

PREFACE

Hello,

We are with you again with our 24th issue.

In the new issue of our quarterly newsletter, you can find details about current advancements in endometriosis and adenomyosis and updates on our society's activities.

In this issue, you will find summaries about the relationship between endometriosis and cancer, the effect of endometriosis on couples, the role of neurogenic inflammation in the aetiology of endometriosis, artificial intelligence in the diagnosis of endometriosis, the effect of pain in endometriosis on daily life and the role of a new digital application in reducing the pain of endometriosis.

ENDO/ADENO Journal Clubs, as a part of the scientific activities of our association, were held on Thursdays, October 6, November 10 and December 15, 2022, which were moderated by Prof. Taner Usta, MD., Prof. Cem Demirel, MD. and Prof. Hulusi Bülent Zeyneloğlu, MD. Hümeyra Özkaya, MD., Nilüfer Cimşit Kemahlı, MD., Ezgi Darıcı, MD., Berivan Güzelbağ, MD., Elif Göknur Topçu MD., and Nilüfer Akgün, MD presented selected articles in these Journal Clubs. The next one will take place in January, and will be moderated by Prof. Murat Sönmezer, MD.

The 16th of our EndoAcademy meetings was held in Malatya on Sunday, December 4, 2022. The meeting was held under the chairmanship of **Prof. Recai Pabuçcu, MD.** and **Assoc. Prof. Engin Yıldırım** with the scientific contributions of valuable professors covering the diagnosis, medical and surgical treatment of endometriosis, and its relationship with infertility and pelvic pain. It was a successful meeting where many physicians dealing with endometriosis from Malatya and the surrounding provinces participated and benefited.

The 36th and 37th of our Instagram question and answer broadcasts that we started during the pandemic were held with the contribution of **Assoc. Prof. Yusuf Aytac Tohma, MD., Hümeyra Özkaya, MD., Prof. Servet Hacivelioğlu MD.,** and **Begüm Ertan, MD.** You can follow the dates of the upcoming sessions on our association's Instagram account.

Women's Health and Menstrual Hygiene Meetings organized by our society with the Institute of Loans and Accommodations were held in Istanbul, Ankara, Samsun, and Edirne. These meetings will continue to be held in other provinces throughout 2023.

Among the upcoming scientific activities of our society, the 1st Gaziosmanpaşa OB&GYN Days will be held on 13-14 January 2023 at Gaziosmanpaşa Training and Research Hospital.

The 'Multidisciplinary Approach to Endometriosis and Adenomyosis Symposium' will be held on February 26 in Ankara and will be chaired by Prof. Ümit İnceboz, MD. and Assoc. Prof. Yusuf Aytaç Tohma, MD. We are happy to invite all our colleagues who are interested in the field to this comprehensive meeting where different disciplines will share their knowledge on endometriosis.

On **10-11 March 2023, ESGE (European Society of Gynecological Endoscopy) Regional Workshop** will be held at Istanbul Taksim Sofitel Hotel. The workshop will be chaired by **Prof. Dr Ertan Saridoğan, MD.** and **Prof. Taner Usta, MD**.

The guest of our interview with a specialist section in this month's issue is Dan Martin. He is the scientific director of the Endometriosis Foundation of America. You can find this interview and his future projects in this issue.

We hope to be together again with developments from the world of endometriosis and adenomyosis in our next issue.

Best regards.

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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 you would like to ask, you can contact us via e-mail at drcihankaya@gmail.com.

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TABLE OF CONTENTS

A SELECTED ARTICLES

- 1. Partners matter: The psychosocial well-being of couples when dealing with endometriosis Schick M, Germeyer A, Böttcher B, et al. 2022 Jul 28;20(1):115.. Health Qual Life Outcomes.
- 2. Living with endometriosis: Comorbid pain disorders, characteristics of pain and relevance for daily life

Leuenberger J, Kohl Schwartz AS, Geraedts K, et al. Eur J Pain. 2022;26(5):1021-1038.

- 3. Neurogenic Inflammation in the Context of Endometriosis—What Do We Know? Velho RV, Taube E, Sehouli J, Mechsner S. Int J Mol Sci. 2021;22(23):13102.
- 4. Machine learning algorithms as new screening approach for patients with endometriosis. Bendifallah S, Puchar A, Suisse S, et al. Scientific Reports. 2022 Jan 12;12(1):1-2.
- 5. Pain Reduction With an Immersive Digital Therapeutic Tool in Women Living With Endometriosis-Related Pelvic Pain: Randomized Controlled Trial

Merlot B, Dispersyn G, Husson Z et al. J Med Internet Res. 2022 Sep; 24(9): e39531.

6. Predictive factors of endometriosis progression into ovarian cancer Varga J, Reviczká A, Háková H, et al. J Ovarian Res. 2022;15(1):5.

- **B- NEWS FROM OUR SOCIETY**
- C- NEWS FROM THE WORLD OF ENDOMETRIOSIS
- **D-INTERVIEW WITH AN ENDO SPECIALIST**
- E- ARTICLES ON ENDOMETRIOSIS FROM OUR COUNTRY FROM THE LAST THREE MONTHS
- F- SOCIAL MEDIA

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A SELECTED ARTICLES

1

Partners matter: The psychosocial well-being of couples when dealing with endometriosis

Schick M, Germeyer A, Böttcher B, et al. 2022 Jul 28;20(1):115. Health Qual Life Outcomes.

Abstract

Background Endometriosis is often associated with severe dysmenorrhea, pelvic pain and dyspareunia and has a high impact on daily life as well as sexuality. Quality of partnership positively influences the course of various diseases and ability to cope with emotional and physical distress. However, studies focusing on the male partners of endometriosis patients are rare, and even less is known about the reciprocal relationship in these couples. Therefore, this study aims to explore the interrelations in couples with endometriosis in matters of psychological distress, sexual and partnership satisfaction and social support.

Methods The cross-sectional study was conducted in two university-affiliated fertility centres in Germany and Austria with n = 104 female/male couples affected by endometriosis. Participants completed a questionnaire regarding endometriosis, partnership, sexuality, stress, anxiety, depression and social support. Both women and men were asked about the impact of women's endometriosis-related pain (IEP) on their everyday life (e.g. leisure time). Data were analysed using the Actor-Partner-Interdependence Model..

Results Significant partner effects were evident: High depression, anxiety and stress scores in women were associated with a higher IEP in men (all $p \le 0.01$), reciprocally high stress and depression scores in men were correlated with a higher IEP in women (all $p \le 0.05$). Less sexual satisfaction in women was associated with a



higher IEP in men (p = 0.040). There was a significant reciprocal association between the perceived lack of understanding from the social environment and a higher IEP, for both women (p = 0.022) and men (p = 0.027).

Conclusions The male partner should be taken into account when counselling or treating women with endometriosis. Our study shows a high interdependence and reciprocal influence from both partners—positively and negatively—concerning psychological distress and sexual satisfaction. Furthermore, there ought to be more awareness for the psychosocial impact of endometriosis, especially in regard to social support and understanding. Talking about and improving sexual satisfaction as well as enhancing stress reducing techniques may hold great benefits for dealing with endometriosis.

2 Living with endometriosis: Comorbid pain disorders, characteristics of pain and relevance for daily life

Leuenberger J, Kohl Schwartz AS, Geraedts K, et al. Eur J Pain. 2022;26(5):1021-1038.

Background: Pain plays a central role in endometriosis. The complex relationship among pain characteristics, comorbid pain disorders and daily life represents a challenge for medical support. This multicentre cross-sectional case-control study analysed the association between endometriosis-related chronic pain and functions of daily life in 510 women with endometriosis, 265 (52%) who experienced chronic pain, either from endometriosis alone (N = 134, 26.3%) or in association with additional pain disorders (N = 131, 25.7%).

Methods: Self-administered questionnaires from the Brief Pain Inventory and the Pain Disability Index were used to investigate associations between pain characteristics (frequency, duration, intensity) and daily life. Also, associations between different endometriosis characteristics (rASRM stage, presence of adhesions, localisation of lesions) and pain were evaluated.



Results: Chronic pain is negatively associated with almost all (12/14) aspects of daily life investigated, including standing, walking, sitting, defaecation, sleep, sports activities, family and domestic responsibilities, sexuality, social functioning, professional life, mood, and joy of life. Altogether, 33.7% of women with chronic pain reported moderate and 27.5% severe limitations. Comorbid pain disorders resulted in significantly more limitations. The length of pain episodes showed a particularly especially important influence for family/domestic responsibilities (OR 22.94, p < 0.001), professional life (OR 16.56, p < 0.001) and social functioning (OR 41.03, p < 0.001).

Conclusions: Our data confirm that despite treatment, about 50% of women experience pain. Pain was associated with at least moderate negative effects on almost all areas of daily life;

additional pain comorbidities increased limitations. Improving pain management is essential for improving quality of life in women with endometriosis.

Significance: The study provides an accurate overview of the impact of endometriosis-associated pain on daily life. This is important because pain plays a central role in women living with endometriosis, and despite modern therapies, many women continue to suffer from chronic pain. The detailed analysis of its impact with a comprehensive survey of all aspects of daily life in a very large study population is unique. We expect an improved understanding of the consequences of pain to significantly advance medical support in these patients.

Neurogenic Inflammation in the Context of Endometriosis—What Do We Know?

Velho RV, Taube E, Sehouli J, Mechsner S. Int J Mol Sci. 2021;22(23):13102.

Abstract

Endometriosis (EM) is an estrogen-dependent disease characterized by the presence of epithelial, stromal, and smooth muscle cells outside the uterine cavity. It is a chronic and debilitating condition affecting ~10% of women. EM is characterized by infertility and pain, such as dysmenorrhea, chronic pelvic pain, dyspareunia, dysuria, and dyschezia. Although EM was first described in 1860, its aetiology and pathogenesis remain uncertain. Recent evidence demonstrates that the peripheral nervous system plays an important role in the pathophysiology of this disease. Sensory nerves, which surround and innervate endometriotic lesions, not only drive the chronic and debilitating pain associated with EM but also contribute to a growth phenotype by secreting neurotrophic factors and interacting with surrounding immune cells. Here we review the role that peripheral nerves play in driving and maintaining endometriotic lesions. A better understanding of the role of this system, as well as its interactions with immune cells, will unearth novel disease-relevant pathways and targets, providing new therapeutics and better-tailored treatment options.



inflammation, **Keywords:** endometriosis. neurogenic neuroimmune modulation, nerve signalling, peripheral nerve, inflammation, non-hormonal treatment

Machine learning algorithms as new screening approach for patients with endometriosis.

Bendifallah S, Puchar A, Suisse S, et al. Scientific Reports. 2022 Jan 12;12(1):1-2.

Abstract

Endometriosis—a systemic and chronic condition occurring in women of childbearing age—is a highly enigmatic disease with unresolved questions. While multiple biomarkers, genomic analysis, questionnaires, and imaging techniques have been advocated as screening and triage tests for endometriosis to replace diagnostic laparoscopy, none have been implemented routinely in clinical practice. We investigated the use of machine learning algorithms (MLA) in the diagnosis and screening of endometriosis based on 16 key clinical and patient-based symptom features. The sensitivity, specificity, F1-score and AUCs providers. Introducing MLA in this setting represents a paradigm of the MLA to diagnose endometriosis in the training and change in clinical practice as it could replace diagnostic validation sets varied from 0.82 to 1, 0-0.8, 0-0.88, 0.5-0.89, and from 0.91 to 0.95, 0.66–0.92, 0.77–0.92, respectively. Our data suggest that MLA could be a promising screening test for general symptoms and initiate dialogue with physicians about diagnosis practitioners, gynecologists, and other front-line healthcare



laparoscopy. Furthermore, this patient-based screening tool empowers patients with endometriosis to self-identify potential and treatment, and hence contribute to shared decision-making.

5

Pain Reduction With an Immersive Digital Therapeutic Tool in Women Living With Endometriosis-Related Pelvic Pain: Randomized

Controlled Trial

Dalkalitsis A, Salta S, Tsakiridis I, et al. Taiwan J Obstet Gynecol 61 (2022) 24e33.

Abstract

Background: Chronic pelvic pain is a common and disabling condition in women living with endometriosis. Pharmacological and surgical treatments are not always effective at controlling pain and present important restrictions. Digital therapeutics (DTx) are emerging as major nonpharmacological alternatives that aim to extend the analgesic therapeutic arsenal of patients.

Objective: In this randomized controlled trial (RCT), we aimed to measure the immediate and 4-hour persisting effects of a single use 20-minute DTx (Endocare) on pain in women experiencing pelvic pain due to endometriosis.

Methods: A total of 45 women with endometriosis participated in a randomized controlled study comparing the analgesic effect of a single use of a virtual reality digital treatment named Endocare (n=23, 51%) to a 2D digital control (n=22, 49%). Perceived pain and pain relief were measured before the treatment and 15, 30, 45, 60, and 240 minutes after the end of the treatment.

Results: The clustered posttreatment pain was significantly reduced compared to the pretreatment for both Endocare and the control group (all P<.01). Endocare was significantly more effective than the control group (all P<.01). Endocare decreased the mean pain intensity from 6.0 (SD 1.31) before the treatment to 4.5 (SD 1.71) posttreatment, while the control only decreased it from 5.7 (SD 1.36) to 5.0 (SD 1.43). When comparing each posttreatment measure to the pretest, Endocare significantly reduced pain perception for all points in time up to 4 hours posttreatment. The differences did not reach significance for the control group. Moreover, Endocare was significantly superior to



the control group 15, 30, and 45 minutes after the treatment (all P<.001). The mean perceived pain relief was significantly higher for Endocare at 28% (SD 2%) compared to the control, which was 15% (SD 1%) for all the posttreatment measurements (all P>.05).

Conclusions: Our study aimed to test the effects of a single use of a DTx treatment on reported pain at different time points in women diagnosed with endometriosis experiencing moderate-to-severe pelvic pain. Importantly, our results support that Endocare, a virtual reality immersive treatment, significantly reduce pain perception compared to a digital control in women living with endometriosis. Interestingly, we are the first to notice that the effect persisted up to 4 hours posttreatment.

Keywords: RCT; chronic pain; digital health; digital intervention; digital therapeutics; digital treatment; eHealth; effectiveness; efficacy; endometriosis; endometrium; gynecologist; gynecology; pain; pelvic; pelvic pain; pelvis; randomized controlled trial; reproductive health; sexual health; virtual reality; women's health.



Predictive factors of endometriosis progression into ovarian cancer

Varga J, Reviczká A, Háková H, et al. J Ovarian Res. 2022;15(1):5.

Abstract

Background In recent years, endometriosis has overcome a noteworthy renaissance in the recognition of its potential. In certain patients, a demonstrable malignant progression of ectopic foci leading to the development of ovarian cancer is seen. The knowledge of endometriosis overthrow background endometriosis associated ovarian cancer is of paramount importance for selection of patients at risk. The goal of the presented study was to review a malignant potential of endometriosis and to specify predictive factors of endometriosis progression into ovarian cancer. Altogether 189 patients were included in the study. Conventional cytogenetics as well as measurement of transcriptional activity of CTNNB1 (β -catenin) and HIF1A (HIF1- α) genes were prospectively studied in 60 endometriosis patients and 50 control group patients. The retrospective histopathological analysis was performed in 19 endometriosis associated ovarian cancer patients and 60 patients with histologically confirmed endometriosis.



Results Five endometriosis patients showed a deviation from normal cytogenetics finding without affecting of their phenotype. In 6 cases of endometriosis associated ovarian cancer ectopic endometrium was not confirmed. The remaining 13 cases demonstrated either benign or atypical endometriosis or even structures of borderline carcinoma. Atypical endometriosis was histologically confirmed in 20% of 60 endometriosis patients. Determination of gene expression (CTNNB1, HIF1A) formed two subgroups. Transcriptionally incipient endometriosis subgroup with insignificant genes expression compared to control group. In transcriptionally evident endometriosis subgroup were genes expressions significantly higher compared to control group (p < 0.01) as well as transcriptionally incipient endometriosis subgroup (p < 0.05).

Conclusions Significant structural abnormalities of chromosomes are not included in genetic rigging of endometriosis patients. Atypical endometriosis represents a histopathologically detectable intermediate of endometriosis progression. Determination of genes expression CTNNB1 and HIF1A helps to allocate risk patients with endometriosis where more precise management is needed.

B NEWS FROM OUR SOCIETY PAST ACTIVITIES

On the 6th of October 2022, we discussed the articles presented by **Humeyra Ozkaya**, **MD.** and **Nilufer Cimsit Kemahli**, **MD.** The session was moderated by **Prof. Taner Usta**, **MD.**



On the 10th of November 2022, we discussed the articles presented by **Ezgi Darici**, **MD.** and **Berivan Guzelbag**, **MD.** The session was moderated by **Prof. Cem Demirel**, **MD.**



On the 15th of December 2022, we discussed the articles presented by **Elif Göknur Topçu, MD.** and **Nilüfer Akgün, MD.** The session was moderated by **Prof. Hulusi Bülent Zeyneloğlu, MD.**



The 36th and 37th of our Instagram Question and Answer broadcasts which were initiated during the pandemic were held with the participation of **Assoc. Prof. Yusuf Aytaç Tohma, MD., Hümeyra Özkaya, MD., Prof. Servet Hacıvelioğlu, MD. and Begüm Ertan, MD.** You can follow the upcoming broadcast dates on our society's Instagram account.





Women's Health and Menstrual Hygiene meetings organized by our association in collaboration with the Institute of Loans and Accommodations were held in Istanbul, Ankara, Samsun, and Edirne. These will continue in other cities throughout 2023.















The president of our society **Prof. Ümit İnceboz, MD.** gave a presentation about "What is endometriosis (chocolate cyst disease) and how to improve social awareness?" in the meeting organized by the Endometriosis and Adenomyosis Society in partnership with Aydın Adnan Menderes University Faculty of Health Sciences, Department of Midwifery.



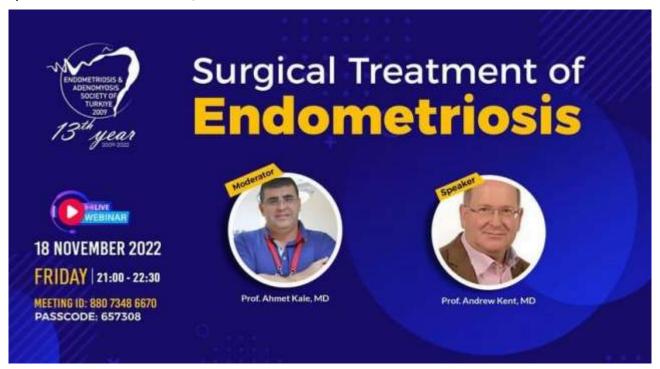
Konuşmacı: Prof. Dr. Ümit İNCEBOZ Kadın Hastalıkları ve Doğum Uzmanı Endometriozis ve Adenomyozis Dernek Başkanı

On the 2^{oth} of October 2022, upon the invitation of Ege University Faculty of Agriculture, Department of Soil Science and Plant Nutrition, in the conference titled "Healthy Soil, Healthy People", our society's president Prof. Ümit İnceboz, MD gave a presentation titled "The importance of nutrition in endometriosis as in other fields of medicine". In the same meeting, a member of our society's advisory committee, Assoc. Prof. Pınar Yalçın Bahat, MD made her presentation about "We draw our future with what we eat".





In November, the president of BSGE **Prof. Andrew Kent, MD.** from England was our guest in the webinar titled **'Surgical treatment of endometriosis',** which was moderated by our vice president **Prof. Ahmet Kale, MD.**



Prof. Kutay Biberoğlu, MD., a member of the Discipline Committee of our society, gave a presentation titled **'How to manage Endometriosis Associated Infertility'** at The 10th Asian Conference on Endometriosis and Adenomyosis.



The 16th EndoAcademy Meeting was held on the 4th of December in Malatya. The meeting was chaired by **Prof. Recai Pabuçcu, MD. and Assoc. Prof. Engin Yıldırım, MD.** and specialists contributed to the meeting on topics covering the diagnosis of endometriosis, its medical and surgical treatment, and its relationship with infertility and pelvic pain. Many physicians from Malatya and surrounding provinces attended the meeting where they benefited from the experiences of valuable professors in the field.

















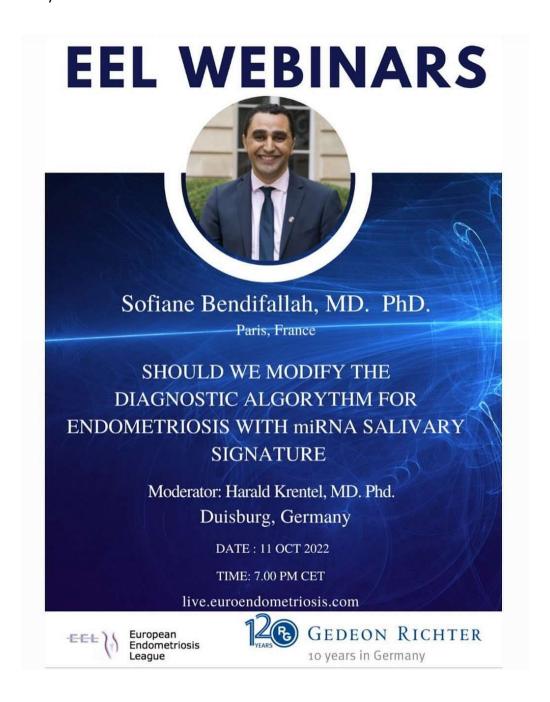


C NEWS FROM THE WORLD OF ENDOMETRIOSIS

EEL WEBINAR Program 2023

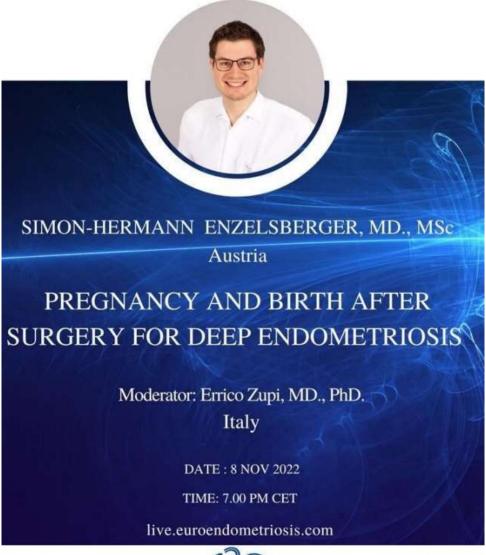
European Endometriosis League Webinar programs organized by the European Endometriosis League (EEL) continued during 2022.

The EEL webinar 'Should we modify the diagnostic algorithm for endometriosis with miRNA salivary signature was held by Sofiane Bendifallah, MD. PhD. from France in October, which was moderated by Harald Krentel.



The EEL Webinar 'Pregnancy and Birth after surgery for deep endometriosis' was held in November by Simon-Hermann Enzelberger, MD., MSc. and moderated by Errico Zuppi, MD., PhD.

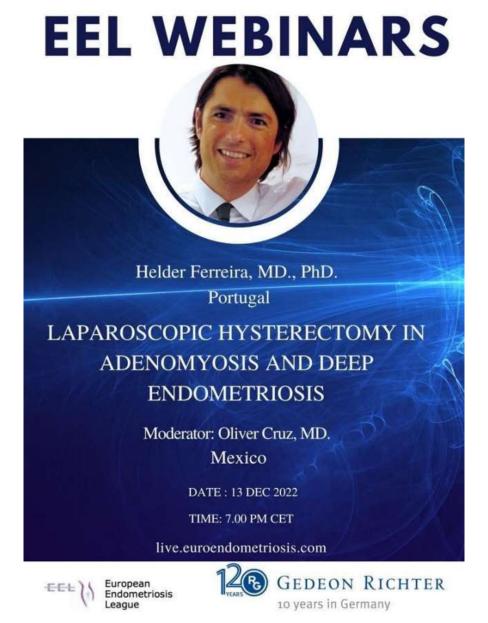
EEL WEBINARS







In December, the EEL Webinar 'Laparoscopic hysterectomy in adenomyosis and deep endometriosis' was held by Helder Ferreira, MD., PhD. and moderated by Oliver Cruz, MD.



The European Endometriosis League Webinar program organized by the European Endometriosis League (EEL) will continue in 2023.

For more information visit https://www.endometriosis-league.eu/home or follow the European Endometriosis League or Euro Endo League accounts on social media.

FUTURE ACTIVITIES

In January the ENDO/ADENO Journal Club Meetings will continue with the presentations prepared by **Eda Üreyen Özdemir, MD. and Assoc. Prof. Murat Bozkurt, MD.** The session will be moderated by Prof. Murat Sönmezer, MD.

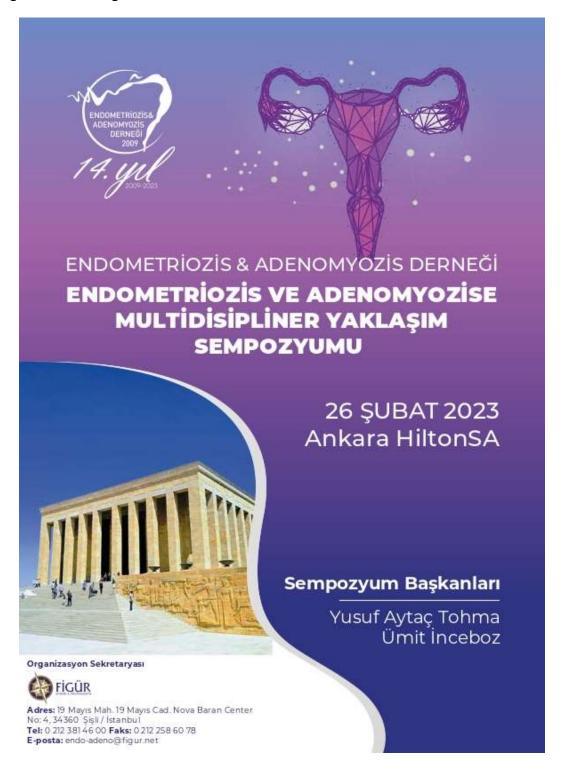


The 1st Gaziosmanpaşa Obstetrics and Gynecology Days will be held on the 13th and 14th of January 2023 at the University of Health Sciences Turkey, Istanbul Gaziosmanpasa Training and Research Hospital.

You may find the program and details below.



A Multidisciplinary approach to endometriosis and adenomyosis symposium will be held in Ankara and will be chaired by **Prof. Ümit İnceboz, MD. and Assoc. Prof. Yusuf Aytaç Tohma, MD.** on the 26th of February. We are glad to invite all our colleagues who are interested in the subject to this comprehensive meeting, which will include colleagues from different specialities sharing their knowledge on endometriosis.



On the 10th and 11th of March 2023, ESGE Regional Workshop is planned to take place at Taksim Sofitel Otel, Istanbul, Turkey. The workshop will be chaired by **Prof. Ertan Sarıdoğan, MD. and Prof. Taner Usta, MD**. https://www.esgeendoturkiye.org/en/scientific-program.html



12:00 - 12:45 12:45 - 13:00	Registration Opening speeches Ertan Saridogan, Taner Usta
	Workshop: Imaging for Endometriosis (US and MR)
	SESSION 1: Basic principles of transvaginal ultrasound and pelvic MRI for the diagnosis of endometriosis Chairs: Cem Atabekoglu, Cihan Kaya
13:00 - 13:20	How to perform ultrasound examination for pelvic endometriosis/adenomyosis: Uterus and ovaries Stefano Guerriero
13:20 - 13:40	How to perform ultrasound examination for pelvic endometriosis/adenomyosis: deep endometriosis of pelvic side walls, rectovaginal space, rectosigmoid, bladder Stefano Guerriero
13:40 - 14:00	Basic principles of MRI scanning: Description of different MRI sequences, patient preparation and MRI protocol Isabelle Thomassin-Negarra
14:00 - 14:20	MRI findings of adenomyosis and ovarian, deep and superficial endometriosis Isabelle Thomassin-Negarra
14:20 - 15:00	Discussion
15:00 - 15:30	Coffee break
	SESSION 2: Live ultrasound demonstration and case presentations of ultrasound and MRI Moderators: Ahmet Kale, Elif Cansu Gundogdu
15:30 - 17:30	Panelists: Stefano Guerriero, Isabelle Thomassin-Negarra
DAY 2 11 r	NARCH 2023, SATURDAY
100	SESSION 3: Management of endometriosis associated infertility Chairs: Umit Inceboz, Pinar Yalcın Bahat
09.00 - 09:20	Initial evaluation of infertile women with possible endometriosis associated infertility and patient selection for MAR versus surgery Engin Oral
09:20 - 09:50	Surgical management of endometriosis associated infertility Grigoris Grimbizis
09:50 - 10:20	Medically assisted reproduction (IUI and ART) for endometriosis associated infertility Stratis Holibianakis

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10:20 - 10:50	Disscussion
10:50 - 11:15	Coffee break 💮
10.00 11.10	
	SESSION 4: Surgical management of endometriosis Chairs: Yucel Karaman, Tolga Karacan
11:15 - 11:35	Surgery for superficial/peritoneal endometriosis
	Michelle Nisolle
11:35 - 11:55	Surgery for ovarian endometrioma Ertan Saridogan
11:55 - 12:15	Surgery for deep endometriosis
	Ahmet Kale
12:15 - 12:35	Management of complications of endometriosis surgery Helder Ferreira
12:35 - 13:00	Discussion
13:00 - 14:00	Lunch (
	SESSION 5: Management of endometriosis associated pain Chairs: Levent Senturk, Hale Goksever Celik
14:00 - 14:30	Medical management of endometriosis associated pain Paolo Vercellini
14:30 - 15:00	Surgical Management of pelvic pain Taner Usta
15:00 - 15:30	Management of endometriosis associated pain: The role of pain management team Sawsan As-Sanie (Live video conference)
15:30 - 16:00	Discussion
16:00 - 16:30	Coffee break
1000	SESSION 6: Panel and case discussions Moderator: Ertan Saridogan
16:30 - 18:30	Panelists: Sawsan As-Sanie (Live video conference), Helder Ferreira, Grigoris Grimbizis, Umit Inceboz, Stratis Kolibianakis, Michelle Nisolle, Paolo Vercellini
18:30 - 19:00	Closing Ertan Saridogan, Taner Usta
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INTERVIEW WITH AN 'ENDO SPECIALIST'



Dan Martin
Interviewer: Goknur Topcu

Turkish Endometriosis and Adenomyosis Society (EAD): You have been involved in endometriosis for a long time. Could you tell us how did this journey begin?

Dan Martin (DM): My journey began with my grandmother. My grandmother wanted all their grandkids to become surgeons, as we all are now. The other two are pathologists and gastroenterologists. She supported us in succeeding in this. My father was a surgeon. I've always leaned towards a surgical speciality. We had a doctor in our medical school who had a ruptured aneurysm in the brain. You are paralysed on one side of your body when this happens. He used to be a brilliant gynaecological surgeon; he was still able to walk but he couldn't move his arm. Therefore, he became a wonderful lecturer who teaches everything about surgery. In 1970, A. Hindy was very serious about endometriosis, and I got my training from him. We had many doctors in the 70s who took endometriosis very seriously. As far as I understand this is not the case for every medical faculty considering how the diagnosis of endometriosis is delayed 8.3 years in 50%, 1.8 years in 25% in the normal population whereas the time is 2 months for gynaecologists. We know that at least 25% of doctors are aware of endometriosis.

During my residency at Hopkins, I worked with a surgeon who used to receive endometriosis patients from other hospitals. My thesis at the university was on lasers. In 1981 a surgeon came to visit from Clermont-Ferrand and taught us how to use lasers in laparoscopic endometriosis surgery. The same year another surgeon from Germany came and said that coagulation treatment didn't work at nodules. Later partial excision was used on nodules to coagulate the base. We were very close to going from partial excision to total excision. After learning how to do total excision between 1981-1983, I decided that total excision was easier than partial excision. And all the work that I have done and the prizes I have been given were consequences of these thoughts.

EAD: How is your daily routine nowadays?

DM: I retired from my clinical duties at the age of 70 and I am 76 years old now. I am the Scientific and Medical Director of the Endometriosis Foundation of America. What I do for them is mostly about checking the articles and making sure they are all medically correct and revise them accordingly. The Endometriosis Foundation of America is a patient advocacy group.

EAD: What do you think is the hardest thing about endometriosis?

DM: First, it resembles many other conditions such as primary dysmenorrhea, adenomyosis, interstitial cystitis, and irritable bowel syndrome... etc. It is very difficult to detect endometriosis for someone not focusing on finding it. And the worse is, acute conditions such as ectopic pregnancies, abortus, and pelvic inflammatory disease are the ones many people think and care about at first as these situations can threaten one's life. Although endometriosis can disrupt your daily life, it is hardly life-threatening. The only life-threatening result of endometriosis is untreated depression. Additionally, endometrioma cyst ruptures in people using anticoagulants or bowel obstructions are very rare. Bowel obstructions develop slowly, so it is hard to detect the progression. The second important problem of endometriosis is the normalization of pain. Your mom, your friends and even you are used to normalizing pain, so you cannot expect doctors to behave differently. We can only change this habit of normalizing pain by educating not only the doctors but the whole of society. The third challenge with endometriosis is surgical treatment. No one would operate on an adolescent with 2 months of period pain. Even when you want to do research no ethical board would allow you. However, those ages are when all the progression of endometriosis occurs. The implantation, growth and inflammation happen before the age of 21. This could be explained by a theory of neuroimmune maturation which doesn't happen until the age of 20. After the age of 21, it is not a new implantation.

EAD: What is the most important part of evaluating and examining a patient with endometriosis?

DM: We diagnose 72% of our patients in our population. In our case, they just have to come through the door. I don't need to screen them for endometriosis, of the patients who are advised to have surgery come to me. If a patient is referred to me with a diagnosis of endometriosis there is a 90% chance that the diagnosis is accurate. You can only guess for the pediatric population. What you can do is search for some changes which indicate the presence of endometriosis at advanced stages. Due to the prostaglandins secreted from a bleeding superficial peritoneal lesion, diarrhoea, stomachache with cramps and unlocalized pain can occur. And when you operate on these patients you would see extensive lesions throughout the peritoneum. You would often see non-specific symptoms in young people. It is very difficult to diagnose endometriosis in this population but luckily the treatment of pain and endometriosis often are the same, so you can treat endometriosis when you want to treat pain. Non-steroid anti-inflammatory drugs and combined oral contraceptives are the easiest treatment options. New medications are being developed as well. Take pain seriously and do not normalize it.

EAD: What would you advise young doctors in terms of education as a pioneer in the surgery of endometriosis?

DM: There are a few centres and mentors that can educate you on endometriosis. It all depends on your goals. If you want to do research, try to find out if these people are available and join their group. Find someone with many papers and a research facility. If you get connected with one person, your network will get bigger. There are many types of training and many kinds of different people who are involved in endometriosis so you wouldn't want to get stuck with only one person. You would have to choose people whether you want to do clinic or surgery.



FROM THE LAST THREE MONTHS

1. Comparison of immunohistochemical characteristics of endometriomas with non-endometriotic benign ovarian cysts

Eur Rev Med Pharmacol Sci 2022 Oct;26(20):7594-7599. doi: 10.26355/eurrev_202210_30034. F T Cagiran 1, Z Kali, P Kirici, O Celik PMID: 36314331 DOI: 10.26355/eurrev_202210_30034

Abstract

Objective: The aim of the study was to investigate the existence of neuroendocrine cells and to compare the density of those in normal ovarian tissue, endometriotic and non-endometriotic benign ovarian cysts.

Patients and methods: Twenty patients with the diagnosis of endometrioma and 30 control subjects consisting of ovarian serous cystadenoma (n=10), ovarian mucinous cystadenoma (n=10) and normal ovarian tissue (n=10) were included. The tissues were prepared and assessed according to staining density by using the H-score method.

Results: Tissues with mucinous cystadenoma were significantly more stained with PAS and VanGieson, when compared to women with endometrioma. Macrophage deposition was higher in cyst samples with endometrioma and in normal ovarian tissue when compared to serous cystadenoma and mucinous cystadenoma. Normal ovarian tissue was significantly more stained with PGP9.5, NSE and SYN when compared to endometrioma and non-endometriotic benign ovarian cyst. PGP9.5 staining was higher in normal ovarian tissue when compared with endometriotic lesions (p<.001). Endometrioma samples were significantly more stained with p53 when compared to non-endometriotic cysts and normal ovarian tissue. c-Kit staining was mild and not statistically significant among all groups.

Conclusions: During endometrioma transformation, expression intensity of neuroendocrine markers decreases compared to normal ovarian tissue and other benign ovarian cysts.

2. The Phytochemical Profile and Biological Activity of Malva neglecta Wallr. in Surgically Induced Endometriosis Model in Rats

Molecules. 2022 Nov 15;27(22):7869. doi: 10.3390/molecules27227869. Esra Küpeli Akkol 1, Büşra Karpuz 2, Gizem Türkcanoğlu 1, Fatma Gül Coşgunçelebi 1, Hakkı Taştan 3, Michael Aschner 4, Anurag Khatkar 5, Eduardo Sobarzo-Sánchez 6 7 PMID: 36431970 PMCID: PMC9695446 DOI: 10.3390/molecules27227869

Abstract

Leaves and aerial parts of Malva neglecta Wallr. have been traditionally used in Anatolia for the treatment of pain, inflammation, hemorrhoids, renal stones, constipation, and infertility. This study investigated the effects of M. neglecta leaves in a rat endometriosis model. The dried plant material was extracted with n-hexane, ethyl acetate, and methanol, successively. Experimental endometriosis was surgically induced in six-week-old female, non-pregnant, Wistar albino rats by autotransplant of endometrial tissue to the abdominal wall. After twenty-eight days, rats were evaluated for a second laparotomy. Endometrial foci areas were assessed, and intraabdominal adhesions were scored. Rats were divided into five groups as control, n-hexane, ethyl acetate, methanol, and aqueous extracts, as well as reference. At the end of the treatment, all rats were sacrificed and endometriotic foci areas and intraabdominal adhesions were re-evaluated and compared with the previous findings. Moreover, peritoneal fluid was collected to detect tumor necrosis factor- α (TNF- α), vascular endothelial growth factor (VEGF), and interleukin-6 (IL-6) levels, and cDNA synthesis, and a quantitative real-time polymerase chain reaction (PCR) test was done. The phytochemical content of the most active extract was determined using High-Performance Liquid Chromatography (HPLC). Both endometrial volume and adhesion score decreased significantly in the group treated with methanol extract. In addition, significant decreases were observed in TNF- α , VEGF, and IL-6 levels in animals administered methanol extract. HPLC results showed that the activity caused by the methanol extract of M. neglecta was due to the polyphenols. Taken together, these novel findings indicate that M. neglecta may be a promising alternative for the treatment of endometriosis.

3. Serum kisspeptin levels in deep-infiltrating, ovarian, and superficial endometriosis: A prospective observational study

Observational Study Medicine (Baltimore). 2022 Nov 11;101(45):e31529. doi: 10.1097/MD.000000000031529. Mesut Önal 1, Pervin Karli 2, Ayşe Zehra Özdemir 1, Adem Kocaman 3, Yunus Katirci 1, Gülnur Çoban 1, Gülen Kübra Nakişli 1, Yeşim Civil 3, Bahattin Avci 4 PMID: 36397399 PMCID: PMC9666188 DOI: 10.1097/MD.00000000031529

Abstract

The diagnosis of endometriosis may delay for many years due to non-deterministic symptoms and avoiding surgical interventions. Kisspeptins are hormones that interact with endometrial tissue to limit invasions during placentation and various cancers and are suggested to be also associated with endometriosis. This study evaluated if serum kisspeptin levels are associated with the invasion depth in endometriosis. Forty patients between 18 and 45 years of age and admitted to a tertiary-care Obstetrics and Gynecology Department between 2020 and 2021 with a diagnosis of endometriosis, and 40 patients without endometrioma were included in the study. Demographic, obstetric, clinical, and biochemical characteristics were evaluated in

patients with superficial (SE) and deep infiltrating (DIE) endometriosis and healthy controls. Twenty patients (50%) had SE, 14 (35%) had DIE, and 22 (55%) had endometrioma in the patient group. Fertility rates were higher among controls, but similar between patients with SE and DIE. CA125 levels were significantly higher in the DIE group. SE and DIE groups had similar kisspeptin values, significantly higher than controls. CA125 and kisspeptin levels were not correlated in study groups. Serum kisspeptin levels were significantly different between endometriosis patients and healthy controls. However, kisspeptin levels were unable to differentiate endometriosis severity. Our results suggest that kisspeptins might play a role in the pathogenesis of endometriosis, which needs further assessment in more comprehensive studies.

4. The Role of Inflammatory Markers in the Diagnosis of Extraperitoneal Endometriosis

Journal of Experimental and Clinical Medicine Year 2022, Volume 39, Issue 4, 1004 - 1007, 29.10.2022 Selim GÜLÜCÜ Neşet GÜMÜŞBURUN

Abstract

OBJECTIVE: This study was concerned with the examination of patients who underwent surgery for subcutaneous endometriosis in our clinic and the relationship between subcutaneous endometriosis and inflammatory markers.

MATERIALS AND METHODS: Patient demographics and information on history and duration of previous surgery, lesion size, number of lesions, location, recurrence, symptoms, type and number of deliveries, recurrence status, and imaging method were recorded. Laboratory analysis recorded TSH, blood count (Hb), WBC, mean platelet volume (MPV), neutrophil/lymphocyte ratio (NLR), monocyte/platelet ratio (MPR), lymphocyte/monocyte ratio (LMR), platelet/lymphocyte ratio (PLR) and CA -125 values of patients. RESULTS: The study included 28 patients and it was found that the mean age of the patients was 32.67±5.56 years. Five (17.9%) and 18 (64.3%) of the patients complained of a palpable mass and cyclic pain, respectively. Five patients (17.9%) were asymptomatic. Endometriosis associated with the scar line was localized in 18 (64.3%) of the patients. In three (10.7%) of the patients, the endometriosis was localized in the perineal line and in 7 (25%) of the patients in the rectus abdominis. No significant difference was found in the patients' routine laboratory results and inflammatory markers.

CONCLUSION: In the present study, there was no significant association between the levels of inflammatory markers in patients who underwent surgery for subcutaneous endometriosis at different sites and with different symptoms.

5. Effects of polyamine synthesis enzymes on angiogenesis and apoptosis during endometriosis

Caglar Yildiz1, Veysel Kenan Celik1, Begum Kurt1, Serkan Kapancık2, Hasan Kılıcgun3 DOI: 10.5603/GP.a2022.0097

Abstract

Objectives: Since we assumed that endometriosis is a benign cell division disorder, our study was conducted to investigate the effects of the relationships between polyamine synthesis and angiogenesis in the formation of endometriosis.

Material and methods: Thirty-five patients with endometriosis and 35 healthy female women were included in the study. The patient and the control groups were compared regarding the blood levels of agmatine, argininecarboxylase (ADC), ornithinecarboxylase (ODC), agmatinase, arginase, ornithine, and the vascular endothelial growth factor (VEGF).

Results: There is a statistically significant difference between the patient and the control groups regarding the agmatinase, arginase and VEGF levels (higher in the patient group) (p < 0.05). There is no statistically significant difference between the patient and the control groups regarding the ODC, ornithine and the ADC levels (p > 0.05). There is a statistically significant difference between the patient and the control groups regarding the agmatine levels (higher in the control group) (p < 0.05).

Conclusions: The increase in the serum levels of polyamine synthesis enzymes may contribute to the formation of endometriosis. It is anticipated that the study of the relationship between enzymes and molecules in the polyamine synthesis pathway and angiogenesis in patients with endometriosis will contribute to the literature.

6. Is the presence of deep infiltrative endometriosis underestimated in the surgical management of endometriosis?

Ginekologia Polska Sabahattin Anil Ari1, Ali Akdemir2, Gurdeniz Serin3, Murat Ulukus2, Fatih Sendag2 DOI: 10.5603/GP.a2022.0150

Abstract

Objectives: The aim of the study was to determine the presence of deep infiltrative endometriosis (DIE) in the surgical management of endometriosis.

Material and methods: Operation notes and histopathological reports of women with endometriosis were retrospectively analyzed in the Ege University Hospital between 2008 and 2018. A total of 191 women with suspicious of endometriosis but without clinical signs of DIE were enrolled in the study. Laparoscopic diagnosis of DIE was compared with histopathological reports. There was no histopathology before surgery. Endometriosis was suspected only based on symptoms.

Results: A total of 213 lesions that were thought to be DIE were removed from 191 women with endometriosis. Among these 213 lesions, 179 specimens were reported as endometriosis and 34 lesions as fibro-adipose tissue. Forty-nine right uterosacral ligaments were excised, and endometriosis was detected in 44 out of 49 specimens. Histopathological examination of 45 left uterosacral ligaments revealed endometriosis in 35 specimens. Finally, 25 endometriotic nodules were removed from the rectovaginal space, and 22 of these were verified as endometriosis by a pathologist. The positive predictive value of laparoscopic

visualization for DIE in the group suspected of endometriosis but without any clinical findings of DIE was 84%.

Conclusions: Women with the suspicious of endometriosis, qualified to surgery, because of infertility or pain, should be prudently investigated to confirm or to exclude coexistence of DIE even if no preoperative sign of DIE was observed to provide complete resection. Otherwise, DIE continues to grow, causes pain postoperatively, and complicates subsequent surgery.

7. Telemedicine and Artificial Intelligence in the Management of Endometriosis: Future Forecast Considering Current Progress

GebFra Science | Letter to the Editor Authors Cihan Kaya1, Taner Usta2, Engin Oral3

8. Validation Of Turkish Version Of Quality Of Life Questionnaire For Women With Endometriosis: Endometriosis Health Profile Questionnaire – Ehp-30

ABSTRACT ONLY | VOLUME 118, ISSUE 4, SUPPLEMENT, E222, OCTOBER 01, 2022 Pinar Yalcin Bahat, M.D. Miray Nilufer Cimsit Kemahli, MD Ezgi Darici, MD Burak Yücel, MD Engin Oral, MD, Prof DOI:https://doi.org/10.1016/j.fertnstert.2022.08.630



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