UTERINE
BENIGN DISORDERS
2021

TURKISH ENDOMETRIOSIS & ADENOMYOSIS SOCIETY 2009

12th year

ENDOMETRIOSIS BULLETIN

OCTOBER 2021 / ISSUE XIX

SELECTED ARTICLES

The Formidable yet Unresolved Interplay between Endometriosis and Obesity

Endometriosis and polycystic ovary syndrome are diametric disorders

Risk of melanoma in women with endometriosis: A Scottish national cohort study

Special Interview

Deborah Bush

www.endometriozisdernegi.org

PREFACE

Hello,

We are here with you again with our 19th issue.

You can find the newest updates on endometriosis and adenomyosis here in this bulletin.

In this issue, we included the abstracts of studies on the coexistence of endometriosis and polycystic ovarian syndrome, the incidence of malignant melanoma in endometriosis patients, the reasons for discontinuation of Dienogest treatment for endometriosis, the frequency of appendiceal involvement in endometriosis, and the relationship between endometriosis and obesity.

During the summer, we took a break from our live webinar meetings and Instagram live sessions. Hereby we inform you that we will continue these meetings from where we left off with experienced scholars in the upcoming months.

The webinar series organized by European Endometriosis League continued during July, August and September with valuable presentations by **Simone Ferrero**, **Philippe Koninckx** and **Paolo Vercellini**. The webinar series will continue with monthly presentations until the end of the year. You can find the monthly webinar program for 2021 in our bulletin.

We are very proud to announce that the founding president of our society, **Engin Oral,** has been nominated for the vice presidency of American Society of Reproductive Medicine Endometriosis Subgroup. We congratulate him for this achievement, which also sets an example for our young colleagues. In addition, we congratulate the president of our society **Taner Usta**, for joining the advisory board of the European Society of Gynecological Endoscopy.

On 26-27 November 2021, **'Workshop on Uterine Benign Disorders'** will be held by our society in Istanbul, in which current diagnosis and treatment approaches will be discussed and live surgery sessions will be held. For the limited registration, you can visit www.uterusunselimhastaliklari.org.

In our next issue we hope to share new updates on endometriosis and adenomyosis.

Best regards,

Board Members of Turkish Endometriosis & Adenomyosis Society

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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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1 The Formidable yet Unresolved Interplay between Endometriosis and Obesity

Pantelis A, Machairiotis N, Lapatsanis DP. ScientificWorldJournal. 2021 Apr 20;2021:6653677.

Abstract

Obesity and endometriosis are two very common entities, yet there is uncertainty on their exact relationship. Observational studies have repeatedly shown an inverse correlation between endometriosis and a low body mass index (BMI). However, obesity does not protect against endometriosis and on the contrary an increased BMI may lead to more severe forms of the disease. Besides, BMI is not accurate in all cases of obesity. Consequently, other anthropometric and phenomic traits have been studied, including body adiposity content, as well as the effect of BMI early in life on the manifestation of endometriosis in adulthood. Some studies have shown that the phenotypic inverse correlation between the two entities has a genetic background; however, others have indicated that certain polymorphisms are linked with endometriosis in females with increased BMI. The advent of metabolic bariatric surgery and pertinent research have led to the emergence of biomolecules that may be pivotal in understanding the pathophysiological interaction of the two entities, especially in the context of angiogenesis and inflammation. Future research should focus on three objectives: detection and interpretation of obesity-related biomarkers in experimental models with endometriosis; integration of endometriosis-related queries into bariatric registries; and multidisciplinary approach and collaboration among specialists.

2 Endometriosis and polycystic ovary syndrome are diametric disorders

Dinsdale NL, Crespi BJ. Evol Appl. 2021 May 14;14(7):1693-1715.

Abstract

Evolutionary and comparative approaches can yield novel insights into human adaptation and disease. Endometriosis and polycystic ovary syndrome (PCOS) each affect up to 10% of women and significantly reduce the health, fertility, and quality of life of those affected.

PCOS and endometriosis have yet to be considered as related to one another, although both conditions involve alterations to prenatal testosterone levels and atypical functioning of the hypothalamic–pituitary–gonadal (HPG) axis. Here, we propose and evaluate the novel hypothesis that endometriosis and PCOS represent extreme and diametric (opposite) outcomes of variation in HPG axis development and activity, with endometriosis mediated in notable part by low prenatal and postnatal testosterone, while PCOS is mediated by high prenatal testosterone. This diametric disorder hypothesis predicts that, for characteristics shaped by the HPG axis, including hormonal profiles, reproductive physiology, life-history traits, and body morphology, women with PCOS and women with endometriosis will manifest opposite phenotypes. To evaluate these predictions, we review and synthesize existing evidence from developmental biology, endocrinology, physiology, life history, and epidemiology. The hypothesis of diametric phenotypes between endometriosis and PCOS is strongly supported across these diverse fields of research. Furthermore, the contrasts between endometriosis and PCOS in humans parallel differences among nonhuman animals in effects of low versus high prenatal testosterone on female reproductive traits. These findings suggest that PCOS and endometriosis represent maladaptive extremes of both female life-history variation and expression of sexually dimorphic female reproductive traits. The diametric disorder hypothesis for endometriosis and PCOS provides novel, unifying, proximate, and evolutionary explanations for endometriosis risk, synthesizes diverse lines of research concerning the two most common female reproductive disorders, and generates future avenues of research for improving the quality of life and health of women.

Keywords: anogenital distance, endometriosis, folliculogenesis, polycystic ovary syndrome, testosterone

3 Appendectomy in the surgical management of women with endometriosis and pelvic pain

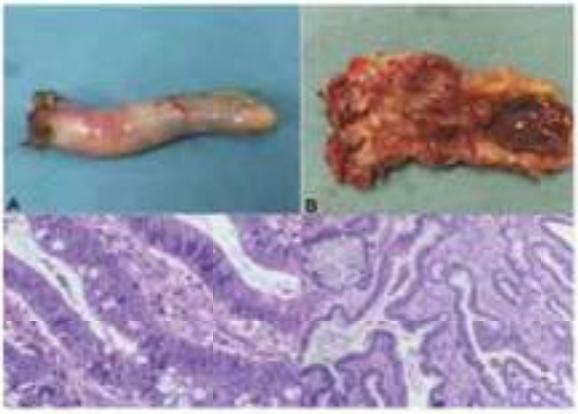
Ross WT, Chu A, Li L, Kunselman AR, Harkins GJ, Delmling TA, Benton AS. Int J Gynaecol Obstet. 2021 Sep;154(3):526-531.

Abstract

Objective: To evaluate the role of appendectomy in surgical excision of endometriosis and to assess complications associated with appendectomy.

Methods: Retrospective study of women undergoing appendectomy for pelvic pain and/or endometriosis during a primary gynecologic procedure.

Results: Record review was performed for 609 women who underwent appendectomy between 2013 and 2019 for pelvic pain (6.9%, 42/609), stage I-II endometriosis (63.7%, 388/609), or stage III-IV endometriosis (29.4%, 179/609). Appendiceal endometriosis (AppE) was present in 14.9% (91/609); 2.4% without endometriosis (1/42, reference group), 7.0% with stage I-II endometriosis (27/388, odds ratio [OR] 3.06, 95% confidence interval [CI] 0.41-23.11, P = 0.278), and 35.2% with stage III-IV endometriosis (63/179, OR 22.24, 95% CI 2.99-165.40, P = 0.002). AppE was significantly associated with endometriosis present in other locations (OR 5.27, 95% CI 2.66-10.43, P < 0.001). The predicted probability of identifying AppE ranged from 6% with 0 positive endometriosis sites to 56% when 4 or more sites were identified. There were no complications related to the performance of an appendectomy.



Conclusion: Women with chronic pelvic pain and/or endometriosis have an increased risk of AppE. Modern appendectomy at the time of gynecologic surgery is safe, with no associated complications in this study. Our findings support the consideration of appendectomy as part of the comprehensive surgical management of endometriosis.

Keywords: appendiceal endometriosis; benign hysterectomy; chronic pelvic pain; coincidental appendectomy; minimally invasive gynecologic surgery.

4 Risk factors for non-response and discontinuation of Dienogest in endometriosis patients: A cohort study

Nirgianakis K, Vaineau C, Agliati L, McKinnon B, Gasparri ML, Mueller MD. Acta Obstet Gynecol Scand. 2021 Jan;100(1):30-40.

Abstract

Introduction: Progestins are commonly prescribed first-line drugs for endometriosis. High rates of non-response and intolerance to these drugs have been previously reported. However, no study to date has investigated the characteristics and comorbidities of patients taking progestins in relation to treatment outcomes, so identifying which patients will respond to or tolerate the treatment is currently impossible. The purpose of this study, therefore, was to identify risk factors for non-response and discontinuation of Dienogest (DNG) in women with endometriosis.

Material and methods: This is a retrospective cohort study including women currently taking, or newly prescribed, DNG for endometriosis-associated pain presenting in the Endometriosis Clinic of the University Hospital of Bern between January 2017 and May 2018. Women with initiation of treatment directly after surgery for endometriosis were excluded. For all participants the symptoms and comorbidities were documented. Effectiveness, tolerability and discontinuation of DNG were the primary end points. Univariate and multivariate binary logistic regression models were carried out to identify risk factors for non-response, intolerance and discontinuation of DNG.

Results: A sufficient or excellent treatment response was reported by 85/125 (68%) participants. Genital bleeding during the DNG treatment was negatively (OR 0.185, 95% CI 0.056-0.610, P = .006) and rASRM endometriosis stages III and IV were positively (OR 3.876, 95% CI 1.202-12.498, P = .023) correlated with the DNG response. When accounting for exclusively pretreatment factors, primary dysmenorrhea (OR 0.236, 95% CI 0.090-0.615, P = .003) and suspicion of adenomyosis (OR 0.347, 95% CI 0.135-0.894, P = .028) were inversely correlated with DNG response, and the latter was also correlated with treatment discontinuation (OR 3.189, 95% CI 1.247-8.153, P = .015).

Conclusions: Genital bleeding during the DNG treatment and low rASRM stages are independent risk factors for DNG non-response. Before treatment initiation, primary dysmenorrhea and suspicion of adenomyosis correlate with DNG non-response. The results could assist the clinician first to provide detailed information to women before treatment initiation, second to identify and possibly modify in-therapy factors correlated to treatment effectiveness and lastly to switch treatment on time if needed.

Keywords: Dienogest; endometriosis; hormonal treatment; medical treatment; progestin; progestin-only pill; response; side effects.

5 Risk of melanoma in women with endometriosis: A Scottish national cohort study

Saraswat L, Ayansina D, Cooper KG, Bhattacharya S. Eur J Obstet Gynecol Reprod Biol. 2021 Feb;257:144-148.

Abstract

Objective: To explore the risk of melanoma in women with endometriosis.

Study design: A retrospective cohort study using Scottish national population-based data was conducted. The study comprised 281,937 women with nearly 5 million-person years (4,923,628) of follow up from 1981 to 2010. 17,834 women with a new surgical diagnosis of endometriosis were compared with 83,303 women with no evidence of endometriosis at laparoscopy, 162,966 women who underwent laparoscopic sterilisation and 17,834 age-matched women from the general population to determine the risk of melanoma. Cox proportional hazards regression was used to calculate crude and adjusted Hazards ratios with 95 % Confidence Intervals.

Results: Women with endometriosis had a significantly higher risk of melanoma when compared to women with no evidence of endometriosis at laparoscopy (HR 1.59, 95 % CI 1.19-2.13), women who had undergone laparoscopic sterilisation (HR 1.82, 95 % CI 1.39-2.40) and age-matched women from the general population (HR 1.63, 95 % CI 1.08-2.45).

Conclusion: A diagnosis of endometriosis was associated with an increased risk of developing melanoma compared to those without endometriosis. These findings highlight the need for further research to explore shared pathways in the pathogenesis of the two conditions. It is important to acknowledge that the absolute increase in the risk of melanoma in women with endometriosis remains low, which should be considered when counselling women.

Keywords: Endometriosis; Melanoma; Shared risk factors.

B NEWS FROM OUR SOCIETY
PAST ACTIVITIES

Workshop on Uterine Benign Disorders 2021

Following the suspension of the face-to-face meetings due to the pandemic, the Workshop on Uterine Benign Disorders, which is organized by Prof Dr Taner Usta and Prof Dr Engin Oral at Acıbadem Altunizade Hospital in Istanbul on 26-27 November, 2021 will be held on site. Live surgeries are planned as a part of this workshop. Members of the board of directors of our society and experienced physicians both natioal and international interested in the subject will be present at the workshop.
For registration and detailed program, visit http://uterusunselimhastaliklari.org/tr/

C NEWS FROM THE WORLD OF ENDOMETRIOSIS

EEL WEBINAR Program 2021

European Endometriosis League (EEL) Webinar programs continued in 2021 as well.

PROGRAMME

19.01.2021 | Joerg Keckstein - Austria
THE ROLE OF CLASSIFICATION OF ENDOMETRIOSIS: FROM R-ASRM TO #ENZIAN, THE COMMON LANGUAGE FOR DIAGNOSTICS AND TREATMENT

16.2.2021 | Gernot Hudelist - Austria
COMPLICATIONS OF DE SURGERY

16.03.2021 | James English - Netherlands
APPROACH TO NERVE SPARING RADICAL PELVIC SURGERY: THE REASONS WHY, THE ANATOMY AND THE SURGICAL APPROACH

13.04.2021 | Mario Malzoni - Italy
NAVIGATION IN THE LABYRINTH OF PARAMETRIAL ENDOMETRIOSIS: FROM ACCURATE DIAGNOSIS TO PROPER SURGICAL MANAGEMENT

18.05.2021 | Mohamed Bedaiwy - Canada
ADENOMYOSIS-ASSOCIATED INFERTILITY

15.06.2021 | Mohamed Mabrouk - UK
DEEP ENDOMETRIOSIS SURGERY: BE PREPARED FOR THE CHALLENGE

13.07.2021 | Simone Ferrero - Italy
UPDATE IN HORMONAL TREATMENT OF DEEP ENDOMETRIOSIS

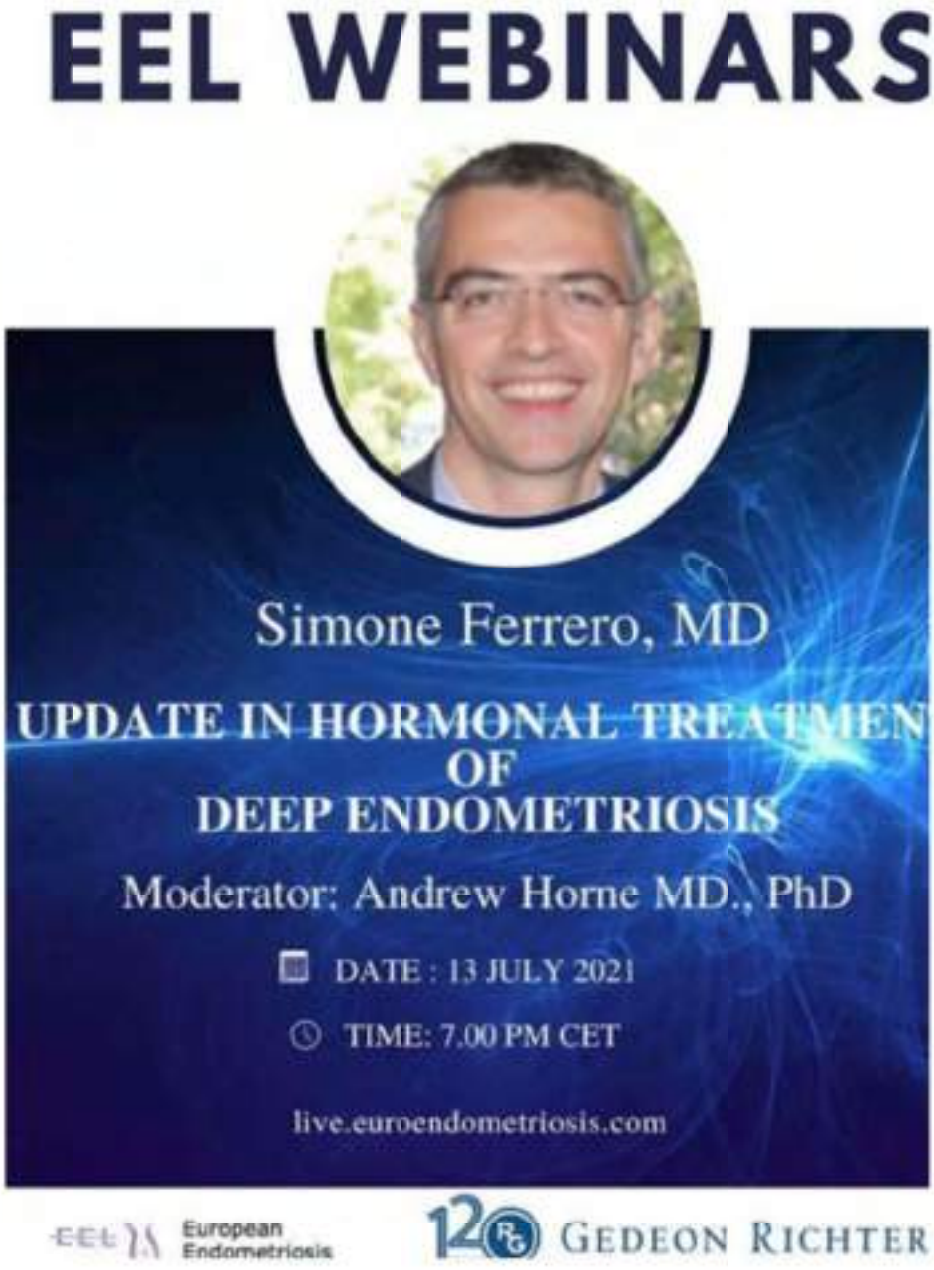
17.08.2021 | Philippe Koninckx - Belgium
GENETIC- EPIGENETIC PATHOPHYSIOLOGY OF ENDOMETRIOSIS

14.09.2021 | Paolo Vercellini - Italy
ENDOMETRIOSIS AND OVARIAN CANCER

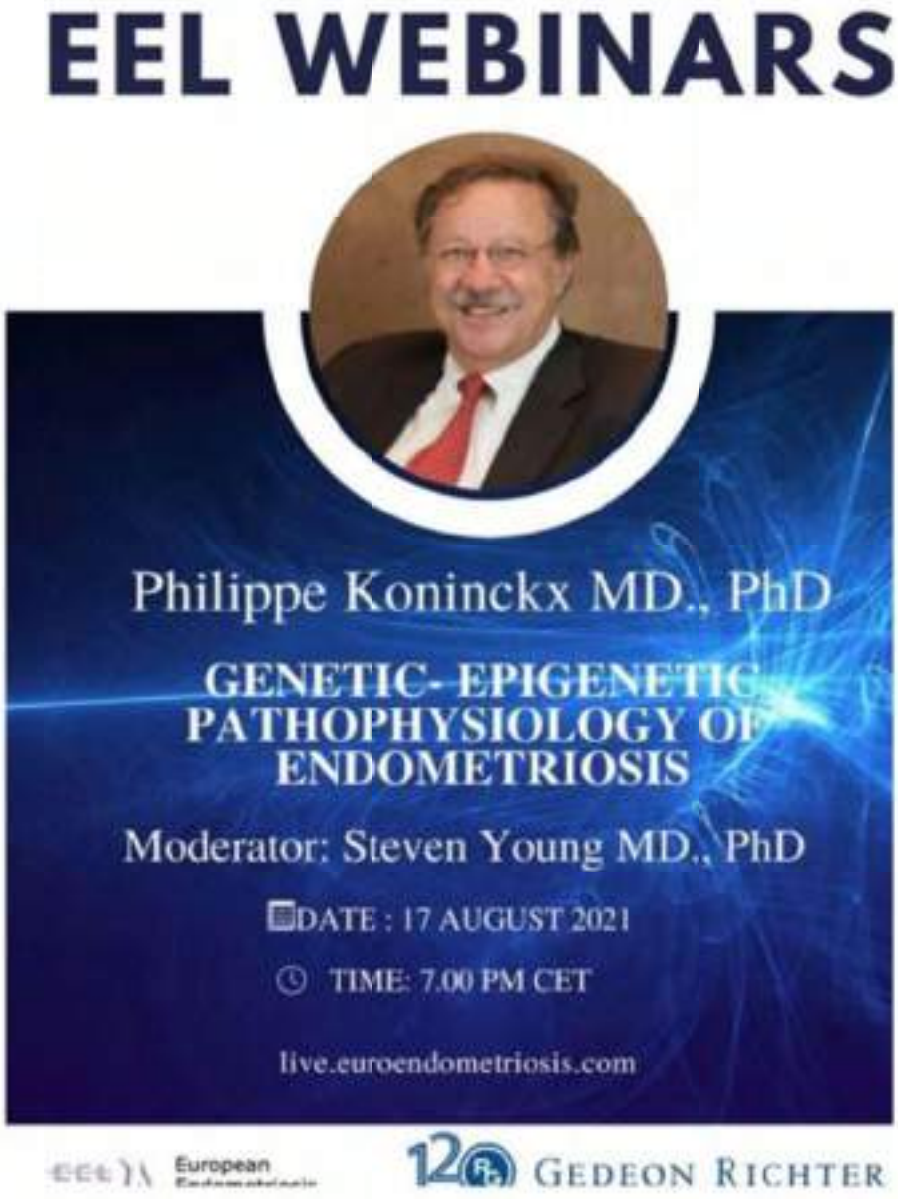
19.10.2021 | Luk Rombauts - Australia
SURGERY OR IVF FOR ENDOMETRIOSIS-RELATED INFERTILITY?

16.11.2021 | Carla Tomassetti - Belgium

In the EEL webinar held in July, Dr. Simone Ferrero explained hormone treatment in deep endometriosis with the title "Update in hormonal treatment of deep endometriosis".



The EEL webinar "Genetic-epigenetic pathophysiology of endometriosis ", which was held in August, was presented by Dr. Philippe Koninckx, one of the leading names in endometriosis.



EEL webinar series continued in September with a comprehensive presentation titled as "Endometriosis and ovarian cancer" and presented by Dr. Paolo Vercellini.

As a part of the EEL webinar program, which is planned to be held every month, international physicians experienced in endometriosis will share their knowledge on different subjects.
For more information, visit https://www.endometriosis-league.eu/home or follow the European Endometriosis League or Euro Endo League accounts on social media.

ACE 2020

The 9th Asian Endometriosis Congress, which is planned to be organized together by the Sri Lanka Endometriosis Association and the Asian Endometriosis and Adenomyosis Association, will be held on 28-30 October, 2021 due to the pandemic. From our country, our founding president, Prof. Engin Oral, MD and Prof. Kutay Biberoglu, MD will contribute to the scientific program of the congress with the topic "Endometriosis after the age of 40" and "Endometriosis-related infertility management" and "Dienogest in endometriosis-related pain" respectively.

6th EEC - France

The 6th European Endometriosis Congress, which is planned to be held in Bordeaux, France in December this year, has been postponed to 16-17 June 2022.

AAGL 2021

The 50th Global Minimally Invasive Gynecological Surgery (MIGS) Congress, organized by AAGL, will be held on 14-17 November 2021 in Austin Texas, USA.

SEUD 2021

The 7th Congress of Endometriosis and Uterine Pathologies is planned to be held in Stockholm, Sweden in December this year.

FIGO 2021

The World Congress of Gynecology and Obstetrics (FIGO) is scheduled to be held in Sydney, Australia in October this year.

D INTERVIEW WITH AN 'ENDO SPECIALIST'

Deborah Bush

Interviewer: Fitnat Topbaş Selçuki, MD

A Short Curriculum Vitae

Deborah Bush MNZM QSM is the co-founder and chief executive of Endometriosis New Zealand. She is also the founder and director of Endometriosis and Pelvic Pain (EPP) Coaching and Consulting. She is a board trustee of World Endometriosis Society (WES) and the founding Principal of the World Endometriosis Organizations (WEO). Deborah Bush developed the world's first Menstrual Health and Endometriosis me® program for schools in 1997, which has significantly influenced early recognition of symptoms and timely intervention in adolescents in New Zealand. Her private practice EPP Coaching and Consulting integrates into four treatment centers offering multi-disciplinary expertise in New Zealand and focuses on education and evidence-based lifestyle management options and well-health coaching to nurture wellbeing.

Turkish Endometriosis & Adenomyosis Society (EAD): Today we will interview Deborah Bush from New Zealand. Thank you for agreeing to do this interview with our society.

Deborah Bush: Hello Fitnat, thank you for inviting me to this interview, it is a pleasure to be with you.

EAD: Could you tell us about yourself and how you became involved in endometriosis?

DB: I am a health professional involved with endometriosis. I say health professional, but I come from a totally different background than a clinician or a researcher. My interest in endometriosis arose when I was diagnosed with the disease in 1985. I have a teaching degree and Letters in the performing arts. At the time, I was teaching secondary school and running my own speech, drama and media training studio and dance academy. When I was diagnosed with endometriosis no one seemed to know what to do or how to treat it. In those days, it wasn't as appropriate to talk about your story publicly. So, I met two other professional women, who were also recently diagnosed with endometriosis. We all had the same experiences of not being believed and lobbed off in care. We articulated our concerns and knew something needed to be done. We established The New Zealand Endometriosis Foundation, later operating as Endometriosis New Zealand. For me having endometriosis was the catalyst that sparked my interest in women's health and endometriosis. We ran public seminars throughout New Zealand for 8 years. From those seminars it became clear to me that this wasn't a 'white women's career disease' like the article in the Time magazine reported. In fact, it was clear that this disease started very young and didn't discriminate on any grounds. Hearing the hundreds of stories and feeling the desperation of those suffering and their family members, I knew that I could use my areas of expertise to start influencing change. Then, in 1997 I started to think about educating adolescents and began planning the Menstrual Health and Endometriosis (me®) program. I used the NZ curriculum to set standards, held focus groups with teenagers to assess knowledge and need, managed to find a group of students willing to design the first hard copy resources and piloted the program in a few local schools who were willing to give it a go! Endometriosis was virtually unheard of amongst colleagues, friends and the community in general. The program was relatable, engaging and fun and the first pilot was very well received. During the pilot trials in 1997 and 1998, I reviewed and evaluated each session and used feedback from the evaluation forms to edit and make changes. I kept these records in a notebook – yes, paper and pen! It was clear there were many girls in every session experiencing dreadful period pain and other symptoms such as lower back pain and bowel symptoms. Some reported that they were off school every month. I was proud of the resources being developed and dropped these off to youth health clinics. Some schools separated the girls and boys but now of course it reaches all genders.

We also ran programs alongside me® which we shared amongst the three of us. We assisted women to navigate their way through the health system and listened to and validated their stories and developed resources to help them cope. We weren't always popular with the medical professionals and we occasionally received rude and unnecessary comments. However, a small group of gynecologists who had a special interest in endometriosis supported us and our work.

In the late 1990s I decided to develop a career specializing in endometriosis from a completely different perspective. There was no job to apply for and certainly no money but we did have a charitable trust by that stage and I had a set of very unique skills. I was very conversant and comfortable working with people from a variety of backgrounds. I began contacting government officials; clinicians; health professionals and of course we worked daily with all those with endometriosis and their families. More than that though, the three of us had passion, drive and determination to influence change and improve the situation for those with endo. It has never made sense to me why endometriosis was never important, why women were dismissed, not listened to, fobbed off with silly unfounded comments from health professionals and health decision makers and isolated because of societal attitudes. I knew the suffering was immense and my own story was far behind me. Sadly, Joan Moultrie RN, co-founder of ENZ, passed away in 1997 of ovarian cancer. She was still young, never got to meet her grandchildren and suffered miserably (though was very stoic) with stage IV endometriosis and severe endometrioma – the type which can cause ovarian cancer. In her final days as I sat with her, she urged me to continue with my work. I promised.

In 2001 I started my own private practice called Endometriosis and Pelvic Pain (EPP) Coaching and Consulting - a well-health coaching clinic to nurture well-being. It now runs in four NZ Endometriosis Centres of Expertise as part of a multi-disciplinary approach to care. Gynaecologists in those clinics refer their patients to me. I started seeing my Auckland patients by Zoom in 2020 because of Covid-19 lockdown and I have a clinic at Oxford Women's Health in Christchurch every week. This is separate to being CEO of Endometriosis New Zealand though I have transferred the learning from my private practice to develop more ENZ services such as EndoHelp and workplace programs and accept speaking engagements to CME meetings and academic conferences. I established an ENZ advisory Board known as ESIG (Endometriosis Special Interest Group) which ensures that we provide medically responsible expertise and knowledge to those we represent. I would like to further the expansion of the workplace wellness program (WISE) which runs under the banner of Endometriosis New Zealand and our beautiful dance program promoting exercise as the best non-drug treatment for pain (endorsed by the Royal New Zealand Ballet).

In 2017 I set up the World Endometriosis Organisations (WEO) to be the global Organisation representing those with endometriosis, adenomyosis and pelvic pain. It seemed inequitable that researchers, doctors and specialists have their representative societies and medical colleges, but where was that association for patients? This was an area sadly lacking given the prevalence of endometriosis world-wide and the degree of misinformation, misunderstanding, absence of country specific Clinical Guidelines and the fact that many of those with endo, adeno and pelvic pain still get such a raw deal in our health systems. Each WEO member organisation must be a Registered Charitable Trust or Society in their own country and approved by a wonderful global Steering Committee. I want to grow WEO and ensure that it has good representation to influence global change. There is much to be done.

I love writing and when Dr Susan Evans, Adelaide Australia, invited me to contribute to her book 'Endometriosis and Pelvic Pain', I jumped at the chance. The book is fabulous and has helped so many patients. I have gifted royalties from sales of the book in NZ to Endometriosis New Zealand. Early recognition of symptoms and timely intervention for endometriosis is vital for change and I am now ready to launch 'me® online'. This is timely also with so many students now learning from home and engaging more in eLearning due to the global pandemic. The aim is for the program to be place based, agile and personalised and available to everyone in schools and at home. It's also a very cost-effective way of reaching a larger audience.
In essence, my career has been based on good ideas because it's the right thing to do and then making it happen. It's always vital to me that any new program or service I initiate, is medically responsible, part of a wider vision from Endometriosis New Zealand and the World Endometriosis Society and true to our Trust Deed. When I was teaching, I always saw a topic or learning holistically and that is the way I work now, integrating our services and programs into the big picture and vision to benefit all.

My career was sparked by having endometriosis, but I never told my story. I think it is irrelevant to the many stories that I have heard over the years and continue to hear today. My career was never based on my story, but rather on the 200 million stories of often avoidable suffering, despair and pain. That's what resonates with me. What makes my blood boil is that girls and women with endometriosis are often marginalised, discriminated against and fobbed off and the disease, despite it being a major life-altering public health issue, is not given priority by our health decision makers. That has never made sense to me. So, in 2015, despite being rejected multiple times by the NZ Government, I presented the case again to government and established a Task Force with our Ministry of Health, Medical Colleges and patients to develop the Clinical Pathway on the Treatment and Management of Endometriosis in New Zealand. That was launched in the New Zealand Parliament on March 2, 2020. I am working with the Ministry to ensure the Clinical Pathway is implemented to improve health outcomes for those with endometriosis in New Zealand. I am experiencing some resistance making headway because of Covid-19 taking precedence. We all understand this, but endometriosis does not stop disrupting the lives of millions for a pandemic. I am totally committed to implementing the Clinical Pathway. I front the media campaigns we have run with consistent strong messages and I am still very passionate and enthusiastic about my work and new ideas.

I am now involved in multiple research studies that fit with our vision, as making headway and progress is challenging without robust published data and evidence. I am thoroughly enjoying working with research teams and making a contribution to the literature.

EAD: Let's go back to the education program you initiated in 1997. Could you tell us more about the program and how it is going right now?

DB: It is referred to as the me® program (menstrual health and endometriosis) and it has been operating for 23 years in areas of New Zealand where we have secured funding. It has also been trialed successfully in Mumbai and South Australia and we are waiting for the trial results from British Columbia. It is the only education program of its type in the world which is published in the medical literature (ANZJOG 2017). Data from the published research from the me® program shows 27% of secondary school aged girls are off school every or most months with severe dysmenorrhea. The me® program is evaluated regularly to ensure it is medically responsible and accurate and is meeting current educational developments and student needs in different settings. I am always keen to know if the program translates into the clinical setting. I mean, are we actually seeing more young people presenting with symptoms suspicious of endometriosis? From my own experience through EPP (Endometriosis and Pelvic Pain) Coaching, I can say this is the case. My records show that in 2001, 12% of the patients referred to me by gynaecologists were under the age of 20, whereas at the end of 2019 this number had escalated to 62% following a growth trend year by year. All had a confirmed laparoscopic diagnosis of endometriosis with 49% having stage I disease. When I asked them how they first knew they might have endometriosis they said that they heard the me® program at school and from there, discussed it at home and sought review with their doctors. I do recognise that it is a biased cohort in that these data are from a private tertiary center. Nonetheless, I believe that the me® program allows for early recognition of symptoms and early intervention. It really is the only preventative tool we have. By intervening and diagnosing early we can at least improve quality of life, nurture their well-being and monitor them to adulthood, to avoid the possibility of their future fertility being compromised down the track if that is their wish.

EAD: So, do you believe that you were able to reach young women/adolescents from different parts of New Zealand with this program and it was a nationwide success?

DB: The me® program is funded by philanthropic funds and therefore we are somewhat restricted. However, the program has now reached hundreds of thousands of students over two decades so we are seeing a much larger number of young people presenting with symptoms. What we must do is also ensure they are able to access the care they need in a timely manner. It's essential that the program is funded by government as part of the National Curriculum and I am currently working to that end. We still have some way to go but we'll get there! In 2019 me® reached 105 schools and approximately 13,500 students. There are almost 300,000 secondary school students in New Zealand at this time. It therefore makes sense to get me® online rolled out nationally. This year, 2021, we plan to do both; that is me® in-school and me®online. We are currently collaborating with the University of Otago in Dunedin (New Zealand) to test and evaluate me® online as part of a robust assessment study. I am working with educationalists to develop the content in Maori through a consultative process with Maori. It is a matter of bringing the right people together to ensure me® is equitable and accessible to all. It's an exciting time. The me® program has been very successful and over 21 years 100% of schools who have had the program want it back the next year. Feedback from students is positive and they thoroughly enjoy the interactivity and that it's relatable to them personally and their health and well-being. me® online has been built in modules so that it can be adapted for use everywhere.

EAD: Can we also talk a little about World Endometriosis Organisation (WEO)?

DB: I run WEO voluntarily. WEO is a very young organisation which I initiated in 2017 at the World Congress on Endometriosis in Vancouver. It seemed to me that while the Clinicians and researchers were well represented by their University or Medical College's, patients did not have a global representative body. WEO has enormous (yet untapped) potential and a strong future to advocate and positively influence change and health outcomes for all those with endometriosis. There are currently 31-member organisations including groups in Africa, Australasia, Europe and the UK, Scandanavia, the Caribbean and the Americas. We are starting to be recognised. To belong, an organisation must be a Registered Charitable Trust or similar in their own country and membership is approved by the Steering Committee. The WEO Memorandum of Understanding respects each member organisation's rules and regulations, processes and procedures. Most organisations in WEO such as Turkish Endometriosis & Adenomyosis Society, have their own clinical advisory boards. I am very comfortable to say that WEO is a professional body of organisations, which will be a useful adjunct to improving the health status of millions with endometriosis world-wide. WEO can be helpful in recruiting participants for research. Recently for instance, WEO disseminated a research study to investigate the impact of Covid-19 on those with endometriosis. It attracted a large number of participants from across the world. This research is so helpful to every country and I will certainly be using these data as evidence for need when planning the implementation of the Clinical pathway with our Ministry of Health over the coming weeks. This is just one example of the benefits of how we can achieve great things for those with endometriosis by professional, global collaboration and cooperation. That is my vision. WEO is not there yet, but it will be and I am sure, will have a strong place alongside major stakeholders in the field in the future.

EAD: Is there anything else you would like to add as a final note?

DB: I have reached a point in my career when succession planning is vital to continue the work of Endometriosis New Zealand and ensure longevity. I am wanting to pass on my experience and knowledge to the next group of advocates so that the work continues . I have been very privileged to be honored with national and international awards but my biggest privilege has been

meeting and working with absolutely wonderful people – patients, scientists, academics and clinicians who have incredible selfless aspirations and a purpose to commit to the cause within their own field of expertise. To be able to call these people my dear friends is indeed an honour. We all have expertise and skills we can contribute, and looking through the lens of our own experiences, proficiency and skill, a great deal to offer. If I have contributed to the cause to positively influence change for this generation with endometriosis and those to come then I am indeed very blessed.

EAD: Thank you for this wonderful interview.

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

1. Non-invasive diagnosis of endometriosis and moderate-severe endometriosis with serum CA125, endocan, YKL-40, and copeptin quadruple panel.

Guralp O, Kaya B, Tüten N, Kucur M, Malik E, Tüten A. J Obstet Gynaecol. 2021 Aug;41(6):927-932. doi: 10.1080/01443615.2020.1803245..

Abstract

Considering the complex pathogenesis of endometriosis, which is associated with many cellular or molecular processes, such as proliferation, angiogenesis, inflammation, we evaluated the diagnostic value of a quadruple panel of serum markers CA125, endocan, YKL-40 and copeptin, for the prediction of endometriosis and moderate - severe endometriosis. Seventy women with endometriosis and 70 women without endometriosis were evaluated. Serum CA125, endocan, copeptin and YKL-40 levels were significantly increased in women with endometriosis compared to the women without endometriosis and in the minimal - mild endometriosis group compared to the no-endometriosis group. YKL-40, endocan and copeptin levels were significantly increased in the moderate - severe endometriosis group compared to the mild -moderate endometriosis group but the difference in CA125 levels remained non-significant. The quadruple panel score had an AUC of 0.954, a sensitivity of 96.5% and specificity of 84.6% for prediction of moderate - severe endometriosis. Zero or one positive marker had a sensitivity of 91.4% and specificity of 88.57% to rule out endometriosis. In conclusion, a quadruple panel of serum markers-CA125, endocan, YKL-40, and copeptin may be beneficial for the diagnosis of endometriosis and especially moderate - severe endometriosis. Further studies are needed to prove the efficacy of this panel.

What is already known on this subject? Many serum markers including CA125 have been investigated so far and suggested to be associated with endometriosis. However, none of these markers is sensitive and specific enough to diagnose endometriosis.

What do the results of this study add? A quadruple panel score (CA125, endocan, YKL-4 and copeptin) had an AUC of 0.954, a sensitivity of 96.5% and specificity of 84.6% for prediction of moderate - severe endometriosis.

What are the implications of these findings for clinical practice and/or further research? A high score may be beneficial to warn the surgeon about the risk of moderate to severe endometriosis if the patient will be operated anyway. A negative test of the quadruple panel may show high odds that there is no endometriosis which may prevent unnecessary surgery.

2. Evaluation of depression and sleep disorders in the preoperative and postoperative period in stage 4 endometriosis patients.

Goksu M, Kadirogullari P, Seckin KD. Eur J Obstet Gynecol Reprod Biol. 2021 Jul 24;264:254-258. doi: 10.1016/j.ejogrb.2021.07.037.

Abstract

Objectives: Endometriosis is a disease that significantly affects the quality of life of patients. Continuous pelvic pain seen in patients disrupts their well-being. The aim of this study is to examine the changes in depression and sleep disorders in patients with endometriosis before and after the operation.

Study design: Forty-two women aged 18-49 with an indication for operation due to the diagnosis of stage 4 endometriosis and without a known psychiatric disorder were included in the study. Pittsburgh Sleep Quality Index and Beck Depression Inventory were used to compare sleep quality and mood of endometriosis patients before and after surgery.

Results: The mean age of the patients was 33.8 ± 7.6. The mean BMI of the patients was 24.6 ± 4.1. Endometrioma diameter was 248.42 ± 95.7 cm3 in patients with poor sleep quality, while it was 296.11 ± 271.53 cm3 in patients with good sleep quality, and a significant difference was observed ($p < 0.05$). Poor sleep quality and severe depression were significantly higher in patients with infertility complaints. It was observed that sleep quality was not significantly correlated with bilateral endometrioma, a nodule in the Douglas, sacrouterine tenderness and mean ASRM scores ($p > 0.05$). A significant decrease in depression complaints and a significant increase in sleep quality were observed in patients who underwent stage-4 endometriosis surgery ($p < 0.05$).

Conclusion: We showed that there was a significant increase in sleep quality and a significant decrease in depression symptoms in patients who underwent stage-4 endometriosis surgery. Since endometriosis affects the social life of patients in many ways, it is necessary to increase the knowledge and experience about the treatment of endometriosis with larger studies to be done. We believe that surgical treatment can reduce social problems and increase the quality of life of endometriosis patients.

3. The Effects of Micronized Progesterone and Cabergoline On a Rat Autotransplantation Endometriosis Model: A Placebo Controlled Randomized Trial.

Karslıoglu T, Karasu AFG, Yildiz P. J Invest Surg. 2021 Aug;34(8):897-901. doi: 10.1080/08941939.2019.1705442.

Abstract

Aim: The etiology of endometriosis is complex and various theories have been postulated. Endometriosis pathogenesis involves genetic susceptibility, immunologic alterations and inflammatory prerequisite pathways. In this pilot experimental animal study we wanted to investigate the effects of cabergoline and micronized progesterone on a rat endometriosis model.

Material and methods: All rats were provided and housed in the animal laboratory of the Experimental Research Center of Bezmialem Vakif University. This was a placebo controlled randomized trial. The endometriosis model consisted of autotransplantation of endometrial tissue on 21 adult Sprague-Dawley rats. Endometriosis formation by second-look laparotomy was confirmed 8 weeks later. After measuring the endometriosis implant area the rats were randomized into three intervention groups: cabergoline treatment group, micronized progesterone treatment group and the control group. Four weeks after treatment, a third laparotomy was performed to remeasure implant volumes. Endometriotic implants were obtained for histopathological and immunohistochemical analysis.

Results: After 4 weeks of treatment endometriosis implant sizes diminished in all groups. There was no statistically significant difference regarding implant size volume before and after treatment among the groups. The peritoneal histopathology and immunohistochemistry showed no difference with regards to IL-6 and TNF-α staining among groups.

Conclusion: We conclude that oral treatment of cabergoline and micronized progesterone for 4 weeks was not statistically effective in endometriotic implant regression. However, we believe further studies are warranted. Treatment for longer durations or via different routes may be investigated in further studies. When ethically applicable other mammals may be considered such as baboons.

4. The Effects Of Etanercept And Cabergoline On Endometriotic Implants, Uterus And Ovarıes In Rat Endometriosis Model.

Keleş CD, Vural B, Filiz S, Vural F, Gacar G, Eraldemir FC, Kurnaz S. J Reprod Immunol. 2021 Aug;146:103340. doi: 10.1016/j.jri.2021.103340.

Abstract

The pathophysiology of endometriosis is still unknown and treatment options remain controversial. Searches focus on angiogenesis, stem cells, immunologic and inflammatory factors. This study investigated the effects of etanercept and cabergoline on ovaries, ectopic, and eutopic endometrium in an endometriosis rat model. This randomized, placebo-controlled, blinded study included 50 rats, Co(control), Sh(Sham), Cb(cabergoline), E(etanercept), and E + Cb(etanercept + cabergoline) groups. After surgical induction of endometriosis, 2nd operation was performed for endometriotic volume and AMH level. After 15 days of treatment: AMH level, flow cytometry, implant volume, histologic scores, immunohistochemical staining of ectopic, eutopic endometrium, and ovary were evaluated at 3rd operation. All groups had significantly reduced volume, TNF-α, VEGF, and CD 146/PDGF-Rβ staining of endometriotic implants comparing to the Sh group ($p < 0.05$).TNF-α staining of eutopic endometrium in all treatment groups was similar to Sh and Co groups ($p > 0.05$). E and E + Cb groups significantly decreased TNF-α staining in the ovary comparing to Sh, Co, and Cb groups ($p < 0.05$). All treatment groups had significantly higher AFC compared to the Sh group. CD25+ Cells' median percentage was significantly increased in the E + Cb group compared to Co, Sh, Cb, and E group. E + Cb group had a significantly higher CD5+ Cells' level than the Co group ($p = 0.035$). In conclusion; Etanercept and/or Cabergoline decreased volume, TNF-α, VEGF, and CD 146/PDGF-Rβ staining of the ectopic endometrial implant. E and E + Cb treatment decreased TNF-α levels in the ovary. E + Cb also increased peripheral blood CD25+ & CD5+ Cell's.

5. Thoracic Endometriosis: A Review Comparing 480 Patients Based on Catamenial and Noncatamenial Symptoms.

Topbas Selcuki NF, Yilmaz S, Kaya C, Usta T, Kale A, Oral E. J Minim Invasive Gynecol. 2021 Aug 8:S1553-4650(21)00384-8. doi: 10.1016/j.jmig.2021.08.005.

Abstract

Objective: This review aimed to categorize thoracic endometriosis syndrome (TES) according to whether the presenting symptoms were catamenial and to evaluate whether such a categorization enables a better management strategy.

Methods of study selection: The following keywords were used in combination with the Boolean operators AND OR: "thoracic endometriosis syndrome," "thoracic endometriosis," "diaphragm endometriosis," and "catamenial pneumothorax."

Tabulation, integration, and results: The initial search yielded 445 articles. Articles in non-English languages, those whose full texts were unavailable, and those that did not present the symptomatology clearly were further excluded. After these exclusions, the review included 240 articles and 480 patients: 61 patients in the noncatamenial group and 419 patients in the catamenial group. The groups differed significantly in presenting symptoms, surgical treatment techniques, and observed localization of endometriotic loci ($p < .05$).

Conclusion: This review points out the significant differences between patients with TES with catamenial and noncatamenial symptoms. Such categorization and awareness by clinicians of these differences among patients with TES can be helpful in designing a management strategy. When constructing management guidelines, these differences between patients with catamenial and noncatamenial symptoms should be taken into consideration.

6. Diagnosis of endometriosis using endometrioma volume and vibrational spectroscopy with multivariate methods as a noninvasive method.

Guleken Z, Bulut H, Depciuch J, Tarhan N. Spectrochim Acta A Mol Biomol Spectrosc. 2021 Aug 3;264:120246. doi: 10.1016/j.saa.2021.120246.

Abstract

Endometriomas are typically an advanced form of endometriosis that leads to the formation of scar tissue, adhesions, and an inflammatory reaction. There is no certain serum marker for the diagnosis of endometriosis. This study aims to research the correlation between the amount of peaks corresponding to proteins and lipids with the volume of endometrioma and determine the chemical structure of blood serum collected from women suffering from endometriosis patients with endometrioma and healthy subjects using Fourier Transform Infrared (FTIR) spectroscopy. FTIR spectroscopy is used as a non-invasive diagnostic technique for the discrimination of endometriosis women with endometrioma and control blood sera. The FTIR spectra of 100 serum samples acquired from 50 patients and 50 healthy individuals were used for this study. For this purpose, multivariate analyses such as Principal Component Analysis (PCA), Partial Last Square analysis (PLS) with Variables Importance in Projection (VIP), and probability models, were performed. Our results showed that FTIR range 1500 cm-1 and 1700 cm-1 and around 2700 cm-1 - 3000 cm-1, regions may be used for the diagnosis of endometriosis. Also, we find that proteins and lipids fraction increase with the volume of endometrioma. Moreover, PLS and VIP analysis suggested that lipids could be helpful in the diagnosis of endometriosis women with endometrioma.

7. Uterine involvement by endometriosis: Sonographic features from elusive findings to apparent adenomyosis.

Olgan S, Dirican EK, Ozsipahi AC, Sakinci M. Eur J Obstet Gynecol Reprod Biol. 2021 Jul;262:93-98. doi: 10.1016/j.ejogrb.2021.05.013. Epub 2021 May 9.

Abstract

Objective: The primary aim of this study is to investigate whether there are any minor sonographic uterine findings, not typical for adenomyosis, in endometriosis patients. The secondary objective is to determine the prevalence of sonographic features of adenomyosis in an infertile population with endometriosis.

Study design: The investigation was of 291 infertile women with endometriosis, either manifesting endometrioma (OMA) or diagnosed through laparoscopy, who were investigated for two-dimensional transvaginal sonographic (2D-TVS) features of adenomyosis. These patients were grouped as either having endometriosis with adenomyosis (EwA,n = 121) or without adenomyosis (EwoA, n = 170). Additionally, patients without both endometriosis and 2D-TVS features of adenomyosis constituted the control group (n = 170).

Results: At least one 2D-TVS feature of adenomyosis was detected in 41.6 % (n = 121) of women with endometriosis. Asymmetrical myometrial thickening of uterine walls (57.9 %), hyperechogenic islands (47.1 %), and fan-shaped shadowing (46.9 %) were relatively more prevalent 2D-TVS findings among EwA patients. Multiple OMA ($p = 0.038$), OMA ≥ 4 cm ($p = 0.034$), and total OMA volumes were found to be higher ($p = 0.004$) in the EwA group. Additionally, uterine volumes were found to be 96.7 cm3, 73.0 cm3, and 64.2 cm3 in the EwA, EwoA, and control groups, respectively (EwA vs EwoA, $p < 0.001$; EwoA vs control, $p < 0.001$). Multivariate linear regression analysis revealed that the presence of endometriosis was independently associated with an increase in uterine volume ($\beta = 0.243$, $p < 0.001$).

Conclusion: A stepwise and statistically significant volume increase from the control group to the EwoA and then to the EwA group may reflect a spectrum of uterine involvement in endometriosis. This might indicate that many uterine endometriosis cases are still hidden from view, possibly demonstrating an "iceberg phenomenon".

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