



**ENDOMETRIOSIS
BULLETIN
JULY 2022 /
ISSUE XXII**



**Special
Interview**

SELECTED ARTICLES

**Endometriosis and Isthmocele:
Common or rare?**

**Relationship between endometriosis
and atherosclerosis**

**Robotic surgery in the
management of endometriosis**



David Redwine

PREFACE

Hello,

We are with you again with our 22nd issue.

In this new issue of our quarterly newsletter, you can find details about current advancements in endometriosis and adenomyosis and updates on our society's activities. You will find abstracts on various topics such as, the relationship between endometriosis and infertility, impact of race/ethnicity on endometriosis, the coexistence of endometriosis and isthmocele, the risk of heart diseases in patients with endometriosis, the place of robotic surgery in endometriosis, and a systematic review on inguinal endometriosis.

In May, the book "**Endometriosis and Adenomyosis-Global Perspectives Across the Lifespan**", edited by our founding president **Prof Engin Oral, MD**, was published by Springer publishing house, which included scientific contribution of 87 authors from 19 countries. Our president **Prof. Taner Usta, MD**, **Fitnat Selcuki, MD**, and **Ezgi Darici, MD** from our country have also contributed to this book.

On May 15, TJOD Istanbul Branch's '**Where are we with Endometriosis in 2022**' meeting was organized by **Prof Engin Oral, MD** and one of our board members **Assoc. Prof. Hale Goksever Celik, MD**. In this meeting, our president **Prof Taner Usta, MD** had a presentation on '**Surgical treatment of endometriosis and pain**'.

On **May 28, World Menstrual Hygiene Day**, the first results of the project on menstrual hygiene and awareness level throughout Turkey, implemented by our society together with Hayat Chemistry and Bayer companies, were shared with the press. Detailed results of this population-based survey, which is the first in this field, will be shared in the upcoming days.

On 27-28 May, the 3rd International Endometriosis School Istanbul, chaired by **Prof. Engin Oral, MD**, **Prof. Taner Usta, MD**, and **Prof. Ertan Saridogan, MD** took place fruitfully. This meeting had theoretical and laparoscopic training by experts in the field of endometriosis from Turkey and abroad. The applied laparoscopic surgery training in the animal laboratory had both national and international participants.

The 14th EndoAcademy meeting was held in Adana on June 12. **Prof. Turan Cetin, MD** and **Assoc. Prof. Dr. Cihan Kaya**, chaired this meeting. Substantial professors attended the session, which covered the diagnosis, medical and surgical treatment of endometriosis with a focus on endometrioma, and its relationship with infertility and pelvic pain. It was a successful meeting that was attended and benefited by many physicians dealing with endometriosis from Adana and surrounding cities.

At the **European Endometriosis League (EEL)** congress held in Bordeaux, France, **Prof. Engin Oral MD**, conveyed the latest developments in the field with his presentation on "**Should AMH be requested from every patient with endometriosis?**". Junior group member of our society **Elif Gökür Topçu, MD** gave a presentation about the activities that young physicians can take part in within international endometriosis study groups.

During this period, the webinar series organized by the European Endometriosis League continued with the presentation of **Christian Becker** on May 10.

Endo-Specialist interview guest of this month's issue was **David Redwine, MD** from USA. **Miray Nilüfer Cimşit Kemahlı, MD**, one of the junior group members of our society, conducted this valuable interview with him.

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

Best regards,
Prof. Taner Usta, MD
President of the Endometriosis & Adenomyosis Society

Turkish Endometriosis & Adenomyosis Society Board of Directors 2019-2022

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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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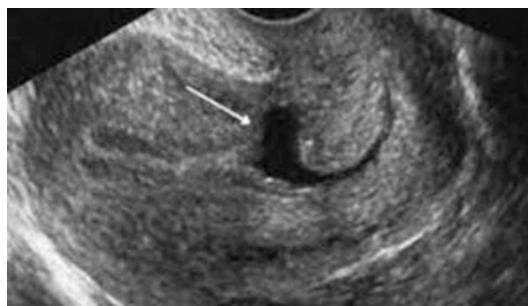
A SELECTED ARTICLES

1 Endometriosis and Isthmocele: Common or Rare?

Gulz M, Imboden S, Nirgianakis K et al. *J. Clin. Med.* 2022, 11, 1158

Abstract

Higher cesarean section rates and better ultrasound diagnostics have led to a more frequent diagnosis of isthmocele, a cesarean scar defect. Sometimes, endometriosis is found in the isthmocele, but simultaneous extrauterine endometriosis and endometriosis in the isthmocele have not yet been reported. Additionally, the surgical technique to repair the isthmocele is the subject of ongoing controversy. The aim of this study is to analyze a possible correlation between uterine scar (isthmocele) endometriosis and extrauterine endometriosis and to investigate the outcome of laparoscopic isthmocele resection in the rendezvous technique. In this single-center retrospective study, we included 83 women of reproductive age with symptomatic isthmocele undergoing laparoscopic isthmocele repair in rendezvous technique from 2004 to 2020 at the University of Bern. We collected data on patient and surgical characteristics as well as on postoperative outcomes (symptoms, further pregnancy, and pregnancy outcomes) retrospectively. We analyzed and compared these data for patients with and without endometriosis. Endometriosis was diagnosed during surgery in 22 out of 83 operated patients (26.5%). Diagnosis of isthmocele endometriosis (n = 9, 11%) was significantly higher in patients with extrauterine endometriosis (n = 6, p = 0.004). While the duration of surgery was significantly longer for patients with endometriosis (p = 0.006), the groups did not differ with regard to blood loss or complications. In addition, both groups showed similar indications for isthmocele repair (infertility, abnormal uterine bleeding, or dysmenorrhea). Surgery significantly improved abnormal uterine bleeding (χ^2 p < 0.001), dysmenorrhea (χ^2 , p = 0.03), and infertility (χ^2 , p < 0.001).



Regardless of the presence of endometriosis, 25 of 40 (63%) infertile patients became pregnant after surgery. In one out of eight pregnancies, however, we observed scar complications during pregnancy such as uterine scar pregnancy (n = 3), uterine scar dehiscence (n = 3), and placenta previa (n = 1). Endometriosis is a non-negligible intraoperative finding in patients with symptomatic isthmocele. The laparoscopic approach in the rendezvous technique is safe and effective. Therefore, this method should be recommended, especially in women with secondary infertility, and preoperatively simultaneous endometriosis resection should be discussed with the patient. In follow-up, postoperative pregnancies have to be monitored with care.

Keywords: isthmocele; uterine scar defect; laparoscopic isthmocele repair; rendezvous technique; endometriosis; infertility

2 Endometriosis promotes atherosclerosis in a murine model

Mamillapalli R, Toffoloni N, Habata S, et al. *Am J Obstet Gynecol.* 2022

Background: Epidemiologic studies have demonstrated an association between endometriosis and the subsequent development of cardiovascular disease. The direct effect of endometriosis on the progression of atherosclerosis, if any, has not been previously characterized. Endometriosis leads to systemic inflammation that could have consequences for cardiovascular health. Here, we reported the effects of endometriosis on the development of atherosclerosis in a murine model.

Objective: This study aimed to determine the contribution of endometriosis in promoting cardiovascular disease in a murine model of endometriosis.

Study design: Endometriosis was induced in 18 apolipoprotein E-null mice, the standard murine model used to study atherosclerosis. Mice of the same strain were used as controls (n=18) and underwent sham surgery without inducing



endometriosis. The formation of endometriotic lesions was confirmed after 25 weeks of induction. Atherosclerotic lesions were subjected to hematoxylin and eosin staining followed by measurement of the aortic root luminal area and wall thickness. The whole aorta was isolated, and Oil Red O staining was performed to quantify the lipid deposits or plaque formation; moreover, biochemical assays were carried out in serum to determine the levels of lipids and inflammatory-related cytokines.

Results: Apolipoprotein E mice with endometriosis exhibited increased aortic atherosclerosis compared with controls as measured using Oil Red O staining (7.9% vs 3.1%, respectively; $P=.0004$). Mice with endometriosis showed a significant 50% decrease in the aortic luminal area compared with sham mice (0.85 mm² vs 1.46 mm²; $P=.03$) and a significant increase in aortic root wall thickness (0.22 mm vs 0.15 mm; $P=.04$). There was no difference in the lipoprotein profile ($P<.05$) between mice with endometriosis and sham mice. The serum levels of inflammatory cytokines interleukin 1 alpha, interleukin 6, interferon gamma, and vascular endothelial growth factor were significantly ($P<.05$) increased in the endometriosis mice.

Conclusion: Our study used a murine model to determine the effect of endometriosis on atherosclerosis. Inflammation-related cytokines interleukin 1 alpha, interleukin 6, interferon gamma, and vascular endothelial growth factor (angiogenic factor) released by endometriotic lesions may contribute to the increased cardiovascular risks in women with endometriosis. To reduce the risk of cardiovascular disease, early identification and treatment of endometriosis are essential. Future treatments targeting inflammatory cytokines may help reduce the long-term risk of cardiovascular disease in women with endometriosis.

Keywords: apolipoprotein E mice; atherosclerosis; cardiovascular disease; cytokines; endometriosis; inflammation; plaques.

3 Revisiting the impact of race/ethnicity in endometriosis

Bougie O, Nwosu I, Warshafsky C. *Reprod Fertil.* 2022;3(2):R34-R41.

Abstract

Endometriosis is a chronic, multisystemic disease often presenting with significant phenotypic variation amongst patients. The impact of race/ethnicity on the prevalence of endometriosis, as well as disease presentation, is a question of interest which has been explored for the last century. This narrative review explores the historical perspective of endometriosis and race/ethnicity as well as the evidence available to date. Furthermore, we discuss the potential implication of the bias perpetuated on this topic, specifically in the areas of medical education, research, and clinical care. In consideration of these intersecting realms, we suggest priorities for future consideration of race/ethnicity as it pertains to the delivery of care for endometriosis patients.

Lay summary: The relationship between race/ethnicity and endometriosis has been explored for over a century. Historical bias and poorly conducted research have led to the idea that this condition is less likely to be diagnosed in certain racial groups, such as Black women. We review the current state of evidence



and highlight important limitations within medical education and research on this topic. Finally, we advocate for a shifting viewpoint as we strive to deliver equitable and outstanding care for all endometriosis patients.

Keywords: endometriosis; ethnicity; pelvic pain; race.

4 Infertility workup: identifying endometriosis

Pirtea P, Vulliemoz N, de Ziegler D, et al. *Fertil Steril.* 2022; 11;S0015-0282(22)00205-9.

Abstract

Endometriosis was classically diagnosed during diagnostic laparoscopies, which used to be routinely performed up until a decade ago or so. This practice fitted with the long-held belief that surgery was the gold standard for diagnosing endometriosis. Today, the abandon of routine diagnostic laparoscopies-in favor of assisted reproductive technology-first therapeutic approaches-has created a void for diagnosing endometriosis. Modern-day imaging techniques-ultrasound and magnetic resonance imaging-when used with a systematic approach have offered a reliable replacement option for diagnosing endometriosis. In infertility, endometriosis should be identified or excluded on the basis of past history or confirmation or exclusion suspicion on the basis of history and/or physical examination.



Keywords: Endometriosis; MRI; diagnosis; infertility; ultrasound.

5 Inguinal endometriosis: A systematic review.

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

Abstract

Inguinal endometriosis is a very rare entity with uncertain pathophysiology, that poses several diagnostic and therapeutic challenges. This study aimed to summarize published literature on the diagnosis and treatment of this condition. Thus, a systematic literature search was conducted in PubMed/MEDLINE, Scopus and the Cochrane Library. An effort was made to numerically analyze all parameters included in case reports and retrospective analyses, as well. The typical and atypical features of this condition, investigations used, type of treatment and histopathology were recorded. More specifications about the surgical treatment, such as operations previously performed, type of surgery and treatment after surgery have been acknowledged. Other sites of endometriosis, the presence of pelvic endometriosis and the follow-up and recurrence have been also documented. Overall, the search yielded 61 eligible studies including 133 cases of inguinal endometriosis. The typical clinical presentation includes a unilateral inguinal mass, with or without catamenial pain. Transabdominal or transvaginal ultrasound was typically used as the first line method of diagnosis. Groin incision and exploratory surgery was the treatment indicated by the majority of the authors, while excision of part of the round



ligament was reported in about half of the cases. Chemotherapy and radiotherapy were initiated in cases of coexisting endometriosis-related neoplasia. Inguinal recurrence or malignant transformation was rarely reported. The treatment of inguinal endometriosis is surgical and a long-term follow-up is needed. More research is needed on the effectiveness of suppressive hormonal therapy, recurrence rate and its relationship with endometriosis-associated malignancies.

6 The current role of robotic surgery in endometriosis management

Andres MP, Souza C, Villaescusa M et al. Expert Review of Endocrinology & Metabolism, 17:1, 63-73.

Abstract

Introduction: Endometriosis is a chronic inflammatory disease that affects approximately 10%-15% of women of childbearing age. Laparoscopic surgery is the preferred surgical approach. Recently, robotic surgery has been used for benign gynecologic surgery, but its role in the treatment of endometriosis is still unknown.

Areas covered: We included studies that evaluated the outcomes of robotic surgery for endometriosis. Using the keywords 'endometriosis' and 'robotics', a comprehensive literature search on PubMed, Embase, and the Cochrane Library was performed in July 2021.

Expert opinion: Robotic surgery for endometriosis has similar outcomes as conventional laparoscopy, with no evidence of increased complication rates. Despite the non-inferiority of the surgical route, the associated costs of robotic surgery limit its availability. Rapid development of robot-assisted surgery necessitates long-term prospective randomized controlled trials. However, the limitations of robotic surgery should not be overlooked. If robotic surgery can facilitate the spread of minimally invasive surgery, it will be necessary to evaluate the cost, availability, complexity of the lesions, and most importantly, the results of patient satisfaction and values of value-based medicine.



Keywords: Deep endometriosis; endometriosis; laparoscopy; robotic surgery; surgical treatment.

B NEWS FROM OUR SOCIETY

PAST ACTIVITIES

The second of our webinar series 'Experts Discuss Endo-Adeno with Real Cases' took place on the 5th of April. Prof. Yucel Karaman, MD, Prof. Umit Inceboz, MD, Prof. Bulent Berker, MD participated in the webinar which was moderated by Prof. Engin Oral, MD.

GERÇEK OLGULARLA ENDO&ADENO UZMANLAR TARTIŞIYOR

Moderatör
Prof. Dr. Engin Oral

Panelist
Prof. Dr. Yücel Karaman

Panelist
Prof. Dr. Ümit Inceboz

Panelist
Prof. Dr. Bülent Berker

Panelist
Doç. Dr. Yusuf Aytac Tohma

5 NİSAN 2022 SALI | 21:00 - 22:30

LIVE WEBINAR

KAYIT OLMAK İÇİN
www.ftsakademi.org

www.info@endometriozisderneği.org | OLGULAR: EndoGenç Grup / Uzm. Dr. Ayşegül BESTEL

EndoSchool

On the 8th of April as a part of our EndoSchool project Assoc. Prof. Pinar Bahat, MD and Hümeyra Ozkaya, MD visited Robert College where they gave a seminar on menstrual hygiene and endometriosis.

ENDO KULDA FARKINDAYIM

Sağlıklı genç bireyler ile daha sağlıklı ve bilinçli bir toplum olmak için hep birlikte el ele...

12:30

8 Nisan 2022

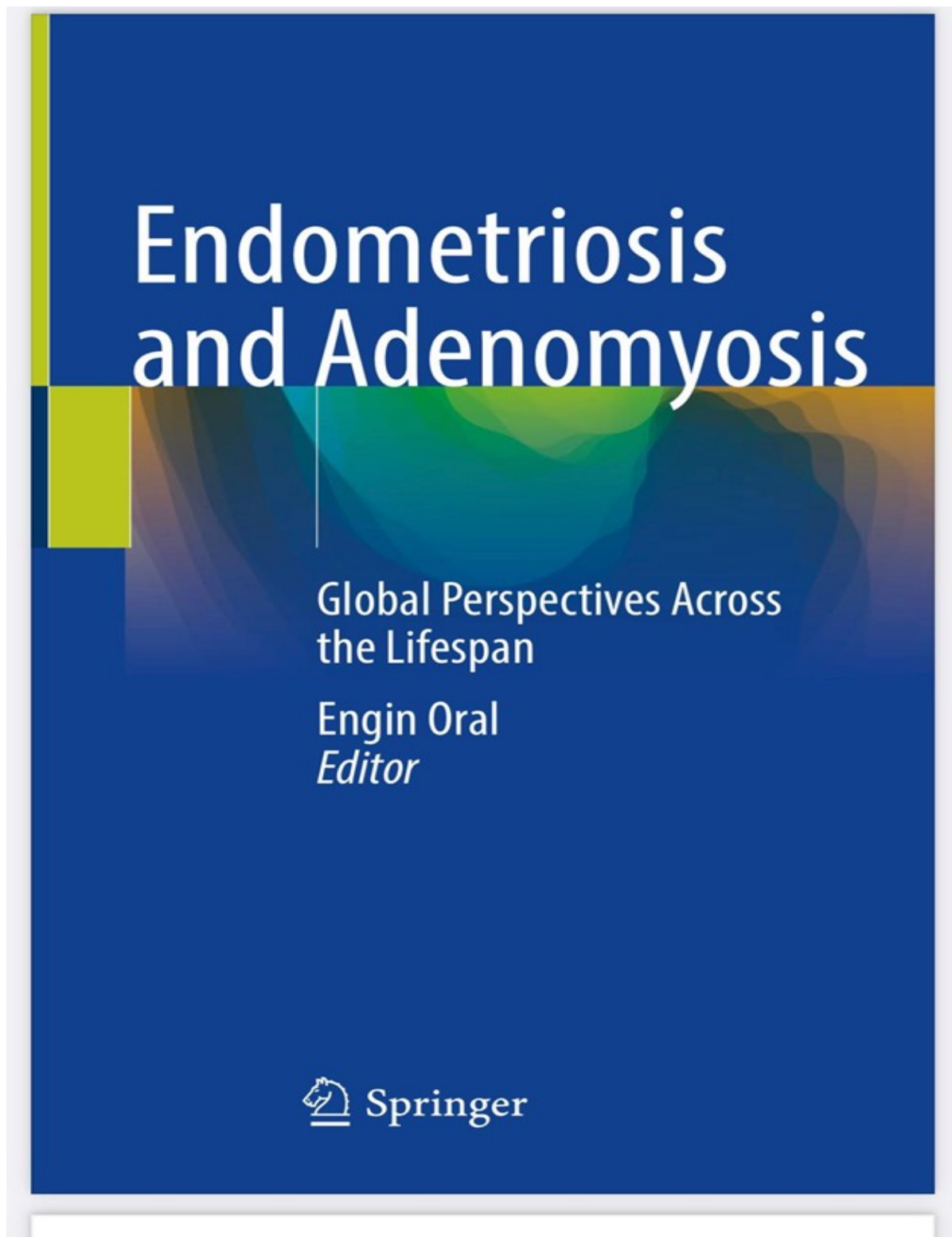
Robert Koleji İstanbul

Doç. Dr. Pinar Yalçın Bahat

Dr. Hümeyra Özkaya

In May 2022 the book titled as 'Endometriosis and Adenomyosis – Global Perspectives Across the Lifespan' has been published by Springer, which was edited by our founding president **Prof. Engin Oral, MD** where 87 authors from 19 different countries participated with their work. A great deal of effort went into the creation of this book and our president **Prof. Taner Usta, MD** and from our junior group **Fitnat Selcuki, MD** and **Ezgi Darici, MD** contributed as well.

<https://link.springer.com/book/9783030972356>



Engin Oral
Editor

Endometriosis and Adenomyosis

Global Perspectives Across the Lifespan

 Springer

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On the 28th of May, which is World Menstrual Hygiene Day, the first results of our joint survey evaluating awareness on menstrual health and hygiene with Hayat Chemistry and Bayer has been made available to the media.

Dünya Adet Hijyeni Günü'nde Türkiye'nin Regl Farkındalık Araştırması Raporu yayınlandı

BEDEN SAĞLIĞI



The meeting titled as 'Where are we with endometriosis in 2022?' organized by TJOD Istanbul Branch, **Prof. Engin Oral, MD** and **Assoc. Prof. Hale Goksever Celik, MD** took place on the 15th of May. Our president **Prof. Taner Usta, MD** gave a talk on surgical treatment of endometriosis and related pain.



15 Mayıs 2022, Pazar



09.00-14.30

Hilton İstanbul Maslak

ENDOMETRİOZİSTE 2022 YILINDA NEREDEYİZ ?

Toplantı Sorumlusu: Engin Oral, Ayşe Seyhan, Hale Göksever Çelik

09.00-09.50 Kahvaltı

09.50-10.00 TJOD İstanbul Derneği Başkan konuşması
Recep Has

10.00-11.40 BİRİNCİ OTURUM
Oturma Başkanları: Altay Gezer, Özlem Dural

10.00-10.20 Endometriozis ilişkili infertilite: Cerrahi tedavinin yeri
Yücel Karaman

10.20-10.40 Endometriozis ilişkili infertilite: Yardımcı üreme tekniklerinin yeri
Bülent Urman

10.40-11.00 Endometriozis ilişkili ağrı: Medikal tedavi
Engin Oral

11.00-11.20 Endometriozis ilişkili ağrı: Cerrahi tedavi
Taner Usta

11.20-11.40 Adenomyozis tanı ve/veya yönetimi
Süleyman Engin Akhan

11.40-12.10 Coffee Break

12.10-12.30 Apikal prolapsusta yeni bir yaklaşım: Self Retaining Support (SRS) implant operasyonu
Fuat Demirci

ATAK
CERRAHI

12.30-14.30 İKİNCİ OTURUM

Panel (Olgular eşliğinde endometriozise yaklaşım tartışılacaktır)

Moderatör: *Engin Oral*

Panelistler: *Yücel Karaman, Bülent Urman, Süleyman Engin Akhan, Taner Usta, Ayşe Seyhan, Hale Göksever Çelik*

www.tjodistanbul.org

Endometriosis School Istanbul, which has been organized several times over the years with the participation of international experts took place this year on 27-28th of May, which was chaired by **Prof. Engin Oral, MD, Prof. Taner Usta, MD and Prof. Ertan Saridoğan, MD**. National and international participants who are experts in their fields contributed to this meeting with their expertise. In addition to theoretical laparoscopy training, hands-on surgical training took place at an animal laboratory.





3rd International
ENDOMETRIOSIS
SCHOOL Istanbul

May 27-28, 2022
Medtronic Innovation Center
Istanbul - Turkey

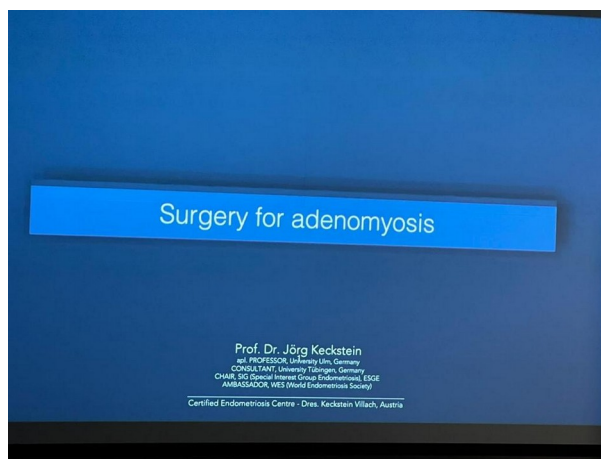
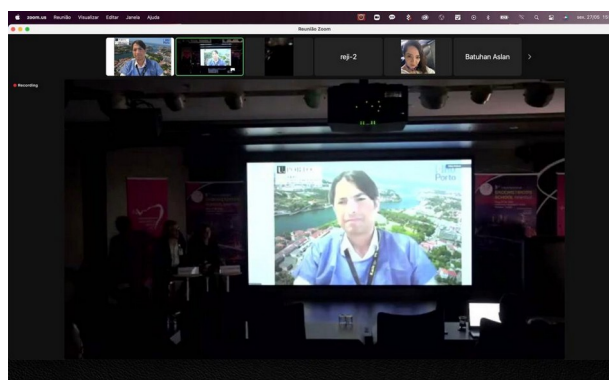
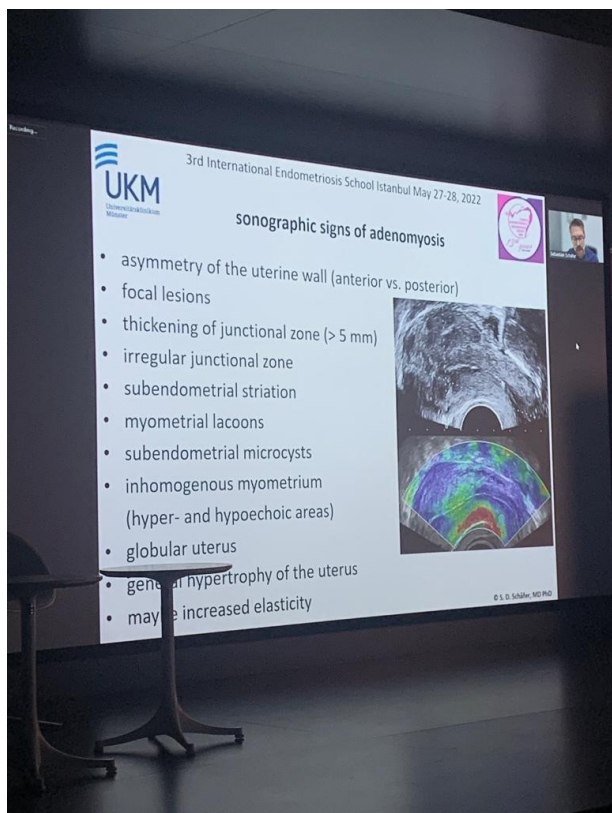
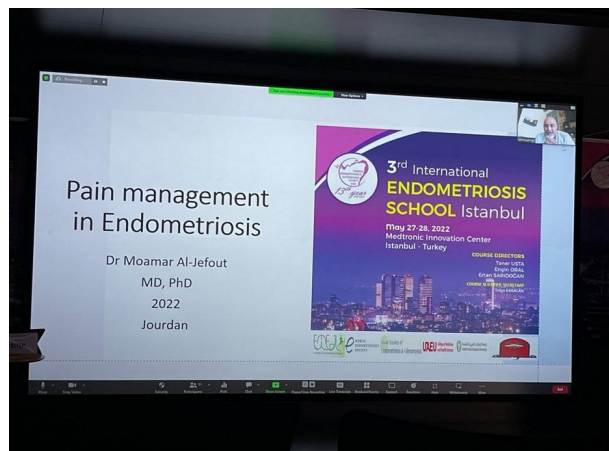
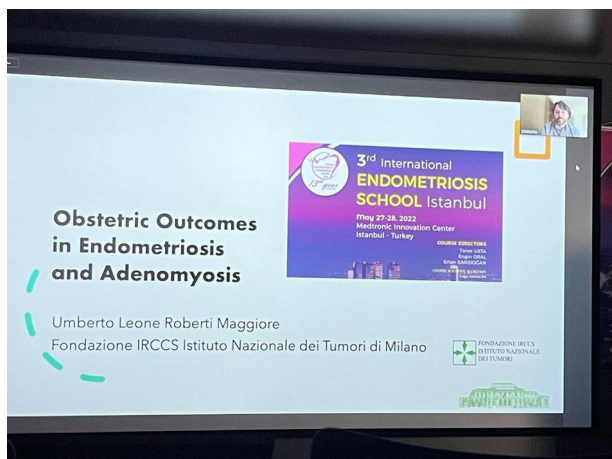
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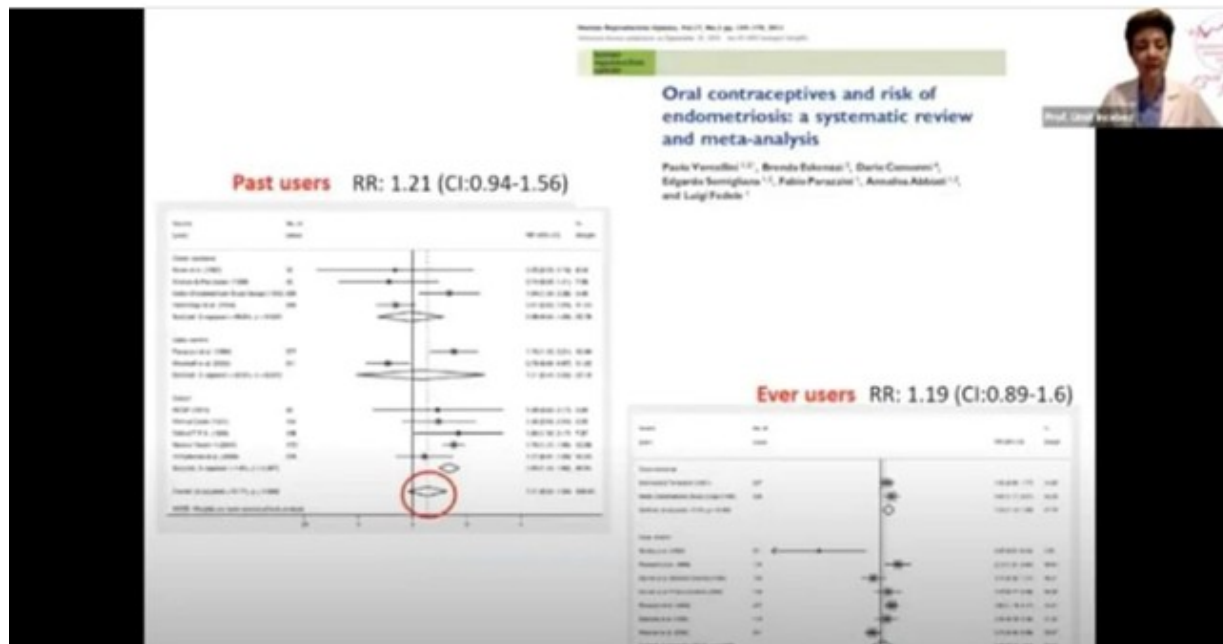


14th EndoAcademy Meeting took place in Adana on the 12th of June. The meeting was chaired by **Prof. Turan Cetin, MD** and **Assoc. Prof. Cihan Kaya, MD**. At this meeting diagnosis, medical and surgical treatment of endometriosis with a focus on endometrioma, infertility and pelvic pain were discussed. Many physicians interested in endometriosis from Adana and from the region participated in the meeting where they listened to experts in the field.





On Sunday the 20th of June our vice president **Prof. Umit Inceboz, MD** gave a web-talk on 'Management of endometriosis in women of post-reproductive years' to physicians from Afghanistan.



On Thursday the 23rd of June **Prof. Engin Oral, MD** participated in the 2nd East African Endometriosis Conference with a talk on 'Management of endometriosis in women of 40 years of age'.

**2ND EAST AFRICAN
 ENDOMETRIOSIS CONFERENCE**
 SAROVA PANAFRIC HOTEL, NAIROBI - KENYA
 22ND - 24TH JUNE, 2022

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 German Academic Exchange Service

EEL
 European Endometriosis League

German Society of Women Health in Developmental Cooperations

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On 25th of June our president **Prof. Taner Usta, MD** gave a talk on Thoracic Endometriosis as a part of the meeting on 'Endometriosis: An Unrecognized Burden in African Women' organized by The African Endometriosis Awareness & Support Group.



The African Endometriosis Awareness & Support Group cordially invite you to this international conference on Endometriosis.

THEME:
ENDOMETRIOSIS: AN UNRECOGNIZED BURDEN IN AFRICAN WOMEN

SPEAKERS:

 Linda G. Griffith Keynote	 Dr John Dulemba Robotics in Endometriosis	 Dr Abayomi Ajayi HIFU in the Management of Adenomyosis	 Dr Francisco Carmona Fertility Preservation in Endometriosis
 Dr Robert Zurawin Adolescent Endometriosis	 Dr Keith Isaacson Differentiating between Endometriosis and Adenomyosis	 Dr Harald Krentel How to establish a robust African Endometriosis Awareness Initiative: Lessons from EEL	 Dr Taner Usta Thoracic Endometriosis

PANELLISTS:

Dr Dickson Francis - Ghana	Dr Femi Olarogun - South Africa	
Dr Busola Amu - Qatar	Dr Julien Bakenga - France	Dr Habib Sadauki - Nigeria

10CPD POINTS

 **25TH JUNE 2022**  **10:00 AM** For enquiries, contact +234 807 760 6677

Venue: Civic Centre, Ozumba Mbadiwe Road, Opposite 1004, Victoria Island, Lagos.

This event is a hybrid event. To participate online, registration is required - <http://bit.ly/3M2uQDH>

C NEWS FROM THE WORLD OF ENDOMETRIOSIS

EEL WEBINAR Program 2022

European Endometriosis League (EEL) are continuing with their Webinars in 2022. In May Christian Becker held the Webinar on 'The ESHRE Guideline - What's Really New?'

A promotional graphic for an EEL webinar. At the top, the text 'EEL WEBINARS' is written in large, bold, dark blue capital letters. Below this is a circular portrait of a man with glasses and a light-colored shirt, identified as Christian Becker. The background of the graphic is dark blue with abstract, glowing light patterns. Below the portrait, the text 'Christian Becker, MD, PhD.' is displayed. Underneath that, the title 'THE ESHRE GUIDELINE - WHAT'S REALLY NEW?' is written in white capital letters. Further down, the text 'Moderator: Attila Bokor, MD, PhD' is shown. Below the moderator's name, the date 'DATE : 10 MAY 2022' and the time 'TIME : 7.00 PM CET' are listed. At the bottom of the graphic, the website 'live.euroendometriosis.com' is provided in white text.

EEL WEBINARS

Christian Becker, MD, PhD.

THE ESHRE GUIDELINE - WHAT'S REALLY NEW?

Moderator: Attila Bokor, MD, PhD

DATE : 10 MAY 2022

TIME : 7.00 PM CET

live.euroendometriosis.com

EEL Webinar series will continue for the rest of the year. For more information, visit <https://www.endometriosis-league.eu/home> or follow the European Endometriosis League or Euro Endo League accounts on social media.

6th EEC - France

The 6th European Endometriosis Congress took place on 16-17 June 2022 in Bordeaux, France. **Prof. Engin Oral, MD** participated the congress with a talk on 'Should we evaluate AMH for each endometriosis patient?'. Additionally, one of our junior members, **Elif Goknur Topcu, MD**, gave a talk on the international study groups and how young physicians could participate in these groups.





D INTERVIEW WITH AN 'ENDO SPECIALIST'



David Redwine

Interviewer: Nilufer Cimsit

Turkish Endometriosis & Adenomyosis Society (EAD): Dr. Redwine, you have been dealing with endometriosis for many years, can you please explain us how did your journey start with endometriosis?

David Redwine: My first wife had endometriosis. Dealing with her case was something totally different than what I was taught and read in the literature. It was like she had a different disease than what was described in the literature, which was at that time primarily concerned with infertility. My wife had various kinds of pain; painful intercourse, pain by just sitting around doing nothing, sharp stabbing pain etc. She did not respond well to birth control pills, and she didn't respond well to danazol. It became clear that all this notion of a good response to medicine that I was reading wasn't working in real life. At the time I was just beginning my private practice. She had a laparoscopy while I was in training where they found small endometriosis lesions and burned them. But, despite all that she was really no better and in fact I have had to diagnose her with endometriosis myself. She's been seen by ex-president of the American fertility society in Houston and the diagnosis was missed.

I made the diagnosis myself. When I went into practice, I was kind of tuned in the pelvic pain and I was taking these patients to surgery and expecting to see these little dots in the pelvis, at that time so-called black powder burn lesion, which were considered as the main lesions. But I was seeing things with different colors; things that had no color, gray, white, and/or yellow. All different colors except black powder. So, I decided to keep track of certain things in my own patients.

I was also interested in the origin of endometriosis. At that time, everybody was talking about Sampson's Theory. So, I thought to myself, I've got two main initial goals. First of which was to try to figure out how many different ways endometriosis can appear. I would evaluate the pelvis at the start of surgery. Most of the disease that I saw was white or clear, a very crude type of color classification scheme. My second focus was on the origin of endometriosis. I was trying to validate Sampson's Theory. If reflux menstruation occurs every month, then the pelvis should fill up like dandelions in a pasture. I did a simple anatomic pelvic mapping system, so that I could keep track of where the endometriosis was. It was kind of an early harbinger of the ENZIAN classification, which is also anatomically based. It was intuitive to me what pelvic involvement was, so I kept track of these patients. My plan was to keep track of what it looks like and where it is in the pelvis. Meanwhile I continued to deliver babies, cover the emergency room, go to staff meetings, deliver more babies, and operate endometriosis patients. After a while I had about 135 patients with descriptions of what the disease looked like and where the lesions were located in the pelvis. I thought to myself 135 patients is a pretty good number and eventually I ended up having operated over 3000 patients. I didn't know what was in store, but I sat down literally at the kitchen table with a handheld calculator and spreadsheets. My first wife was an accountant, so we had manual spreadsheets that I used to keep track of stuff. What I found was that the so-called black powder burn lesion was in the minority and more common in older patients whereas colorless lesions were seen earlier in life, in teenagers and in between you know there could be different appearances. I wrote this in a paper called the visual appearance of an endometriosis and how it changes over time. That was important because it expanded the surgical diagnosis of endometriosis. When I realized that most patients did not have the black powder burn lesions, I realized that most endometriosis apparently had been missed by physicians for many decades. Our understanding was deeply flawed because the diagnosis was based on the presence of the black powder burn lesion, which occurs primarily in older patients. When you go back in the literature, you find patient age groups were frequently between 30 and 50, which is when the black powder and lesion is predominant. So, it is like the self-fulfilling prophecy; if you look at older patients, you are going to find more black powder lesions and you would think that is the predominant manifestation, but it is not. So, this age-related evolution in color appearance of endometriosis was important. Second thing with the pelvic mapping study, I was interested in whether old age groups had more pelvic sights of endometriosis because if Sampson's Theory were operative you would expect aggressive disease and get more and more of it. What I found was that older age groups did not have more disease, in fact the line kind of went down, it certainly didn't go up. I said to myself "Oh man, we have major problems with this disease". I have just found something that was kind of a self-feeding thing and if somebody believes in Sampson's Theory, and observed an age related evolution in appearance they might and if they missed the early subtle lesions, then later did surgery and found that some of them evolved, they would think that it's a new disease and Sampson's Theory is correct and then if they were to re-operate that patient later, the lesions might have evolves in all appearance in a few more areas leading the surgeon to think Sampson's Theory is correct. So, you had this you know kind of two symbiotic errors of thought that combine to support a theory that just didn't make sense. I was living in a small town of 15,000 people just a general Ob & Gyn, still delivering babies, but I had this very important information that has escaped the profession literally for 70-80 years and was clearly a misunderstanding and I needed to tell the world. How do you tell the world, when you live in a small town, 150 miles away from the nearest highway? So, I did two things; first, I began to talk about endometriosis to just anybody, cashier at the grocery store, somebody sitting next to me on the bench, and second, I sent papers for publication. I had my first two publications in Fertility and Sterility. That's how it started, it started out of personal need, personal curiosity, then a desire to spread the word.

I knew as soon as the first biopsy I took came back as endometriosis, I knew at that point that I would be sitting here talking to you today because it was such important news that it was going to propel me into an academic career that I didn't seek but I gladly accepted, because it had to be done. The interesting thing is when I was doing my visual appearance of endometriosis study collection, I had to remove the disease to confirm endometriosis. As I remove the disease, my first way of treating it was laparotomy excision and frequently I would take biopsies through laparoscope to get a specimen frozen section and then perform the laparotomy and pelvic mapping. As time went by the initial laparoscopic biopsies that I took got bigger and bigger. After a while I thought "I can just do this all laparoscopically." It sounds crazy now, but I just dedicated myself to developing laparoscopic excision of endometriosis, which began because of the study of visual appearance but it evolved into now a new treatment and the magnification of the laparoscope made it better than laparotomy. I was armed with good information and a new effective surgical technique. During that time in my early career, I was delivering babies, operating on endometriosis patients in just a local area with patients from 50-100 miles radius. After a year or two, I had a patients come to me from across the mountains over the valley, a friend of a friend. I operated her and went back to delivering babies, covering emergency room, attended committee meetings. Then somebody came down from Portland. A friend of a friend again, I operated her, then I go back to delivering babies and then somebody came down from Canada. I've anticipated this. And this was before the internet, which indicates that there was some networking going on at that time. I knew what's happening was that the surgery was very affective, the reasons were not mysterious and if you do the surgery the word will get out. That's kind of an overview of how I got started. It started out as a personal mission and then it became a professional mission.

EAD: You are one of the pioneers of endometriosis surgery. Can you please tell us tips and tricks on how to avoid complications?

DR: When I came to the small hospital, the only laparoscopic equipment they had was an old Wolf Operating Laparoscope with a 3 mm channel and a pair of 3 mm scissors that went down with it. First, I started off doing sharp excision just with the scissors but then after a few years I reduced my operating times by 2/3. I think the 3 mm scissors was an important part of the whole story since they're smaller than these 5 mm Endo Shears and have smaller electrical footprints, so you can get the scissors into tighter spots and you can do meticulous fine dissection with a smaller instrument, there's less metal exposed so less chance of inadvertent electrical damage. I think one of the ways to reduce complications is to evaluate what kind of instrument you are using. Precise small instruments to me seem better than larger instruments that don't allow fine dissection and they expose more metal for more electrosurgical injury. That's a big part of reducing complications. Know your equipment and limitations and strength. Another thing is always start dissection laterally, outside the area of endometriosis, in normal tissue. With the 3 mm scissors, I had to take small steps. By taking small steps you can see what your next step is. Sometimes with the big scissors, before you know it, you go deeper than you want to go. The instrument you use is a big part of surgical complications, and obviously the experience of the surgeon and how they use their equipment are important. I used small scissors, took small steps and I was able to get around lesions. That's my simple recommendation for trying to avoid complications who just start.

EAD: Do you have any advice to young colleagues who plan to be endometriosis specialist in the future?

DR: You'd better become a surgical specialist for endometriosis soon because probably in 15-20 years there's going to be some kind of vaccine or some kind of targeted immunotherapy. Surgery potentially could be replaced by what is in the future. In the meantime, while we're waiting for these magic bullets, which are not hormonal, because it's clear the hormonal therapy is complete failure, excision is still going to be the best current treatment. You have to be passionate about something about surgery. You either have to be passionate from a personal experience of a family member or a friend with an endometriosis that makes you want to do it or as with many people, you just have to be passionate about doing good and difficult surgery. There's no question that endometriosis surgery is the most difficult surgery that can be done in the human body, when you think of all the other routine surgeries. Of course, I'm not talking about big major trauma and stuff like that. That is attractive to many people especially, when you are growing up as a little child you say "I wanna be a doctor, I wanna be a surgeon". If you do endometriosis surgery, when you leave the operating room, you know you're a surgeon. You just have to have a passion, like I said mine was a combination of personal passion and later professional passion. Professional passion involved doing the surgery and publishing papers. I had several roots of my passion for surgery and if you have passion for something then you will apply yourself diligently and you'll figure out how to make things work in your hands. Just because you see somebody saying something or you read something in a journal, that doesn't necessarily need to apply to your career or what you do. You have to find your own path and whatever that is, don't be afraid. Once you identify that, support it by passion, that's what you do.

EAD: Thank you very much for your time and valuable contributions.

E ARTICLES ON ENDOMETRIOSIS FROM OUR COUNTRY FROM THE LAST THREE MONTHS

1. Analysis of preoperative and postoperative quality of life, sexual function, and sleep in patients with endometriosis: a prospective cohort study.

Halici BNA, Aktoz F, Kabakci M, Kiran G, Ozcan P. Arch Gynecol Obstet. 2022 Apr 22. doi: 10.1007/s00404-022-06562-9.

Purpose: Endometriosis affects the quality of life, sleep, and sexual life of patients due to pain. This study compared the scores of endometriosis patients in these three areas before and after surgery.

Methods: Patients between the ages of 18 and 60 with a prediagnosis of endometriosis were enrolled. Postoperative histopathological diagnosis of endometriosis was confirmed in all patients. This study included 56 patients who completed pre- and postoperative (three months) evaluation of quality scale questionnaires: a visual analog scale for pelvic pain, the Pittsburgh Sleep Quality Index, Morningness-Eveningness Questionnaire, Endometriosis Health Profile-30 Questionnaire, and Female Sexual Function Index were administered prior to and 3 months after each patient's surgery.

Results: Among the 56 female patients included in this study, statistically significant improvement was observed in pain scores, quality of life, sexual function, and sleep of all patients regardless of endometriosis stage.

Conclusion: Endometriosis is a disease that progresses, with increasing pain scores; it has negative effects on the quality of life, sexual function, and sleep of patients. Surgical or medical treatment can be performed considering the complaints and fertility status of the patients.

2. A prospective study examining the effect of dienogest treatment on endometrioma size and symptoms.

Kizilkaya Y, Ibanoglu MC, Kiykac Altinbas S, Engin-Ustun Y. Gynecol Endocrinol. 2022 May;38(5):403-406. doi: 10.1080/09513590.2022.2053956.

Objective: We aimed to determine the effect of dienogest on cyst volume, symptoms, and quality of life in patients with endometrioma.

Method: This prospective cohort study included 37 patients diagnosed with endometrioma and planned for medical treatment. Subjects were treated with a 3-month oral dose of dienogest 2 mg/day. Pre-treatment and post-treatment endometriosis measurements were assessed via 3D ultrasonography, pain symptoms via 100-mm visual analog scale (VAS), and quality of life via Short Form-36.

Results: The mean age of the patients was 36.0 ± 6.6 years. The mean endometrioma volume was significantly reduced by 31% after treatment (26.7 ± 19.7 mm³) compared to the pre-treatment volume (17.4 ± 11.2 mm³, $p < .001$). Post-treatment VAS scores of dysmenorrhea, dyspareunia, and chronic pelvic pain VAS values were significantly decreased by 35.5% ($p < .001$), 37.5% ($p < .001$), and 38.5% ($p < .001$), respectively. The mean physical function score and mental health score significantly increased by 15% ($p = .009$) and 28% ($p < .001$), respectively.

Conclusion: Our findings showed dienogest treatment at oral doses of 2 mg/day for 3 months significantly reducing the size of endometrioma, reducing pain level, and increasing quality of life in women with endometriosis.

3. Correlation between endometriomas volume and Raman spectra. Attempting to use Raman spectroscopy in the diagnosis of endometrioma.

Guleken Z, Bulut H, Bulut B, Paja W, Parlinska-Wojtan M, Depciuch J. Spectrochim Acta A Mol Biomol Spectrosc. 2022 Jun 5;274:121119. doi: 10.1016/j.saa.2022.121119.

The formation of the uterus lining, i.e. the endometrium, outside the uterus (ex. in the abdominal cavity, ovaries, or anywhere in the body) is called endometriosis. The presence of endometrial tissue present in the ovaries, thickens after menstruation, leading to menstrual-like bleeding and to the formation of chocolate cyst (Endometrioma) because of the accumulation of old, brown blood in the ovary. It is still unknown, what triggers the development of endometrioma. However, it leads to excessive bleeding during menstrual periods or abnormal bleeding between periods and infertility. Endometriosis is often first diagnosed in those who seek medical attention for infertility. Therefore, new markers of endometrioma as well as new methods of its diagnosis are sought. In this study we used Raman spectra of serum collected from 50 healthy women and 50 women suffering from endometriosis. The obtained Raman data were used in multivariate analysis to determine the Raman range, which can be used for endometrioma diagnostics. Partial Least Square (PLS), Principal Component Analysis (PCA) and Hierarchical Component Analysis (HCA) showed, that it is possible to distinguish between the serum collected from healthy and un-healthy women using the Raman range between 800 cm⁻¹ and 1800 cm⁻¹ and between 2956 cm⁻¹ and 2840 cm⁻¹, while the first range corresponds to the fingerprint region and the second one to lipids vibrations. Consequently, the Pearson correlation test showed a

significant positive correlation between values of lipid intensity in Raman spectra and volume of endometriomas. Summarizing, Raman spectroscopy can be a helpful tool in endometrioma diagnosis and the lipid vibrations are candidates for being a spectroscopic marker of the disease being studied.

4. Antilipidemic ezetimibe induces regression of endometriotic explants in a rat model of endometriosis with its anti-inflammatory and anti-angiogenic effects.

Tapdıgova R, Bayrak G, Yılmaz BC, Aytan H. *Naunyn Schmiedeberg's Arch Pharmacol.* 2022 Jun;395(6):673-680. doi: 10.1007/s00210-022-02226-2.

To assess the potential therapeutic role of antilipidemic ezetimibe on endometriosis in an experimental rat model. A standard experimental endometriosis model was created with 18 Wistar-Albino rats, and after 1 month, the sizes of the endometriotic explants were measured. The rats were randomized as study and control groups. A total of 1 mg/kg/day ezetimibe and 1 ml/kg/day saline were administered orally to the study and control groups respectively for 28 days. At the end of 28 days, the explants were measured again, excised, and sent for histopathologic assessment for expression of tumor necrosis factor-alpha (TNF- α) and vascular endothelial growth factor (VEGF) and number of mast cells. At the end of the study period, the size of the endometriotic explants decreased significantly in the study group; but not in the control group (from 145.3 ± 120.5 to 89.8 ± 60.1 vs 174.72 ± 88.3 to 87.65 ± 27.1 cm³ respectively); however, the amount of post- and pretreatment differences in explant sizes was similar in the groups. The median TNF- α and VEGF levels were significantly lower in the ezetimibe group when compared to the control group (4 [3-4] vs 2 [1-3], p 0.029; 4 [3-4] vs 2 [2-3], p 0.002; respectively). And numbers of mast cells in all uterine layers were also lower in the ezetimibe group. Ezetimibe decreased the size of the endometriotic explants with its anti-inflammatory and anti-angiogenic properties. This agent alone or with combination of other agents may have a potential role in the treatment of endometriosis.

5. The effects of adalimumab on the rat autotransplantation endometriosis model: A placebo-controlled randomized study.

Kaplan S, Kırıcı P, Türk A. *Adv Clin Exp Med.* 2022 Apr;31(4):417-426. doi: 10.17219/acem/144369.

Background: Endometriosis is a chronic inflammatory pathology that can cause persistent pelvic pain and infertility by affecting women of reproductive age. It is defined as the placement of endometrial tissue outside the uterine cavity. Hormonal, genetic and immunological factors have an effect on the development of endometriotic implants. Adalimumab is a monoclonal antibody specific for tumor necrosis factor alpha (TNF- α), used in the treatment of autoimmune diseases.

Objectives: To investigate the effectiveness of adalimumab on histopathological and biochemical values in rats with experimental endometriosis.

Material and methods: This study is a comparative, prospective, experimental rat study. Wistar albino female rats were divided into 4 groups. Group 1 was separated as the control group. Endometriotic implants were simultaneously induced in group 2 and group 3. After 4 weeks, developing endometriotic foci were measured. Adalimumab (5 mg/kg) was simultaneously intraperitoneally (ip.) administered to group 3 and group 4 for 4 weeks. At the end of the study, histopathological scoring and fibrillin-1 scoring were performed. Total antioxidant status (TAS), total oxidant status (TOS) and malondialdehyde (MDA) values were measured. Findings in all groups were compared.

Results: When group 1 and group 2 were compared, the histopathological score, as well as MDA and TOS levels increased, while TAS levels decreased in group 2 (p < 0.001). After adalimumab treatment, the average endometriotic implant size in group 3 (0.32 ± 0.002 mm) decreased compared to group 2 (0.77 ± 0.04 mm) (p = 0.032). While fibrillin-1 score increased in group 2 and group 3 compared to group 1, it decreased in group 3 compared to group 2 (p < 0.001). Histopathological score decreased, TAS levels increased and MDA levels decreased in group 3 compared to group 2 (p < 0.001).

Conclusions: Adalimumab may play a role in the regression of endometrial implants by showing antioxidant and anti-inflammatory effects on histopathological damage and fibrosis.

6. The rate of oocytes with granular cytoplasm is higher in women with endometrioma in ICSI cycles

Kaplan S, Kırıcı P, Türk A. *Adv Clin Exp Med.* 2022 Apr;31(4):417-426. doi: 10.17219/acem/144369.

The purpose of this study was to investigate the impact of endometrioma on oocyte morphology and fertility outcome in intracytoplasmic sperm injection (ICSI) cycles. The study material was obtained from 114 ICSI cycles of infertile women aged between 20 and 38 years with ovarian endometriomas and unexplained infertility. In total, 644 mature oocytes were included in the analysis. The rates of specific oocyte morphological abnormalities were similar between the two groups however the central granulation rate was significantly higher in the group with endometrioma (p < .05). Fertilisation rate were not significantly different between the groups (p \geq .05) however the numbers of metaphase 2 (MII) oocytes and embryos were lower in the endometrioma group (p \leq .05). Endometrioma was associated with a higher rate of oocytes with granular cytoplasm, despite the fertilisation rate the numbers of the MII oocytes and embryo were affected.

IMPACT STATEMENT

What is already known on this subject? The association between endometrioma and infertility is a well-known condition, but the possible mechanisms of the effects of endometrioma on women's fertility is still debated and controversial. There is limited data on the effect of endometrioma on oocyte morphology. Low oocyte quality and lower fertilisation rates might be the main cause of adverse pregnancy outcomes during in vitro fertilisation/intracytoplasmic sperm injection cycles.

What do the results of this study add? Endometrioma was associated with a higher rate of oocytes with granular cytoplasm, and lower metaphase 2 oocytes and embryos.

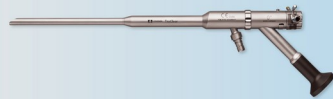
What are the implications of these findings for clinical practice and/or further research? Future studies using further oocyte quality assessment methods and prospective observational studies including live-birth rate should be designed to better understand how endometrioma affects fertility outcomes.

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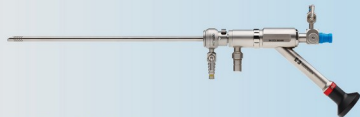
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