest that endometriosis does not alter endometrial receptivity but affects embryo quality, oocyte <u>fertilization</u> ability, and ovarian response. (10)

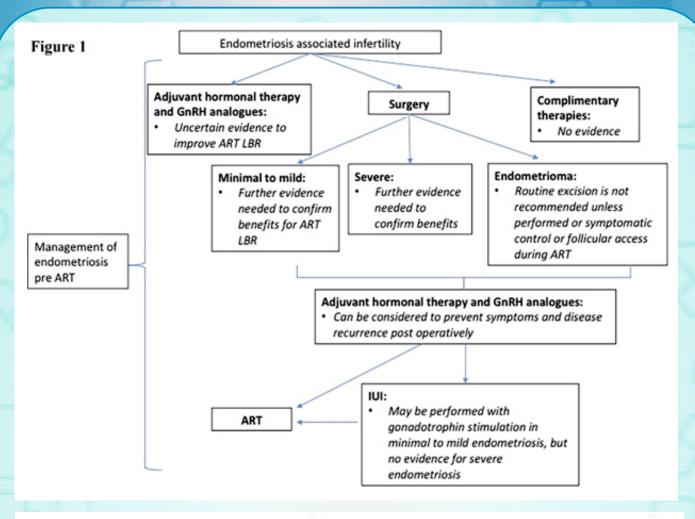


Figure 2

ART

#### Pituitary downregulation:

- Both GnRH analogues can be used;
- Longer GnRH agonist may be considered for symptoms control after surgery but with caution in reduced OR

#### Ovarian stimulation:

No one superiority of gonadotrophin over another

#### Oocyte retrieval:

- Insufficient evidence for routine use of antibiotics but should be considered with endometrioma;
- Elective aspiration of endometrioma at time of oocyte retrieval not recommended

#### Fertilization:

 Insufficient evidence to recommend ICSI over IVF with normal sperm parameters

#### Luteal support:

 Insufficient evidence to recommend any particular luteal support to those with endometriosis compared without endometriosis

#### Frozen embryo transfer:

Insufficient evidence to recommend natural, modified

Management of endometriosis during ART

#### Conclusion

Endometriosis can feel like a heavy burden for those longing to start a family. The pain and frustration often accompany the struggle with fertility can be overwhelming. Many individuals find themselves on an emotional rollercoaster, where hope battles despair. Yet, assisted reproductive techniques (ART) offer a glimmer of hope amid the darkness.

In vitro fertilization (IVF) stands out as a beacon of possibility. This procedure not only circumvents the physical obstacles posed by endometriosis but also allows for tailored approaches, like intracytoplasmic sperm injection (ICSI), to maximize the chances of success. For many, the journey through ART is filled with anticipation and trepidation—each cycle a mix of dreams and heartaches.

Moreover, the emotional toll of navigating this journey cannot be understated. It's vital to seek support, whether through counselling, support groups, or friends who understand the struggle. With compassion and understanding, we can find strength in community.

Though the road may be fraught with challenges, ART can transform despair into hope. Each step taken—whether in the clinic or in one's heart—brings the dream of parenthood a little closer, reminding us that resilience and love can flourish even in the face of adversity.

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Evidence based management of patients with endometriosis undergoing assisted conception: British fertility society policy and practice recommendations

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