TURKISH ENDOMETRIOSIS & ADENOMYOSIS SOCIETY 2009

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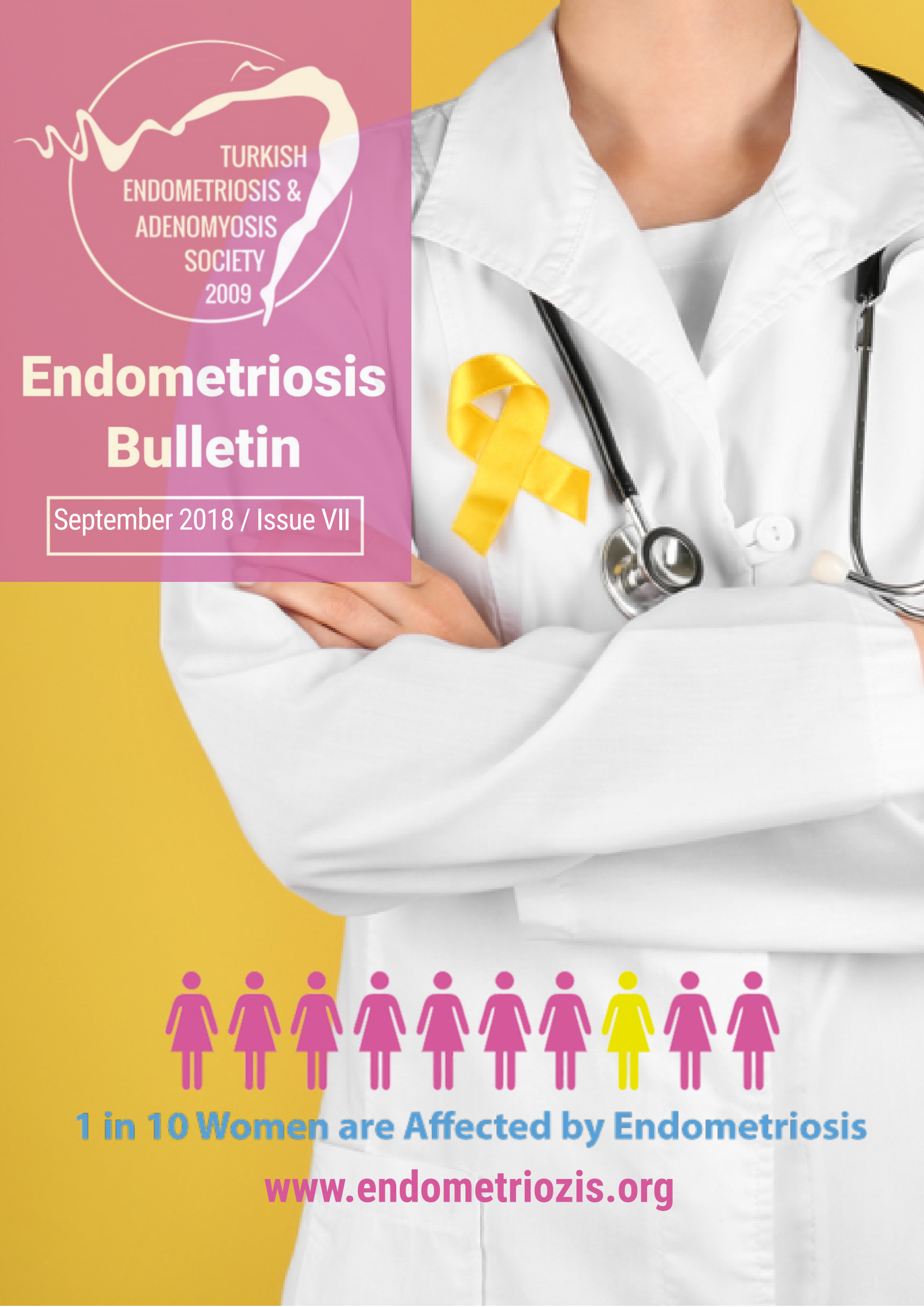

1 in 10 Women are Affected by Endometriosis

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PREFACE

HELLO

Here we are with you again with the 7th issue of our bulletin. We would like to give you a preview of our bulletin and share with you important news from the world of endometriosis.

This year on November 22-24, 2018 we are going to attend the 4th European Endometriosis Congress in Vienna, Austria. Members of our society will participate the congress with oral and poster presentations. We hope to see all our colleagues who are interested in endometriosis in this upcoming congress.

This fall for the first time we are going to initiate Endometriosis School of Turkey project which will take place on December 11-12, 2018 in Istanbul. For two days with national and international participants we are going to discuss endometriosis. Our colleagues will have the opportunity to listen to new subjects on endometriosis and interesting case reports. They will also get a chance to watch live surgery and participate in laparoscopic surgery techniques course in animal laboratory. We will soon share the program online.

In July, 34th ESHRE Annual Meeting took place in Barcelona. Members of our society and young colleagues attended this meeting and acquired new knowledge in the field of endometriosis. First meeting of Endometriosis Guideline Group also took place. It was a very productive and successful meeting.

On August 15th, 2018 Nilufer Rahmioglu joined us in Istanbul to talk about 'Genetics of Endometriosis'. There was a live broadcast of this meeting online on Facebook. We thank Nilufer Rahmioglu for joining us on this day. It was a very informative meeting.

Starting with this bulletin we are going to publish interviews conducted with national or foreign experts on endometriosis. This first interview has taken place online with Ertan Saridogan, PhD. FRCOG. You can read the interview in this bulletin and find the video on our website.

In this bulletin along with the abstracts of chosen international articles we also would like to share with you the abstracts of articles written and published by Turkish researchers in the field of endometriosis.

Hoping to be with you in the next issue with more news and achievements in the field of endometriosis.

Best regards,

Board Members of Endometriosis&Adenomyosis Society

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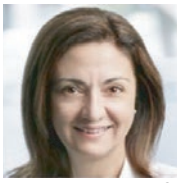

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Endometriosis e-bulletin is prepared by Turkish Endometriosis & Adenomyosis Society. If there are any topics that you would like us to include in the bulletin or any questions that you would like to ask, you can contact us per email via drtanerusta@gmail.com or dr_pinaryalcin@hotmail.com.

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F SOCIAL MEDIA

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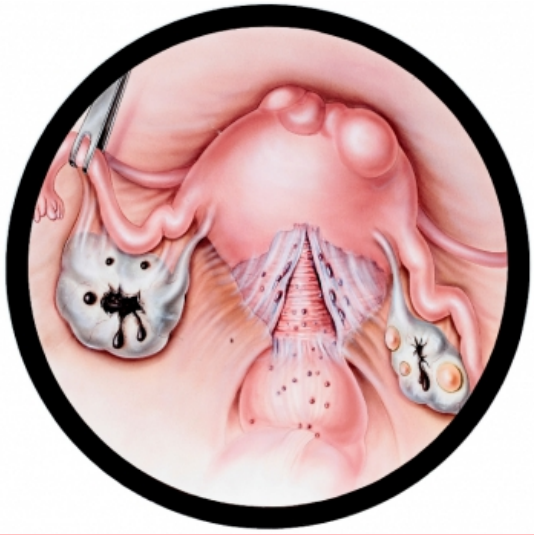
A SELECTED ARTICLES

1 DEEP ENDOMETRIOSIS: A DIAGNOSTIC DILEMMA WITH SIGNIFICANT SURGICAL CONSEQUENCES

Mathew Leonardi, MD; Sukhbir S. Singh, MD; Ally Murji, MD, MPH; Abheha Satkunaratnam, MD; Mostafa Atri, MD, Dipl. Epid; Shannon Reid, MBBS, PhD; George Condous, MBBS(Adel), MD(Lon)

INTRODUCTION

Imagine this common scenario in gynaecology: You have consented a patient for a laparoscopic ovarian cystec- tomy for what appears to be an endometrioma identified on a basic transvaginal ultrasound. Upon inserting the laparoscope, you discover the posterior cul-de-sac is obliterated, with the endometrioma adherent to the pelvic sidewall and rectum **(Figure 1)**.



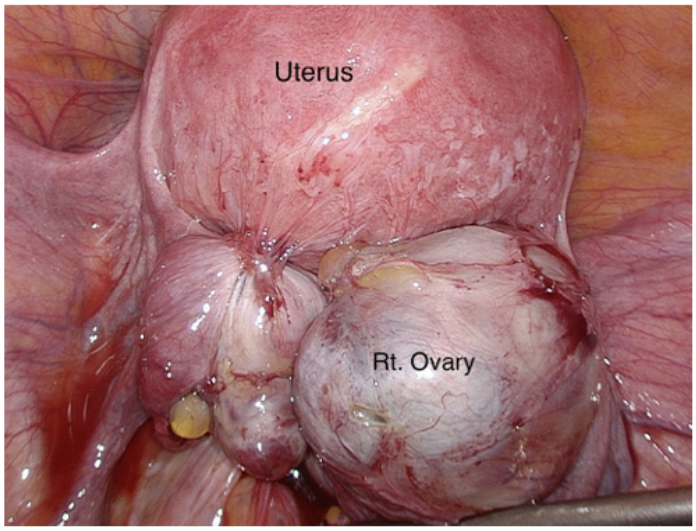
The next step in the described scenario will depend on a number of factors, including the gynaecologist's level of surgical skill, the patient's informed consent, and the availability of surgical support (e.g., minimally invasive general surgeon or urologist). It is possible that in this scenario the objective of a general gynaecologic surgeon should be to perform a comprehensive diagnostic laparoscopy, obtain images of the pelvis and pathology, and subsequently refer the patient to an endometriosis surgeon. Regardless of the surgeon, however, the lack of preoperative data may lead to incomplete surgical resection of disease, a lengthy unplanned operation, and may risk harm to the involved organs.

Care for those with deep endometriosis requires diagnostic and surgical expertise for optimal outcomes. Surgery for DE is not dissimilar to ovarian cancer, where outcomes are superior for patients who are optimally debulked and treated by teams led by gynaecologic oncologists.[1] Patients with DE should ideally be managed by teams led by minimally invasive gynaecologic surgeons with specialized knowledge and training in endometriosis.[2] The difficulty is that disease severity and extent has been traditionally difficult to locate and map preoperatively, creating challenges in matching a patient with the right care team to help facilitate the "ideal" treatment plan.
This commentary highlights current gaps in the diagnosis of DE and proposes new concepts to enhance the care of patients with endometriosis.

THE PROBLEM

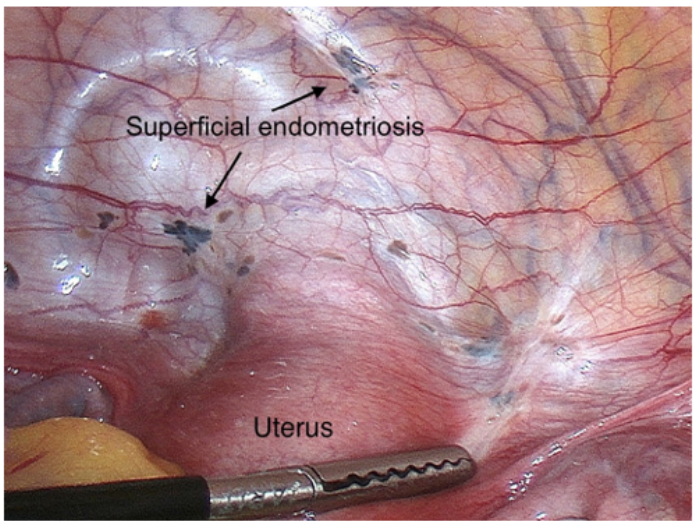
Endometriosis is a common and complex inflammatory condition among women of reproductive age, with a generally accepted prevalence of 10% to 15%.[3] The disease itself encompasses three distinct subtypes: superficial endometriosis **(Figure 2)**, ovarian endometriomas **(Figure 1),** and DE **(Figure 3)**.[3] The contemporary definition of DE is endometrial glands and stroma in fibromuscular tissue (adenomyosis externa), which does not necessarily require a specific depth of measurement.[4,5]

Figure 1. Enlarged and immobile right ovary, containing endometrioma, and completely obliterated cul-de-sac.



Legend: Rt, right

Figure 2. Superficial endometriosis deposits along anterior compartment peritoneum.



The bowel is the most commonly affected nonreproductive organ,[6] with approximately 5% to 10% of patients affected.[7] The prevalence of bowel DE in patients referred to tertiary care centres is significantly higher, estimated between 20% and 25%.[8,9] In the presence of bowel DE, the cul-de-sac is most likely oblitrated. Similarly, when cul-de-sac obliteration is diagnosed, bowel DE is three times more likely to be present.[7,10] The anterior rectum, rectosigmoid junction, and sigmoid colon are the most likely sites of bowel involvement.[11] Unfortunately, this most advanced and morbid subtype of endometriosis has significant negative health impacts on patients, including common issues such as chronic pelvic pain and infertility, but also rare problems such as bowel obstruction and hydronephrosis.

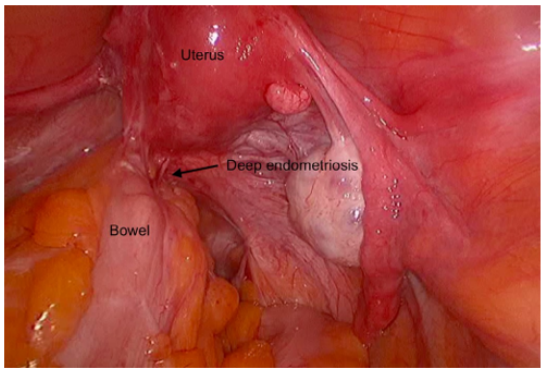
LIMITATIONS OF CURRENT DIAGNOSIS AND MANAGEMENT

The current gold standard method to diagnose pelvic endometriosis is laparoscopy with histopathology.[12,13] However, this approach has limitations,[2] which has led to a surge in interest in developing non-invasive diagnostic methods.[14] With new investigative tools possible, gynaecologists should be questioning whether the rare, though real, surgical risks of a diagnostic laparoscopy are warranted.[15] In addition, not all endometriosis is visible laparoscopically. For example, the rectovaginal septum or the lower (retroperitoneal) anterior rectum are not seen laparoscopically; as such, disease in these locations may be unrecognized. Lastly, laparoscopy may fail to uncover sites and/or the depth of disease, leading to incomplete excision during surgery.

For those who require surgical management, the lack of a thorough preoperative understanding of disease presence and severity may further limit gynaecologists who plan laparoscopic resection of endometriosis procedures. When a gynaecologist encounters unexpected DE or disease severity greater than anticipated, certain issues arise: **(1)** the surgeon's skill does not match the skill level required to adequately and safely address the severity of disease, **(2)** the surgeon's skill level is appropriate but the patient was not consented for all necessary aspects of the procedure to achieve full resection of disease, **(3)** the surgery will take more time than anticipated, affecting subsequent patients (i.e., cancelled surgeries) and the health care team, **(4)** patients experience incomplete surgical management due to unrecognized or masked disease, and **(5)** gynaecologic surgeons have limited support from other surgical specialities that are often required for DE management (e.g., urology, general surgery, thoracic surgery).

Internationally, many centres have recognized the utility and advantages of comprehensive imaging prior to managing patients with endometriosis.[16] Unfortunately, it seems that only a few Canadian sites have adopted an approach to preoperative imaging for the identification and mapping of endometriosis.[17–20] In fact, the most recent Canadian guideline on endometriosis is limited in its comments on preoperative diagnostic imaging, essentially stating that TVS is only useful for the detection of endometriomas.[13] We strongly believe that the current non-invasive ultrasound evaluation for women with suspected endometriosis can be significantly improved.

Figure 3. Partially obliterated cul-de-sac with tethering of bowel adhered to posterior uterus/left uterosacral ligament at site of deep endometriosis lesion of the bowel.



THE PROPOSAL

According to the most recent Cochrane Review, TVS has high specificity for identifying endometriomas and mapping DE of the posterior compartment (i.e., if specificity is high, a positive test rules in pathology; in other words, a highly specific test rarely misclassifies a patient as having disease when none is there).[14] Furthermore, the dynamic nature of TVS allows for accurate assessment of cul-de-sac obliteration using the "sliding sign" technique with high levels of sensitivity and specificity.[21,22] At this time, no evidencebased algorithm exists to decide which patients should undergo conventional basic TVS, which solely evaluates the uterus and ovaries, versus an advanced, expert-guided TVS, which assesses for DE, cul-de-sac obliteration, ovarian mobility, and sitespecific tenderness in addition to the basic TVS components.[23] It may not be appropriate for all patients visiting their primary care provider with dysmenorrhea to undergo an ETVS. However, patients with surgically diagnosed disease, failed medical management, or worsening/progressive symptoms may warrant more comprehensive investigation with the ETVS. Findings on a basic TVS may be predictive of DE. As an example, women who experience severe pain with an endometrioma present have higher rates of DE.[24] Specific symptoms such as dyschezia and dyspareunia should also raise the degree of suspicion for DE.[25] Knowledge of disease prevalence and pretest probabilities in one's patient population will also affect decisionmaking around which ultrasound is most appropriate. **Figure 4** provides a series of findings, during **(1)** clinical history, **(2)** physical examination, **(3)** basic TVS, and **(4)** other investigations, that may be suggestive of severe disease, helping guide clinical practice to more thoroughly investigate with ETVS.[26] A cluster of signs and symptoms found in combination increases the likelihood of DE.[26,27]

An ETVS prior to diagnostic or operative laparoscopy can potentially resolve the many issues just identified. Specifically, a preoperative diagnosis of DE may prevent a diagnostic laparoscopy, saving the patient from repeat surgery, avoiding unnecessary risks, and minimizing the economic footprint on the healthcare system.[2] Instead, if such disease is identified, patients may be triaged to an appropriately trained team with the necessary knowledge and skills to medically manage and/or surgically treat disease. Moreover, these gynaecologic surgeons should have access to appropriate resources, including the assistance of colleagues in other surgical subspecialties (and other supportive services) preoperatively, which allows the patient to be evaluated from different standpoints and to be counselled and consented appropriately.

Figure 4. Features on clinical history, physical examination, imaging, or other investigations that may indicate deep endometriosis.

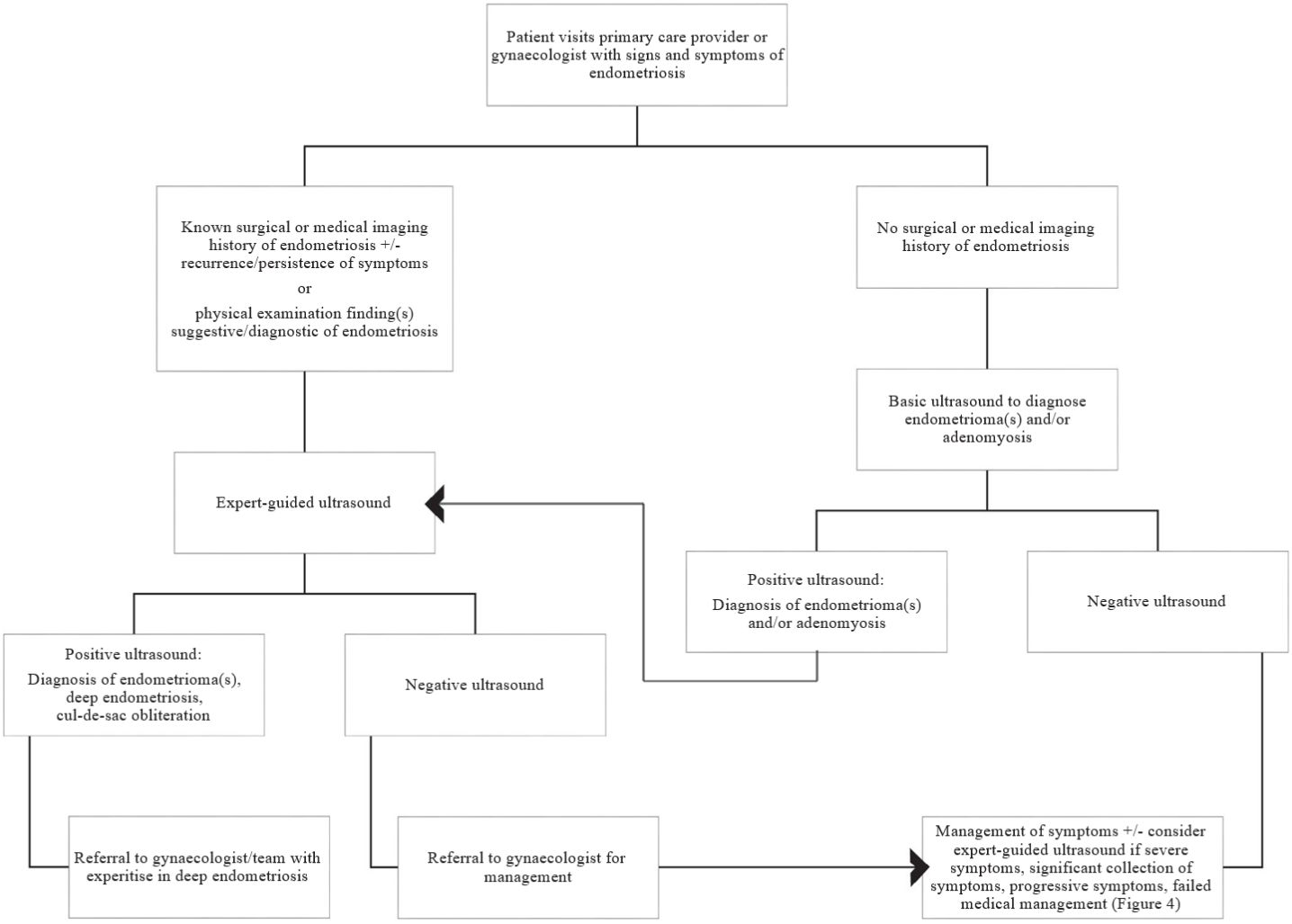
History	Physical Exam	General Imaging	Other Investigations
• dysmenorrhea • deep dyspaurenia • dyschezia • catamenial hematochezia • dysuria • atypical catamenial symptoms • nonmenstrual chronic pelvic pain • infertility	• fixed uterus • mass or tenderness on deep pelvic examination • cul-de-sac nodularity • visual vaginal endometriosis	• endometrioma • adenomyosis • tenderness during TVS	• endometriosis on cystoscopy, colonoscopy, thoracoscopy • previous laparoscopy confirming DE or cul-de-sac obliteration

Legend: TVS – transvaginal ultrasound; DE – deep endometriosis

THE APPLICATION

We propose a stepwise algorithm in the Canadian setting for the diagnosis of endometriosis based on patient history, symptoms, and signs **(Figure 5)**.

Figure 5. Algorithm to guide use of basic and expert-guided ultrasound in the assessment of patients with known or suspected endometriosis.



Essential to the proposed approach is the introduction of ETVS in the care of Canadian patients. The ETVS approach is beyond a simple modification of the basic TVS; it is a highlevel ultrasound performed by experts in endometriosis diagnosis with demonstrated proficiency.[8] Much like an anatomy scan in obstetrics, the utility of an ETVS in identifying patients with DE is contingent on a systematic approach and use of consistent nomenclature[16,23] to facilitate a standardized and accurate communication between imaging specialists and those providing medical and surgical care.

As an example, "rectovaginal" endometriosis is often used to describe complex endometriosis cases that may require surgery. The term "rectovaginal" is vague and encompasses several areas of the posterior compartment, without specifically identifying the site of disease. It may give the surgeon a clue about the location to target treatment, but it remains vague. Ultrasound should distinguish among the posterior vaginal fornix, rectovaginal septum, bowel, and cul-se-sac, all of which can be incorporated in the greater "rectovaginal" area. By localizing disease preoperatively, ultrasound can provide a clear roadmap for the surgeon intraoperatively.
Because this concept of comprehensive diagnostic and/ or preoperative imaging is relatively novel, the present level of knowledge and ability of sonographers, sonologists, radiologists, and gynaecologists will play a large role in initiating and establishing a new model of care. First, key stakeholders should develop an understanding of the steps involved in this type of scan and learn how to perform it accurately.[16,23]
In addition to the direct visualization of disease, dynamic aspects such as the "sliding sign" and assessment of sitespecific tenderness are crucial. Additionally, understanding the current state of ultrasound education in Canada will be important in determining how to integrate new educational objectives to achieve expertise.[28] Ensuring consistent performance and competency with high levels of diagnostic accuracy first requires implementation of a standard educational framework, which can then be maintained. One method to ensure this is to develop close relationships and open communication between the operators and interpreters of TVS and the clinicians managing the patients. This cooperation between the relevant specialists, ideally in an endometriosis multidisciplinary team,[12,29] will be crucial to successfully improving the care of patients with endometriosis. At a higher level, the governing bodies of sonographers, sonologists, radiologists, and obstetrician-gynaecologists should play a role in both advocating for the advancement of ultrasound techniques and the ongoing training and accreditation of these skills.

CONCLUSION

We have proposed an algorithm to address the limitations of the current model of care for patients with endometriosis. This model utilizes the conventional (i.e., basic) TVS technique but adds an expertguided ultrasound approach, which has high levels of diagnostic accuracy in the diagnosis of DE in particular.[14,30] We believe that this modification may significantly improve the care of patients with endometriosis and avoid unexpected surprises in the operating room. We appreciate that introducing a new model of care is challenging due to limitations in education, skill, and resources. In addition, the exact definition of expertise remains unknown in Canada and needs to be clarified. Furthermore, much work remains to be done to standardize anatomic and disease terminology. By enhancing the diagnosis of patients with endometriosis, we may be able to give patients the best chance at optimal management.

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2 ENDOMETRIOSIS CLASSIFICATION ACCORDING TO PAIN SYMPTOMS: CAN THE ASRM CLASSIFICATION BE IMPROVED?

Andres MP, Borrelli GM, Abrão MS. Best Pract Res Clin Obstet Gynaecol. 2018 Aug;51:111-118. doi: 10.1016/j.bpobgyn.2018.06.003. Epub 2018 Jun 15.

Abstract

Endometriosis is a chronic disease that affects 5-15% of women of the reproductive age. Different classifications systems have been proposed to categorize endometriosis. In 1979, the American Fertility Society proposed a new system for the classification of endometriosis to correlate surgical findings of endometriosis with fertility, and this system was revised in 1996 (rASRM).

Despite the fact that the rASRM classification system is widely used and accepted worldwide, it has limitations.

The objectives of this study were to critically assess and discuss the current classification of endometriosis according to pain.

KEYWORDS:
Classification; Endometriosis; Endometriosis fertility index; Enzian classification; rASRM score

3 REVIEWING THE ROLE OF PROGESTERONE THERAPY IN ENDOMETRIOSIS.

Abdul Karim AK, Shafiee MN, Abd Aziz NH, Omar MH, Abdul Ghani NA, Lim PS, Md Zin RR, Mokhtar N. Gynecol Endocrinol. 2018 Jul 25:1-7. doi:10.1080/09513590.2018.1490404.

Abstract

Endometriosis is a benign, chronic inflammatory condition characterized by the presence and growth of endometrial implants outside the uterine cavity.

The cause of endometriosis is multifactorial. It is due to the diversity of hypothesis and plausibility of hormonal alterations which could play a major role. Evidence has shown that progesterone resistance is a key factor for endometriosis sufferers.

Medical therapy can avoid surgical intervention, which may lead to a reduced in ovarian reserve, and its effects of earlier menopause and reduced fecundity. Progesterone receptor isoform has provided new insight as the potential treatment.

Progestin, anti-progestin and selective progesterone receptor modulators usage, which target these receptors, could avoid hypo-estrogenic side effects, which can be debilitating.

Numerous types of these medications have been used on and off labeled to treat endometriosis with varying success. This review aims to consolidate series of clinical trials using progestins in endometriosis.

4 ENDOMETRIOSIS.

Zondervan KT, Becker CM, Koga K, Missmer SA, Taylor RN, Viganò P Nat Rev Dis Primers. 2018 Jul 19;4(1):9. doi: 10.1038/s41572-018-0008-5

Abstract

Endometriosis is a common inflammatory disease characterized by the presence of tissue outside the uterus that resembles endometrium, mainly on pelvic organs and tissues. It affects ~5-10% of women in their reproductive years - translating to 176 million women worldwide - and is associated with pelvic pain and infertility.

Diagnosis is reliably established only through surgical visualization with histological verification, although ovarian endometrioma and deep nodular forms of disease can be detected through ultrasonography and MRI. Retrograde menstruation is regarded as an important origin of the endometrial deposits, but other factors are involved, including a favourable endocrine and metabolic environment, epithelial-mesenchymal transition and altered immunity and inflammatory responses in genetically susceptible women.

Current treatments are dictated by the primary indication (infertility or pelvic pain) and are limited to surgery and hormonal treatments and analgesics with many adverse effects that rarely provide long-term relief. Endometriosis substantially affects the quality of life of women and their families and imposes costs on society similar to those of other chronic conditions such as type 2 diabetes mellitus, Crohn's disease and rheumatoid arthritis.

Future research must focus on understanding the pathogenesis, identifying disease subtypes, developing non-invasive diagnostic methods and targeting non-hormonal treatments that are acceptable to women who wish to conceive.

5 MRI VERSUS LAPAROSCOPY TO DIAGNOSE THE MAIN CAUSES OF CHRONIC PELVIC PAIN IN WOMEN: A TEST-ACCURACY STUDY AND ECONOMIC EVALUATION.

Khan KS, Tryposkiadis K, Tirlapur SA, Middleton LJ, Sutton AJ, Priest L, Ball E, Balogun M, Sahdev A, Roberts T, Birch J, Daniels JP, Deeks JJ. Health Technol Assess. 2018 Jul;22(40):1-92. doi: 10.3310/hta22400

Abstract

BACKGROUND: Chronic pelvic pain (CPP) symptoms in women are variable and non-specific; establishing a differential diagnosis can be hard. A diagnostic laparoscopy is often performed, although a prior magnetic resonance imaging (MRI) scan may beneficial.

OBJECTIVES: To estimate the accuracy and added value of MRI in making diagnoses of idiopathic CPP and the main gynaecological causes of CPP. To quantify the impact MRI can have on decision-making with respect to triaging for therapeutic laparoscopy and to conduct an economic evaluation.

DESIGN: Comparative test-accuracy study with cost-effectiveness modelling.

SETTING: Twenty-six UK-based hospitals.

PARTICIPANTS: A total of 291 women with CPP.

METHODS: Pre-index information concerning the patient's medical history, previous pelvic examinations and ultrasound scans was collected. Women reported symptoms and quality of life at baseline and 6 months. MRI scans and diagnostic laparoscopy (undertaken and interpreted blind to each other) were the index tests. For each potential cause of CPP, gynaecologists indicated their level of certainty that the condition was causing the pelvic pain. The analysis considered both diagnostic laparoscopy as a reference standard for observing structural gynaecological causes and consensus from a two-stage expert independent panel for ascertaining the cause of CPP. The stage 1 consensus was based on pre-index, laparoscopy and follow-up data; for stage 2, the MRI scan report was also provided. The primary analysis involved calculations of sensitivity and specificity for the presence or absence of each structural gynaecological cause of pain. A decision-analytic model was developed, with a 6-month time horizon. Two strategies, laparoscopy or MRI, were considered and populated with study data.

RESULTS: Using reference standards of laparoscopic and expert panel diagnoses, MRI scans had high specificity but poor sensitivity for observing deep-infiltrating endometriosis, endometrioma, adhesions and ovarian cysts. MRI scans correctly identified 56% [95% confidence interval (CI) 48% to 64%] of women judged to have idiopathic CPP, but missed 46% (95% CI 37% to 55%) of those considered to have a gynaecological structural cause of CPP. MRI added significant value, over and above the pre-index information, in identifying deep-infiltrating endometriosis ($p = 0.006$) and endometrioma ($p = 0.02$) as the cause of pain, but not for other gynaecological structural causes or for identifying idiopathic CPP ($p = 0.08$). Laparoscopy was significantly more accurate than MRI in diagnosing idiopathic CPP ($p < 0.0001$), superficial peritoneal endometriosis ($p < 0.0001$), deep-infiltrating endometriosis ($p < 0.0001$) and endometrioma of the ovary ($p = 0.02$) as the cause of pelvic pain. The accuracy of laparoscopy appeared to be able to rule in these diagnoses. Using MRI to identify women who require therapeutic laparoscopy would lead to 369 women in a cohort of 1000 receiving laparoscopy unnecessarily, and 136 women who required laparoscopy not receiving it. The economic analysis highlighted the importance of the time horizon, the prevalence of CPP and the cut-off values to inform the sensitivity and specificity of MRI and laparoscopy on the model results. MRI was not found to be a cost-effective diagnostic approach in any scenario.

CONCLUSIONS: MRI was dominated by laparoscopy in differential diagnosis of women presenting to gynaecology clinics with CPP. It did not add value to information already gained from history, examination and ultrasound about idiopathic CPP and various gynaecological conditions.

6 ABERRANT EXPRESSION OF GENES ASSOCIATED WITH STEMNESS AND CANCER IN ENDOMETRIA AND ENDOMETRIOMA IN A SUBSET OF WOMEN WITH ENDOMETRIOSIS.

Ponandai-Srinivasan S, Andersson KL, Nister M, Saare M, Hassan HA, Varghese SJ, Peters M, Salumets A, Gemzell-Danielsson K, Lalitkumar PGL. Hum Reprod. 2018 Oct 1;33(10):1924-1938. doi: 10.1093/humrep/dey241.

Abstract

STUDY QUESTION: Is there molecular evidence for a link between endometriosis and endometriosis-associated ovarian cancers (EAOC)?

STUDY ANSWER: We identified aberrant gene expression signatures associated with malignant transformation in a small subgroup of women with ovarian endometriosis

MAIN RESULTS AND THE ROLE OF CHANCE: Isolated and expanded SC+ from both control and patient groups showed significantly higher surface expression of W5C5+, clonal expansion and 3D-spheroid formation capacity ($P < 0.05$) compared with SC-. The SC+ cells also undergo mesenchymal lineage differentiation, unlike SC-. Gene expression from paired-endometriosis samples showed significant downregulation of PTEN, ARID1A and TNFα ($P < 0.05$) in endometrioma compared with paired-endometrium SC+ samples. Hierarchical and multivariate clustering from both SC+ and tissue cohorts together identified 4 out of 30 endometrioma samples with aberrant expression of stem cell and cancer-associated genes, such as KIT, HIF2α and E-cadherin, altered expression ratio of ER-β/ER-α and downregulation of tumour suppressor genes (PTEN and ARID1A). Thus, we speculate that above changes may be potentially relevant to the development of EAOC.

WHAT IS KNOWN ALREADY: Epidemiological studies have shown an increased risk of EAOC in women with ovarian endometriosis. However, the cellular and molecular changes leading to EAOC are largely unexplored.

STUDY DESIGN, SIZE, DURATION: CD73+CD90+CD105+ multipotent stem cells/progenitors (SC cohort) were isolated from endometrium (n = 18) and endometrioma (n = 11) of endometriosis patients as well as from the endometrium of healthy women (n = 14). Extensive phenotypic and functional analyses were performed in vitro on expanded multipotent stem cells/progenitors to confirm their altered characteristics. Aberrant gene signatures were also validated in paired-endometrium and -endometrioma tissue samples from another cohort (Tissue cohort, n = 19) of endometriosis patients.

PARTICIPANTS/MATERIALS, SETTINGS, METHODS: Paired-endometrial and -endometriotic biopsies were obtained from women with endometriosis (ASRM stage III-IV) undergoing laparoscopic surgery. Control endometria were obtained from healthy volunteers. Isolated CD73+CD90+CD105+ SC were evaluated for the presence of known endometrial surface markers, colony forming efficiency, multi-lineage differentiation, cell cycle distribution and 3D-spheroid formation capacity. Targeted RT-PCR arrays, along with hierarchical and multivariate clustering tools, were used to determine both intergroup and intragroup gene expression variability for stem cell and cancer-associated markers, in both SC+ and tissue cohorts.

MAIN RESULTS AND THE ROLE OF CHANCE: Isolated and expanded SC+ from both control and patient groups showed significantly higher surface expression of W5C5+, clonal expansion and 3D-spheroid formation capacity ($P < 0.05$) compared with SC-. The SC+ cells also undergo mesenchymal lineage differentiation, unlike SC-. Gene expression from paired-endometriosis samples showed significant downregulation of PTEN, ARID1A and TNFα ($P < 0.05$) in endometrioma compared with paired-endometrium SC+ samples. Hierarchical and multivariate clustering from both SC+ and tissue cohorts together identified 4 out of 30 endometrioma samples with aberrant expression of stem cell and cancer-associated genes, such as KIT, HIF2α and E-cadherin, altered expression ratio of ER-β/ER-α and downregulation of tumour suppressor genes (PTEN and ARID1A). Thus, we speculate that above changes may be potentially relevant to the development of EAOC.

LIMITATIONS, REASON FOR CAUTION: As the reported frequency of EAOC is very low, we did not have access to those samples in our study. Moreover, by adopting a targeted gene array approach, we might have missed several other potentially-relevant genes associated with EAOC pathogenesis. The above panel of markers should be further validated in archived tissue samples from women with endometriosis who later in life developed EAOC.

WIDER IMPLICATIONS OF THE FINDINGS: Knowledge gained from this study, with further confirmation on EAOC cases, may help in developing screening methods to identify women with increased risk of EAOC.

7 EARLY LIFE ABUSE AND RISK OF ENDOMETRIOSIS.

Harris HR, Wieser F, Vitonis AF, Rich-Edwards J, Boynton-Jarrett R, Bertone-Johnson ER, Missmer SA. Hum Reprod. 2018 Sep 1;33(9):1657-1668. doi: 10.1093/humrep/dey248.

Abstract

STUDY QUESTION: Is there an association between physical and sexual abuse occurring in childhood or adolescence and risk of laparoscopically-confirmed endometriosis?

SUMMARY ANSWER: Early life sexual and physical abuse was associated with an increased risk of endometriosis.

WHAT IS KNOWN ALREADY: Previous studies have reported that physical and sexual abuse are associated with chronic pelvic pain (CPP). However, only one study has examined the association between childhood physical abuse and laparoscopically-confirmed endometriosis, and did not observe an association with endometriosis risk.

STUDY DESIGN, SIZE, DURATION: Prospective cohort study using data collected from 60 595 premenopausal women from 1989 to 2013 as part of the Nurses' Health Study II cohort.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Participants completed an exposure to violence victimization questionnaire in 2001. Cases were restricted to laparoscopically-confirmed endometriosis. Cox proportional hazards models were used to calculate rate ratios (RR) and 95% confidence intervals (CI).

MAIN RESULTS AND THE ROLE OF CHANCE: Three thousand three hundred and ninety-four cases of laparoscopically-confirmed endometriosis were diagnosed during 24 years of follow-up. Compared to those reporting no physical or sexual abuse, the risk of endometriosis was greater among those who experienced severe physical abuse (RR = 1.20; 95% CI = 1.06, 1.37) or severe sexual abuse (RR = 1.49; 95% CI = 1.24, 1.79). There was a 79% increased risk of laparoscopically-confirmed endometriosis for women reporting severe-chronic abuse of multiple types (95% CI = 1.44, 2.22). The associations between abuse and endometriosis were stronger among women presenting without infertility, a group that was more likely to have been symptomatic with respect to pain.

LIMITATIONS, REASONS FOR CAUTION: The violence exposure was recalled by the study participants and thus is subject to misclassification as well as recall bias for the cases who were diagnosed prior to 2001. However, our results were similar in a sensitivity analysis including only endometriosis cases incident after their violence history report. In addition, residual or unmeasured confounding is a possibility; however, we were able to adjust for a variety of potential early life confounders. Finally, selection bias is also a possibility if those who chose to return the violence questionnaire did so based jointly on abuse history and endometriosis risk.

WIDER IMPLICATIONS OF THE FINDINGS: Early life sexual and physical abuse was associated with an increased risk of endometriosis. Severity, chronicity and accumulation of types of abuse were associated with greater risk. Understanding the mechanisms underlying these relations may better define the biologic impacts of abuse and the related pathophysiology of endometriosis.

8 EFFECTIVENESS OF AN ANTIOXIDANT PREPARATION WITH N-ACETYL CYSTEINE, ALPHA LIPOIC ACID AND BROMELAIN IN THE TREATMENT OF ENDOMETRIOSIS-ASSOCIATED PELVIC PAIN: LEAP STUDY.

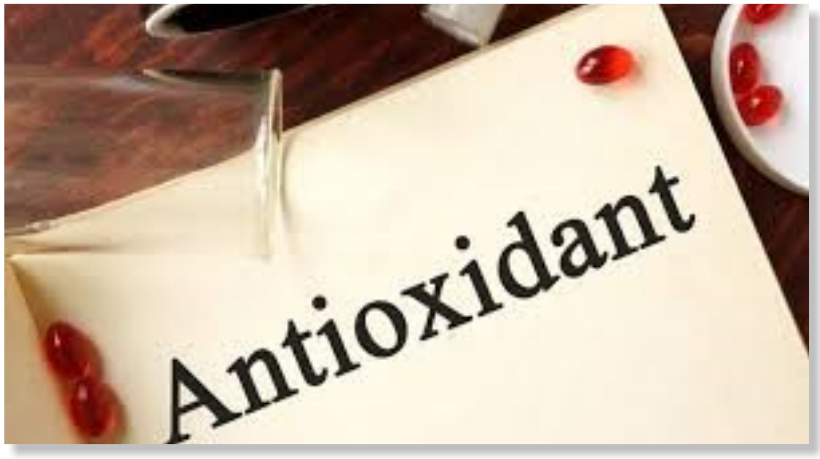
Lete I, Mendoza N, de la Viuda E, Carmona F. Eur J Obstet Gynecol Reprod Biol. 2018 Sep;228:221-224. doi: 10.1016/j.ejogrb.2018.07.002. Epub 2018 Jul 6.

Abstract

OBJECTIVE: To assess the impact of an antioxidant preparation with N-acetyl cysteine, alpha lipoic acid and bromelain on endometriosis-associated pelvic pain.

STUDY DESIGN: Multicenter, open-label, non-comparative clinical trial in a representative sample of women with endometriosis-associated pelvic pain.

RESULTS: In total, 398 patients with a mean age of 34.6±7.2 years were treated with a combination of N-acetyl cysteine, alpha lipoic acid and bromelain for 6 months. At baseline, 92.7% of the patients had pain intensity > 4 on the visual analogue scale (VAS); at 3 months of treatment, this percentage decreased to 87.2% (p=0.074) and at 6 months the percentage was 82.7% (p<0.05).



CONCLUSIONS: Women with endometriosis who wish to become pregnant and are treated with a preparation containing N-acetyl cysteine, alpha lipoic acid and bromelain experienced a significant improvement in endometriosis-associated pelvic pain and required lower intake of rescue analgesics.

9 HIGH POSTOPERATIVE FERTILITY RATE FOLLOWING SURGICAL MANAGEMENT OF COLORECTAL ENDOMETRIOSIS.

Roman H, Chanavaz-Lacheray I, Ballester M, Bendifallah S, Touleimat S, Tuech JJ, Farella M, Merlot B Hum Reprod. 2018 Sep 1;33(9):1669-1676. doi: 10.1093/humrep/dey146.

Abstract

STUDY QUESTION: What are fertility outcomes in patients surgically managed for large deep endometriosis infiltrating the rectum who intend to get pregnant postoperatively?

SUMMARY ANSWER: Surgical management for rectal endometriosis is followed by high pregnancy rates, with a majority of natural conceptions.

WHAT IS KNOWN ALREADY: Optimal management such as surgery versus first-line ART for patients with severe deep endometriosis who desire pregnancy is not defined.

STUDY DESIGN, SIZE, DURATION: The study included the patients enrolled in ENDORE randomized trial who attempted pregnancy after the surgery. From March 2011 to August 2013, we performed a two-arm randomized trial, enrolling 60 patients with deep endometriosis infiltrating the rectum up to 15 cm from the anus, measuring more than 20 mm in length, involving at least the muscular layer in depth, and up to 50% of rectal circumference. Postoperative follow-up was prolonged in 55 patients recruited at Rouen University Hospital, and varied from 50 to 79 months. No women were lost to follow-up.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Patients had either conservative surgery by shaving or disc excision, or radical rectal surgery by segmental resection. One gynecologist experienced in deep endometriosis surgery performed all the procedures, assisted when required by three general surgeons experienced in colorectal surgery. Institutional review board approval was obtained to extend

postoperative follow-up to 10 years after the surgery. Among patients enrolled at Rouen University Hospital, women who intended to get pregnant after surgery were selected and followed up postoperatively every 6 months for 2 years, then every year. Pregnancy intention, fertility outcomes, conception mode, endometriosis recurrences and digestive and urinary outcomes were rigorously recorded. The primary outcome was postoperative pregnancy rate. Secondary outcomes were conception mode, the delay to conception from the day of surgery and the day when hormonal treatment was stopped, and delivery rate. Kaplan Meier curves were used to estimate the probability of conception after surgery.

MAIN RESULTS AND THE ROLE OF CHANCE: Among the 55 patients enrolled at Rouen University Hospital, 25 had conservative and 30 had radical surgery, and their postoperative follow-up varied from 50 to 79 months. No patient was lost to follow-up. Among the 55 patients, 36 intended to get pregnant after surgery, 23 of whom had unsuccessfully attempted to conceive for more than 12 months before surgery (63%). At the end of follow-up, 29 patients achieved pregnancy (81%), and natural conception was recorded in 17 of them (59% of conceptions). As several women had more than 1 pregnancy (range: 0-3), we recorded 37 pregnancies, 24 natural conceptions (65%) and 29 deliveries (78%). The probabilities of achieving pregnancy at 12, 24, 36 and 48 months postoperatively were 33.4% (95% CI: 20.6-51.3%), 60.6% (44.8-76.8%), 77% (61.5-89.6%) and 86.8% (72.8-95.8%), respectively. Women who had been advised to attempt natural conception achieved pregnancy significantly earlier than patients referred for ART (P = 0.008). In infertile patients, the postoperative pregnancy rate was 74%, and 53% of conceptions were natural.

LIMITATIONS, REASONS FOR CAUTION: The main outcomes of the original trial were related to digestive function and not to fertility. Several factors impacting fertility could not be revealed due to small sample size. The study included a high percentage of young women with an overall satisfactory prognosis for fertility, as patients' median age was 28 years. The inclusion of only large infiltrations of the rectum does not allow the extrapolation of conclusions to small nodules of <2 cm in length. Only one skilled gynecologic surgeon performed all the procedures.

WIDER IMPLICATIONS OF THE FINDINGS: First-line surgery can be considered in patients with deep endometriosis infiltrating the rectum and pregnancy intention. Patients receiving advice from experienced surgeons on conception modes were more likely to conceive faster after surgery.

STUDY FUNDING/COMPETING INTEREST(S): This work was supported by a grant from the clinical research program for hospitals (PHRC) in France. The authors declare no competing interests related to this study.

10 ELAGOLIX, AN ORAL GNRH ANTAGONIST, VERSUS SUBCUTANEOUS DEPOT MEDROXYPROGESTERONE ACETATE FOR THE TREATMENT OF ENDOMETRIOSIS: EFFECTS ON BONE MINERAL DENSITY.

Carr B, Dmowski WP, O'Brien C, Jiang P, Burke J, Jimenez R, Garner E, Chwalisz K. Reprod Sci. 2014 Nov;21(11):1341-51. doi: 10.1177/1933719114549848. Epub 2014 Sep 23.

Abstract

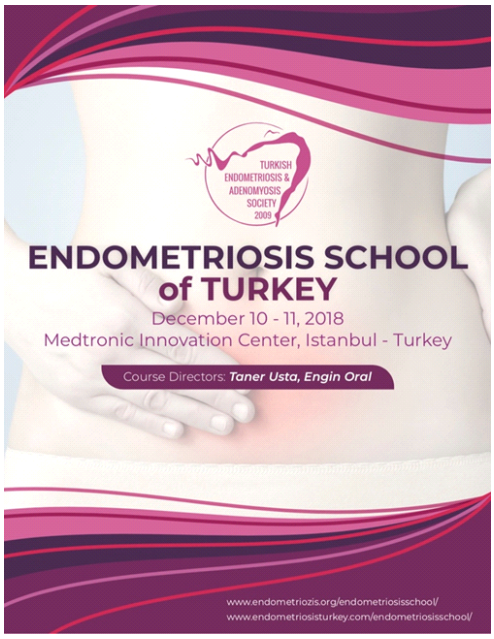
This randomized double-blind study, with 24-week treatment and 24-week posttreatment periods, evaluated the effects of elagolix (150 mg every day, 75 mg twice a day) versus subcutaneous depot medroxyprogesterone acetate (DMPA-SC) on bone mineral density (BMD), in women with endometriosis-associated pain (n = 252). All treatments induced minimal mean changes from baseline in BMD at week 24 (elagolix 150 mg: -0.11%/-0.47%, elagolix 75 mg: -1.29%/-1.2%, and DMPA-SC: 0.99%/-1.29% in the spine and total hip, respectively), with similar or less changes at week 48 (posttreatment). Elagolix was associated with improvements in endometriosis-associated pain, assessed with composite pelvic signs and symptoms score (CPSSS) and visual analogue scale, including statistical noninferiority to DMPA-SC in dysmenorrhea and nonmenstrual pelvic pain components of the CPSSS. The most common adverse events (AEs) in elagolix groups were headache, nausea, and nasopharyngitis, whereas the most common AEs in the DMPA-SC group were headache, nausea, upper respiratory tract infection, and mood swings. This study showed that similar to DMPA-SC, elagolix treatment had minimal impact on BMD over a 24-week period and demonstrated similar efficacy on endometriosis-associated pain.

B NEWS FROM OUR SOCIETY

PLANNED ACTIVITIES

New Project
ENDOMETRIOSIS SCHOOL OF TURKEY

This year for the first time we are going to initiate Endometriosis School of Turkey project which will take place on December 11-12, 2018 in Istanbul. For two days with national and international participants we are going to discuss endometriosis. Our colleagues will get a chance to listen to new subjects on endometriosis and interesting case reports. In addition to the lectures they will also get a chance to watch live surgery and participate in laparoscopic surgery techniques course in animal laboratory. We will soon share the program online.



PAST ACTIVITIES

34TH ESHRE ANNUAL MEETING

On July 1-4, 2018 34th congress of European Society of Human Reproduction and Embryology took place in Barcelona, Spain. Endometriosis was one of the main subjects of discussion. Members of our society who are also a member of the 'ESHRE Endometriosis Guideline Group' joined the congress and attended their first meeting. They also had a chance to discuss with foreign colleagues new updates in the field of endometriosis.

MEETING WITH NILUFER RAHMIOGLU

Genetics of Endometriosis, Where Do We Stand?

On August 15, 2018 we held a meeting and invited Nilufer Rahmioglu, PhD. who has been working for many years at the Wellcome Center for Human Genetics at Oxford University and doing research in the field of endometriosis.

Although there is a variation among different studies endometriosis is seen in 5-10% of women in reproductive age. This number correlates with almost 176 million women worldwide. The time it takes to diagnose endometriosis from the onset of symptoms is approximately 7 years. In addition to this delay invasive procedures are needed for final diagnosis. Thus, finding a noninvasive diagnosis technique is important. As in most of the chronic diseases annual cost of endometriosis is also very high. According to European studies annual cost of a patient with diabetes mellitus or rheumatoid arthritis is approximately 3,000-4,000 Euro per patient. Whereas, this number is almost 9,500 Euro for endometriosis patients due to loss of workforce, medical costs and paid absences from work.

According to American Society of Reproductive Medicine (ASRM)'s guideline written in 1996 endometriosis is classified in four stages. These four stages are further divided in two as stage 3-4 severe and stage 1-2 less endometriosis lesions. Although there is a little correlation between infertility and stage no correlation has been observed between severity of pain and infertility.

Similar to cancer or autoimmune diseases endometriosis is also a complex disease which is affected by many genetic and environmental factors. A study conducted on twins by Treloar et al. in 1999 showed a 51% genetic heritability in endometriosis patients. This genetic heritability consists of factors such as gene mutations, single nucleotide polymorphism or potential modifications.

When studying the underlying genetic mechanism of a disease the starting point should be DNA and variations in DNA sequence (gene variations in a population should always be compared with that population's gene pool). Then the effects of these variations could be analyzed in RNA and protein expression. DNA polymorphisms are variations in a populations DNA sequence which is observed in more than 1% of the population. Mutations are rare variations which are observed in less than 1% of the population. There are many variabilities that affect DNA sequence. One of these variabilities are SNPs (single nucleotide polymorphisms). SNPs are changes in base pairs which can be found in protein coding or noncoding regions of DNA. SNPs which are localized at the protein coding regions can affect gene regulation and thus can alter the phenotype or the function of the gene. Another variability affecting DNA sequence is VNTR (variable number tandem repeats). These are mini/micro satellite base pair repeat variations of different length varying between individuals. Research using VNTR is suitable for diseases with mendelian heritability in family-based studies. In familial endometriosis linkage-based studies can be designed using VNTR. Repeating insertions/deletions and duplications, which are also called copy number, are structure variations affecting DNA sequences. Genes can have different functions depending on the tissue. Furthermore, they can be active or inactive depending on the cell or the surrounding tissue. Thus, RNA studies should be conducted on disease causing tissues or cells. For endometriosis this tissue is eutopic or ectopic endometrium. When a DNA variant is identified it has to be further analyzed on RNA and protein level to assess its functional role in disease mechanism.

Endometriosis research so far has not yet been able to identify a mutation, variation or marker which helps in the identification of deep infiltrative endometriosis, severity of the disease unilateral or bilateral localization or the risk of infertility. Risk described by each SNP is

very low. Thus, one SNP does not count as a risk factor to describe the cause of the disease.

Currently a detailed phenotypic description and classification of endometriosis leads researchers to genotype and map this disease. Since the beginning of 2000 new developments in genotyping techniques and a decline in costs has enabled researchers to design studies with big patient populations.

Each population's ethnic and phenotypic features are described by its genetic background. For this reason, a study designed to find genetic variations in a population should take that population's genetic map as a reference point. This enables the elimination of ethnic or population wide variations and thus enables the identification of the disease related variations.

Sequencing allows mapping of the whole genome base pair by base pair. Whereas, with genotyping reference genome of the population is used to map all the variations with more than 1% frequencies including SNPs. In GWAS studies differences in variation frequencies are identified thus all variations with a frequency of more than 1% are mapped.

In candidate gene association studies, a single gene is chosen and all gene specific mutations and variations are genotyped. The problem with this type of study is that in populations where the ethnic variations are unknown it is impossible to distinguish between disease related mutations and population-based variations. Sometimes the presence of one SNP depending on its location (in the introns or exons) can affect disease mechanism. In order to find significant results these studies should be designed with at least 1000 individuals in the experimental group and at least 1000 individuals in the control group. Therefore, scientific value of these studies is limited.

In GWAS the whole genome is analyzed without a specific hypothesis and all the variations are identified. More than 100,000 SNPs are assessed among an experimental and a control group consisting of 1000 individuals each. When the SNPs are identified they are compared with population-based variations in a quality control study and thus the data is homogenized. Following this quality control study SNPs are graphed and their p-values are calculated (should be <5x108). Areas with disease related SNPs are further analyzed and sequenced. All the variations, promoter sequences and copy numbers in the proximity are identified in that region. Finally, this data is assessed in a meta-analysis.

So far worldwide more than 20,000 GWAS studies for a variety of diseases have been published and more than 15,000 SNPs have been identified. The data is available online www.genome.gov/gwastudies.

In 2011 Painter et al. staged endometriosis patients according to the ASRM classification and designed a GWAS study. They found that 27% of the 51% genetic heritability is caused by SNP variations. Then patients were further staged according to severity. Stages 3-4 were described as severe endometriosis and stages 1-2 were described as light endometriosis. The heritability of severe stages was reported as 34% and light stages 15%. The authors concluded that severe stages have a higher percentage of heritability. In 2017 International Endometriosis Genomics Consortium published the results of 11 different GWAS studies from Europe and Japan where results from 17,000 patients and 190,000 controls were analyzed. They identified 14 loci and all of these loci were seen in endometriosis patients staged as 3-4. These results suggested a difference in terms of genetic heritability among early and late stages. Based on these results researchers ask if endometriosis is a progressive disease or are the stages genetically determined from the beginning.

Genetic variations related with endometriosis are closely associated with ovarian cancer. They share common loci when analyzed in fat tissue. There is a relationship with fat distribution and endometriosis. However, no association has been found between BMI and endometriosis. Thus, it is thought that there is a relationship between fat localization in body and endometriosis.

Currently all GWAS research done in the field of endometriosis worldwide is collected under the International Endometriosis Genomic Consortium (IEGC). So far genomes of 61,634 patients and 768,625 individuals under the control group have been analyzed. Although it has not yet been published as a result of all the research the known loci related with endometriosis has increased to 27 from 14 (first phase results to be published in BioRxiv, September 2018 Rahmioglu et al.). Similar to the previous results 21 of the 27 loci has been found to be associated with stage 3-4 and 1 has been found to be associated with stage 1-2. In contrast to the previous data 17 out of these 27 loci were found to be associated with infertility. These 27 loci are also seen in patients with autoimmune diseases, patients with gynecologic cancers, patients with cardiovascular diseases and also patients with symptoms like chronic pain, dysmenorrhea, altered bone density and there is also a relationship with age of menarche- menopause. Specifically, the relationship with pain symptom suggests a tendency for endometriosis in patients suffering from chronic pain symptoms.

Variations identified with GWAS studies should further be evaluated in tissue studies. To standardize tissue collection for research purposes we recommend the protocol set by WERF (World Endometriosis Research Foundation). You can reach these protocols online on endometriosisfoundation.org's website. (Soon these protocols will be available online in our website.)

As a summary, endometriosis and its genetic associations are still under research. Although there have been some developments a direct association between a genetic variation an endometriosis has not yet been identified.

Bahar Yuksel Ozgur
Nilufer Rahmioglu

VIII. ENDOACADEMIA MEETINGS – DIYARBAKIR

Following the previous meetings held in Gaziantep and Kayseri our society organized the 8th Endocademia Meeting on September 8, 2018 in Diyarbakir at the Radisson Blu Hotel. Our colleagues from Diyarbakir and surroundings joined us in this meeting. We were very happy to see the extensive interest of our colleagues in this meeting. Hope to see everyone again in the upcoming meeting.

NEWS FROM THE WORLD OF ENDOMETRIOSIS

NOVEMBER 22-24, 2018 EUROPEAN ENDOMETRIOSIS CONGRESS VIENNA/AUSTRIA

On November 22-24, 2018 in Vienna European Endometriosis League's (EEL) European Endometriosis Congress will take place. Our vice-president Engin Oral, Prof. MD. will be one of the two secretaries of this congress. We thank Engin Oral for his work and wish him success in this upcoming congress. Engin Oral, Prof. MD. and our general secretary Taner Usta, Assoc. Prof. MD. are also board members of EEL. Our members will represent our society in this congress with 6 oral and 5 poster presentations.
Oral and poster presentations which are accepted:

You can reach the program of the congress under the following link:
For detailed information: http://www.eec2018.com

#:	93
Programm Nr:	93
Type:	Poster Submission
Topic:	13 Other
Title:	Impact of Social Media Accounts on Endometriosis Awareness
Authors:	P. Yalcin Bahat, E. Darici, E. Oral; Istanbul/TR
Jury decision:	Accepted
Your status:	Presentation confirmed

#:	106
Programm Nr:	106
Type:	Poster Submission
Topic:	10 Ovarian endometriosis
Title:	The Change in Coagulation Parameters in Patients who have Ovarian Endometrioma: A 3-Year Analysis
Authors:	P. Yalcin Bahat[1], G. Turan[2]; [1]Istanbul/TR, [2]Hatay/TR
Jury decision:	Accepted
Your status:	Presentation confirmed

#:	161
Programm Nr:	161
Type:	Poster Submission
Topic:	02 Basic research
Title:	The Role of Raman Spectroscopic Analysis for Endometriosis Diagnosis
Authors:	B. Yuksel Ozgor, T. Pesen, U. Parlatan, G. Basar, E. Bastu, E. Oral; Istanbul/TR
Jury decision:	Accepted

#:	96
Programm Nr:	96
Type:	Poster Submission
Topic:	10 Ovarian endometriosis
Title:	The effect of hemostasis by electrocoagulation versus suture on endomerioma recurrence and pregnancy rates after laparoscopic cystectomy in uni/bilateral endometriomas
Authors:	C. Kaya, İ. Alay, M. Ekin, S. Ertaş Kaya, H. Goksever Celik, E. Oral, L. Yaşar; Istanbul/TR
Jury decision:	Accepted

#:	132
Programm Nr:	132
Type:	Poster Submission
Topic:	10 Ovarian endometriosis
Title:	Does immunotherapy have a role in the treatment of endometriosis?
Authors:	H. Goksever Celik, E. Celik, M. Uhri, E. Bastu, I. Polat, E. Oral; Istanbul/TR
Jury decision:	**Accepted**
Your status:	**Presentation confirmed**

#:	149
Programm Nr:	149
Type:	Poster Submission
Topic:	12 Pain
Title:	Impact of Yoga on Endometriosis Related Pelvic Pain
Authors:	E. Darici, P. Yalcin Bahat, E. Oral; Istanbul/TR
Jury decision:	**Accepted**
Your status:	**Presentation confirmed**

#:	116
Programm Nr:	116
Type:	Poster Submission
Topic:	12 Pain
Title:	Effects of an anti-inflammatory diet on chronic pelvic pain
Authors:	N.F. Topbas, P. Yalcin Bahat, K. Cakmak, E. Oral; Istanbul/TR
Jury decision:	**Accepted**
Your status:	**Presentation confirmed**

#:	65
Programm Nr:	65
Type:	Poster Submission
Topic:	10 Ovarian endometriosis
Title:	Intraoperative Diagnosis: Endometrioma imitating a leiomyoma in preoperative evaluation
Authors:	E.G. Topcu, D. Seckin, H. Sadikoglu, H. Kiyak; Istanbul/TR
Jury decision:	**Accepted**
Your status:	**Presentation confirmed**

#:	110
Programm Nr:	110
Type:	Poster Submission
Topic:	12 Pain
Title:	Role of Exercise in Managing Pain for Patients with Endometriosis
Authors:	E.G. Topcu, P. Yalcin, E. Oral; Istanbul/TR
Jury decision:	**Accepted**

#:	70
Programm Nr:	70
Type:	Poster Submission
Topic:	07 Infertility
Title:	Prognostic factors for intracytoplasmic sperm injection cycle success and cancellation rates of endometriosis patients: Does the phenotype of endometriosis matter?
Authors:	G. Uncu, I. Kasapoğlu, E. Külahçı Aslan, K. Aslan, N. Düzok; Bursa/TR
Jury decision:	Accepted

SEPTEMBER 14-16, 2018 7TH ASIAN CONFERENCE ON ENDOMETRIOSIS

On September 14-16, 2018 in Taipei, Taiwan 7th Asian Conference on Endometriosis has taken place. For program details: http://www.acetaiwan2018.org/

The 7th Asian Conference on
ENDOMETRIOSIS

SEPTEMBER 27-28, 2018 ESHRE CAMPUS, COPENHAGEN/DENMARK

How does endometriosis cause pain?

27-28 September 2018 | Copenhagen, Denmark

On September 27-28, 2018 in Copenhagen ESHRE Campus organized a two day congress. The main subject of the congress was 'How does endometriosis cause pain?'. In our next bulletin we are going to report on this congress in more detail.

SEPTEMBER 27-28, 2018 1ST WORLD NEUROPELVEOLOGY CONGRESS, ZURICH, SWITZERLAND

The 1st world congress took place in Zurich. We are going to report on this two-day congress in our next issue.

INTERVIEW WITH AN 'ENDO SPECIALIST'

Surgical Treatment of Endometriosis and the Importance of the ESHRE Guidelines
Ertan Saridogan, PhD. FRCOG

One of the members of our study group **Fitnat Topbas, MD** interviewed **Ertan Saridogan, PhD. FRCOG.** who lives and works in UK over Skype. You can find the video of the interview on our website.

Hello,
We are with Ertan Saridogan who has agreed to give us an interview.

FT: Could you please tell us about yourself?

ES: As you already mentioned I currently live and work as an obstetrics and gynecology physician in UK. It has been almost 26 years since I moved to UK. I graduated from Hacettepe Medical Faculty in Ankara, Turkey. Then I did my residency at the Istanbul University Cerrahpasa Medical Faculty in the Department of Obstetrics and Gynecology in Istanbul. After finishing my residency in 1992 I moved to UK. Since 2000 I have been working as a consultant physician in University College London Hospital.

FT: Our topic is endometriosis. Could you describe us in a few words the importance of surgery in the treatment of endometriosis?

ES: Endometriosis is a chronic disease. Thus, surgery is an important part of the treatment. Medical treatment usually helps in downsizing and controlling the symptoms. However, it is not possible to eliminate endometriosis loci with medical treatment. In surgery the aim is to eliminate the effected tissue as much as possible. But due to the chronic art of this disease the same problem is encountered with surgery as well which is recurrence. However, in contrast to medical treatment surgery can be more successful in terms elimination of the diseased tissue. Thus, surgery plays an important role.

FT: Patients usually inquire if they are going to have a surgery with laparotomy or laparoscopic surgery. How do you decide on the art of the surgery and how do you inform the patients? Or is laparoscopic surgery more preferably nowadays?

ES: In the current treatment of endometriosis surgery with laparotomy is rare. Surgery is done with laparoscopy. Laparoscopic surgery has many advantages. First of all, it enables a sooner postoperative recovery. In addition, due to the small incisions postoperative pain is less compared to surgery with laparotomy. Furthermore, laparoscopic surgery allows a better visualization of the abdominal organs thus a better exploration and a better surgical access. For these reasons surgeons nowadays prefer laparoscopic surgery. However, in some occasions a surgery with laparotomy is required. Surgeons prefer laparotomy on patients with a history of multiple surgeries while abdominal surgeries are known to cause abdominal adhesions which can cause complications when re-entry with laparoscopy is tried. In patients with additional pathologies such as myoma uteri where the size of the myomas could obstruct abdominal visualization in laparoscopic surgery, laparotomy is preferred. Aside from these rare occasions, laparoscopy is almost always the preferable option.

FT: You are in the ESHRE Guideline group. You work in the endometriosis team and prepare the guidelines. Could you explain our patients in a few works what is ESHRE and why the guidelines are important?

ES: ESHRE stands for European Society of Human Reproduction and Embryology. There are several special interest groups in this society and endometriosis is one of them. In 2003 this group got together to publish a guideline on treatment of endometriosis. So far, we have published two guidelines and we are preparing the third one. We started writing the first one in 2003 and we published it in 2005. Some members in the group continued working on the guideline and published the second one. It was published in 2013, so it has been five years since the publication of the previous guideline and during this time there have been some developments. Thus, we started working on the new guideline. It takes almost two years to revise and publish a new guideline, so we are expecting to publish the next issue end of 2019 or beginning of 2020. ESHRE is a world-renowned society. Leading figures in this field are a part of this society. Thus, the guidelines are accepted worldwide as important references and clinicians use these guidelines in their practice.
In addition to the guideline for clinicians we also prepare a guideline for the patients. This is usually published following the one for the clinicians. In 2013 we also published one for the patients and for the next guideline we are also preparing one for the patients.

FT: Can patients find these guidelines online?

ES: Yes, on ESHRE's website patients can find these guidelines and download them.

FT: Endometriosis more commonly known as chocolate cyst disease is not well known in Turkey. Patients usually become aware of this disease once a severe symptom such as infertility is observed, because knowledge on this disease is very limited. How is the situation in UK? Are the patients diagnosed more quickly? Do they have an easier access to treatment? How is the awareness on endometriosis in UK?

ES: Endometriosis has a secretive nature. Therefore, we have similar problems here. First of all, the disease is not known that well. If the patient does not have a relative or a friend with endometriosis most of them are surprised to hear that they have the disease. Thus, in internet we encounter a lot of questions like 'endo'what?'. I think a patient has made a short movie named 'endo'what. I believe the video is available online. Another problem with endometriosis is that the healthcare providers also lack in knowledge on this disease. When a patient is taken care of the possibility of endometriosis does not come that easily to mind. Especially primary care providers or general practitioners do not consider menstruation pain as abnormal so especially symptoms in adolescents are easily overseen. Therefore, delay in diagnosis is common. It is known that worldwide the delay in diagnosis is approximately 5-13 years. These numbers are 8-9 years in UK. This is the time passed from the onset of symptoms until diagnosis. Thus, we also share the same problem. However, due to a better education on health and biology here in UK patients are more aware of their own anatomy and physiology. Therefore, their understanding of the disease is much better compared to other parts of the world. As I mentioned before I have been living in UK for the last 25 years, so I cannot really assess the situation in Turkey. I believe worldwide we share similar problems with endometriosis but maybe on different levels.

FT: On a final note is there a message that you would like to give our patients?

ES: Endometriosis is a common disease, but in contrast to cancer it is a benign disease. It does not require a treatment all the time. If there are symptoms or if the disease is causing other problems, then a treatment is indicated. Two major problems with endometriosis are infertility and pain. When these are observed the patient should receive treatment. It should be taken into account that whether the treatment is medical or surgical they might have side effects. These side effects can sometimes be more severe than the symptoms themselves. Therefore, there has to be balance in treatment. When the patient describes a side effect the physician should not insistent on that specific treatment. Especially with hormonal medications the side effects can be worse. Patients should be thoroughly informed on the management and they should be active in choosing the right type of treatment. However, it is uncertain how much we can apply to this in our daily practice.

Thank you very much for this interview and your time.

ARTICLES ON ENDOMETRIOSIS FROM OUR COUNTRY

J Turk Ger Gynecol Assoc. 2018 Aug 6;19(3):151-157. doi: 10.4274/jtgga.2017.0146.

Does the presence of endometriosis cause a challenge for transvaginal oocyte retrieval? A comparison between patients with and without endometriosis

Kasapoğlu I[1], Türk P[1], Dayan A[1], Uncu G[1].

Abstract

OBJECTIVE: The aim of the study was to compare patients with and without endometriosis regarding performance rates, difficulties, and complications associated with transvaginal oocyte retrieval (TVOR) procedures.

MATERIAL AND METHODS: A prospective cohort study was conducted at the In Vitro Fertilization Unit of the Division of Reproductive Endocrinology and Infertility Department of a university hospital. Fifty-eight patients with endometriosis and 61 patients without endometriosisunderwent TVOR procedures consecutively. Primary outcome measures were; number of needle entries per patient and performance rating defined as the total number of oocytes retrieved per vaginal needle entry. The requirement for manual compression of the abdominal wall (assistance) to reach the ovaries, procedure-related pain, and procedural complications were also evaluated.

RESULTS: The median number of needle entries through the vaginal wall per patient was comparable between the two groups (p=0.45). Performance rates were higher in the control group (p=0.001). Performance rates and total number of the needle entries through the vaginal wall were not significantly correlated with ovarian endometrioma (OMA) diameter (r=0.28; p=0.68; r=0.275, p=0.068, respectively) in the endometriosis group. Body mass index (BMI) scores were found to be correlated with the number of the needle entries and higher BMI scores were associated with higher numbers of vaginal wall punctures (p<0.001). The requirement for manual compression of the abdominal wall was significantly higher in the control group (57.4% vs 27.6%, p=0.001). A similar proportion of women needed analgesic medications after the TVOR procedure in both groups (10.3% vs 16.4%, p=0.33). Hospital readmissions for any symptoms were also comparable between the two groups (p=0.22). Three women were treated for pelvic infection, all of whom were in the endometriosis group.

CONCLUSION: Endometriosis seems to cause a challenge for TVOR that may have reflection on individual surgeon's performance rates for the procedure, independently from the diameter of a pre-existing OMA or ovarian adhesions. Obesity is another factor that may present a challenge for the procedure.

KEYWORDS: Endometriosis, oocyte pickup, obesity, complication, in vitro fertilization

Climacteric. 2018 Aug;21(4):385-390. doi: 10.1080/13697137.2018.1439913. Epub 2018 Mar 1.

Surgical challenges in the treatment of perimenopausal and postmenopausal endometriosis.

Ozyurek ES[1], Yoldemir T[2], Kalkan U[3].

Abstract

Endometriosis is classically defined as a chronic, recurrent and progressive disease. It is known to be estrogen-dependent, but can still be observed during the peri- and postmenopausal periods. Medical management of endometriosis is palliative symptomatic relief. Surgery when properly and timely performed for the right person may treat endometriosis. However, there is always a risk of possible major or minor surgical complications, as well as loss of some functions due to nerve damage. Management of endometriosis in the woman approaching the end of her reproductive life may require special attention both due to the potential for recurrence and transformation into various endometriosis-associated malignancies.

KEYWORDS: Endometriosis; malignant transformation; postmenopausal; recurrence; surgery

Fertil Steril. 2018 Jul 1;110(1):122-127. doi: 10.1016/j.fertnstert.2018.03.015. Epub 2018 Jun 20.

Endometrioma-related reduction in ovarian reserve (ERROR): a prospective longitudinal study.

Kasapoglu I[1], Ata B[2], Uyaniklar O[1], Seyhan A[3], Orhan A[1], Yildiz Oguz S[3], Uncu G[1].

Abstract

OBJECTIVE: To evaluate whether endometrioma is associated with a progressive decline in ovarian reserve, and to compare the rate of decline with natural decline in ovarian reserve.

DESIGN: Prospective, observational study.

SETTING: Tertiary university hospital, endometriosis clinic.

PATIENT(S): Forty women with endometrioma and 40 age-matched healthy controls.

INTERVENTION(S): Women with endometriomas who did not need hormonal/surgical treatment at the time of recruitment and were expectantly managed. Controls were age-matched, healthy women. All participants underwent serum antimüllerian hormone (AMH) testing twice, 6 months apart. Sexually active patients with endometrioma also underwent antral follicle count.

MAIN OUTCOME MEASURE(S): Change in serum AMH levels.

RESULT(S): Median (25th-75th percentile) serum AMH level at recruitment was 2.83 (0.70-4.96) ng/mL in the endometrioma group and 4.42 (2.26-5.57) ng/mL in the control group. The median percent decline in serum AMH level was 26.4% (11.36%-55.41%) in the endometrioma group and 7.4% (-11.98%, 29.33%) in the control groups. Twenty-two women with endometrioma who had antral follicle count (AFC) had median AFC of 10 (8-12) at recruitment and 8 (6.3-10) at 6 months.

CONCLUSION(S): Women with endometrioma experience a progressive decline in serum AMH levels, which is faster than that in healthy women.

KEYWORDS: Antimüllerian hormone; endometrioma; endometriosis; ovarian reserve

Journal of Endometriosis and Pelvic Pain Disorders
https://doi.org/10.1177/2284026518778793
First Published June 19, 2018 Other

Hysteroscopic management of a juvenile cystic adenomyosis
Taner A Usta, Tolga Karacan, Ulviye Hanli, Elif Cansu, Engin Oral

Abstract
Introduction: Hysteroscopic management of juvenile cystic adenomyosis on a virgin patient with non-touch technique.

Description: Juvenile cystic adenomyosis of uterus is a cyst which is surrounded by myometrium and inside of this cyst is filled with hemorrhagic fluid. A 23-year-old virgin patient admitted to endometriosis outpatient clinic. The patient complained of dysmenorrhea, chronic pelvic pain, and abnormal uterine bleeding. A submucosal adenomyotic cyst was, sized 40 mm approximately, determined at posterior wall of uterus by transrectal ultrasonography. She received daily 2 mg dienogest (Visanne®) for 6 months. At the end of 6 months of treatment, the cyst size was still 35 mm. Hysteroscopy was performed with the use of the non-touch technique (vaginoscopic approach). A rigid 2.9-mm hysteroscope with a 12° oblique lens and an outer sheath diameter of 4 mm was used. When the cystic wall was ruptured by bipolar instrument, a chocolate-colored fluid was drained. The operation lasted 10 min. Her postoperative course was uncomplicated. Postoperatively, two dose of leuprolide acetate 11.25 mg (Lucrin depot®—3M; Abbot, Istanbul, Turkey) was prescribed (6 months total). On her sixth month, there was no cyst on transrectal ultrasonography examination. The patient did not exhibit any symptoms.

Conclusions: Because the disease affects adolescent girls, fertility issues should be kept in mind during the workup and when operating on these patients. Hysteroscopy is a mini-invasive, safe, and effective option for the treatment of juvenile cystic adenomyosis.

Keywords: Juvenile cystic adenomyosis, cystic adenomyosis, hysteroscopy

Gynecol Obstet Invest. 2018 Aug 2:1-10. doi: 10.1159/000489494.
The Role of Serum Caspase 3 Levels in Prediction of Endometriosis Severity.
Kaya C[1], Alay I[1], Guraslan H[1], Gedikbasi A[2], Ekin M[1], Ertaş Kaya S[3], Oral E[4], Yasar L[1].
Abstract
BACKGROUND/AIMS: To identify the role of serum caspase 3, Annexin A2 (ANXA2), and Soluble Fas Ligand (sFasL) levels in the prediction of endometriosis severity.

METHODS: The study was performed on 90 women who were candidates for laparoscopic surgery due to endometrioma or any other benign ovarian cysts detected by ultrasound examination, pelvic pain, or infertility. The control group comprised 29 patients. The second group comprised 29 patients with stage I-II endometriosis and the third group comprised 30 patients with stage III-IV endometriosis.

RESULTS: Significant differences were detected between the control and stage III-IV endometriosis groups and between stage I-II and stage III-IV endometriosis groups in terms of caspase-3 levels (both, $p < 0.001$), ANXA2 levels ($p = 0.007$ and $p = 0.002$), and sFasL levels ($p = 0.022$ and $p = 0.044$). After receiver operating characteristic analysis, the area under curve was 93% (95% CI 57-82) at 10.7 ng/mL cut-off level for caspase-3 with 90% sensitivity and 87% specificity.
CONCLUSION: Serum caspase-3 level may be a reliable predictor of endometriosis severity.
KEYWORDS: Apoptosis; Endometriosis; Laparoscopic surgery; Tissue adhesions

Bosn J Basic Med Sci. 2018 Aug 1;18(3):275-278. doi: 10.17305/bjbms.2018.2659.
The clinical characteristics and surgical approach of scar endometriosis: A case series of 14 women.
Tatli F[1], Gozeneli O, Uyanikoglu H, Uzunkoy A, Yalcın HC, Ozgonul A, Bardakci O, Incebiyik A, Guldur ME.

Abstract
Scar endometriosis, also referred to as abdominal wall endometriosis (AWE), is a rare form of endometriosis that usually develops in the scar after obstetric or gynecological surgeries, including cesarean section (CS). Recently, the occurrence of scar endometriosis has been increasing together with the increase of CS incidence. Scar endometriosis can be clinically misdiagnosed as hernia, lipoma, or hematoma. Here we retrospectively analyzed the clinical aspects of scar endometriosis and surgical approach in 14 patients from a tertiary hospital, who were treated by surgery, between 2012 and 2017.

The mean age was 32.71 ± 8.61 years (range: 19-45). Palpable mass and cyclic pain at the scar site were the most common complaints. Twelve patients had previously undergone CS, and two patients had undergone a surgery of ovarian endometrioma. The preoperative diagnosis was determined with ultrasonography (US), magnetic resonance imaging (MRI), or computed tomography (CT). Preoperatively, scar endometriosis was diagnosed in 12/14 patients (85.7%), while 2 patients (14.3%) were diagnosed with inguinal hernia.

The treatment was surgical excision in all patients; in addition, mesh repair surgery was performed in 1 patient with recurrent scar endometriosis. Postoperatively, endometriosis was confirmed by histology in all patients. The average size of endometriomas was 24.71 ± 6.67 mm (range: 11-35). No woman had concurrent pelvic endometriosis. In the follow-up period (mean: 9 months) the recurrence of endometriosis was not observed. Scar endometriosis should be considered in all women of reproductive age presenting with cyclic pain and swelling in their abdominal incision sites.

Journal of Endometriosis and Pelvic Pain Disorders; 2018 Sept 25: doi.org/10.1177/2284026518798331 Review Article
Laparoscopic evaluation of female pelvic neuroanatomy and autonomic plexuses in terms of gynecologic perspective
Ahmet Kale, Gulfem Basol, Taner Usta, Hande G Aytuluk

Abstract
The nerves located in the deepest areas can be exposed and dissected via laparoscopic magnification. This technological innovation does not only help us to avoid surgery-related complications but also allows us to diagnose the vascular entrapment syndromes. The aim of this article is to demonstrate female neuroanatomy and autonomic plexus via enriched photos and videos to reveal the relationship of the pelvic nervous system with gynecological operations.

SUMMARIES OF ENDOMETRIOSIS RELATED ARTICLES

On our website's main page endometriosisturkey.com you can find monthly selected endometriosis related articles which are selected and summarized by **Fatma Ferda Verit, Prof. MD.** You can find the most up-to-date publications on endometriosis under the following link
Article Full texts uploaded by **Banu Kumbak Aygun, Prof. MD.**

http://www.endometriozisdernegi.org/en/library/article-summaries

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