March is Endometriosis Awareness Month

Let's create awareness together
#endometriozisleyasancak #endomarch #endometriozis

You can share your story and your thoughts by using the hashtags above and you can draw attention to this disease that 1 of every 10 women in reproductive age lives with.

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HELLO

In 2018, we are here with the fifth issue of our bulletin. During the last 3 months, our society participated in a variety of scientific programs and at the same time we have prepared several national and international congresses. One of our board members Prof Engin Oral, MD. is going to be one of the congress secretaries at the 4th EEL. Our society is going to be representing our country at this international platform.

Our national and international colleagues will be joining us in Istanbul Altunizade Acibadem Hospital during April 20-21st, 2018 at the 1st Chronic Pelvic Pain Symposium.

As a part of the Endoacademia meetings and with the support of local colleagues we have organized a one-day meeting on ‘Endometrioma’ in Gaziantep on January 28th, 2018, which we also broadcasted live on Facebook. Our colleagues showed great interest and support, and thus we decided to organize a similar meeting on April 1st, 2018 in Kayseri on the subject of ‘Management of Endometrioma’. We are going to share in detail up-to-date information on management of this disease. You can find further information on this meeting on our website or in this bulletin.

Prof Umit Inceboz, MD. is going to deliver a talk on ‘Chronic Pelvic Pain in Endometriosis and Other Organ Related Factors and Treatment’ in Antalya at the 3rd Sexual Health Congress (CISED) organized by The Institute of Sexual Health. This subject will be discussed in detail with the contribution of psychiatrists.

On March 9-10th, 2018 at the 2nd Pelvic Rehabilitation Congress held by The University of Health Sciences, our society organized a course on pelvic pain. With the help of our colleagues from the field of physical therapy and rehabilitation, we have discussed pelvic pain and its treatment in great detail and thus drew a lot of attention.

Due to a lot of requests from our readers we have included more article summaries in this issue.

Owing to the highly vibrant schedule of the next three months we are going to be with you with more news and achievements in our next issue.

Best regards,

Board Members of Endometriosis&Adenomyosis Society

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

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### SOCIAL MEDIA

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Prof. Dr. Umit Inceboz, M.D.
THE RISK OF PRETERM BIRTHS AMONG PREGNANT WOMEN WITH ADENOMYOSIS


Abstract
Objectives—Few studies have examined the effect of adenomyosis on pregnancy outcomes. We aimed to evaluate the risk of preterm birth and low birth weight in women with adenomyosis diagnosed during pregnancy.

Methods—A computerized ultrasonography database was used to identify singleton pregnant women with adenomyosis in the first trimester from January 2010 to December 2011. Only cases with a known pregnancy outcome were included, were viewed the medical records and analyzed pregnancy outcomes according to the presence of adenomyosis and conception method.

Results—Among 11,173 singleton pregnant women, adenomyosis was detected in 88 (0.8%), and 8316 pregnant women (including 72 with adenomyosis) were included. The adenomyosis group was associated with significantly higher rates of preterm birth and low birth weight than the non-adenomyosis group (12.5% versus 4.1%; P < .001; 13.9% versus 3.1%; P < .001, respectively). In a subgroup analysis, according to the conception method, incidences of preterm birth and low birthweight were not different in the non-adenomyosis group. However, the risks of preterm birth and low birth weight in the adenomyosis group were significantly higher in pregnant women who conceived by assisted reproductive technologies than in women who conceived naturally (28.0% versus 4.3%; P < .01; 28.0% versus 6.4%; P < .05, respectively).

Conclusions—Ultrasonographic findings suggesting adenomyosis in early pregnancy were associated with increased risks of preterm delivery and low birth weight in women who conceived with the use of assisted reproductive technologies but not in women who conceived spontaneously.

Key Words—adenomyosis; assisted reproductive technologies; gynecology; low birth weight; obstetrics; premature birth; ultrasonography
Abstract

STUDY QUESTION: What is the degree of patient satisfaction in women with symptomatic colorectal endometriosis who choose medical or surgical treatment after a shared decision-making (SDM) process?

SUMMARY ANSWER: The degree of satisfaction with treatment was high both in women who chose medical treatment with a low-dose oral contraceptive (OCP) or a progestin, and in those who chose to undergo surgical resection of bowel endometriosis.

WHAT IS KNOWN ALREADY: Hormonal therapies and surgery for colorectal endometriosis have been investigated in non-comparative studies with inconsistent results.

STUDY DESIGN, SIZE, DURATION: Parallel cohort study conducted on 87 women referring to our centre with an indication to surgery for colorectal endometriosis. A standardized SDM process was adopted, allowing women to choose their preferred treatment. Median follow-up was 40 [18–60] months in the medical therapy group and 45 [30–67] in the surgery group.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Patients with endometriosis infiltrating the proximal rectum, the rectosigmoid junction, and the sigmoid, not causing severe sub-occlusive symptoms were enrolled. A total of 50 patients chose treatment with an OCP (n = 12) or a progestin (n = 38), whereas 37 women confirmed their previous indication to surgery. Patient satisfaction was graded according to a5-category scale. Variations in bowel and pain symptoms were measured by means of a 0–10 numeric rating scale. Constipation was assessed with the Knowles–Eccersley–Scott Symptom Questionnaire (KESS), health-related quality of life with the Short Form-12 questionnaire (SF-12), psychological status with the Hospital Anxiety and Depression scale (HADS) and sexual functioning with the Female Sexual Function Index (FSFI).

MAIN RESULTS AND THE ROLE OF CHANCE: Six women in the medical therapy group requested surgery because of drug inefficacy (n = 3) or intolerance (n = 3). Seven major complications were observed in the surgery group (19%). At 12-month follow-up, 39 (78%) women in the medical therapy group and 38 (76%) in the surgery group (adjusted odds ratio (OR), 1.37; 95% confidence interval (CI), 0.45–4.15; intention-to-treat analysis). Corresponding figures at final follow-up assessment were 72% in the former group and 65% in the latter one (adjusted OR, 1.74; 95% CI, 0.62–4.85). The 60-month cumulative proportion of dissatisfaction-free participants was 71% in the medical therapy group compared with 61% in the surgery group (P = 0.61); the Hazard incidence rate ratio was 1.21 (95% CI, 0.57–2.62). Intestinal complaints were ameliorated by both treatments. Significant between-group differences in favor of medical treatment were observed at 12-month follow-up in diarrhea, dysmenorrhea, non-menstrual pelvic pain and SF-12 physical component scores. The total HADS score improved significantly in both groups, whereas the total FSFI score improved only in women who chose medical therapy.

LIMITATIONS REASONS FOR CAUTION: As treatments were not randomly assigned, selection bias and confounding are likely. The small sample size exposes to the risk of type II errors.

WIDER IMPLICATIONS OF THE FINDINGS: When adequately informed and empowered through a SDM process, most patients with non-occlusive colorectal endometriosis who had already received a surgical indication, preferred medical therapy. The possibility of choosing the preferred treatment may allow maximization of the potential effect of the interventions.
Innovation drought

Despite the exponential growth in the number of PubMed-indexed publications on endometriosis in the last 60 years (Guo, 2014), a simple reality check can be quite humbling and, perhaps more likely, disheartening. Innovation drought is conspicuous. So far not a single biomarker has been proven to be clinically useful for diagnosing endometriosis (Gupta et al., 2016; Nisenblat et al., 2016a, 2016b). Furthermore, a good disease-staging system that correlates with the severity of symptoms and/or has prognostic predictive capability is lacking.

The innovation drought is most glaring in the research and development of non-hormonal drugs: this is so painfully stagnant that the disappointment is audible (Vercellini et al., 2011). Currently, the top-of-the-line drug for treating endometriosis is dienogest; a drug that was originally synthesized by Jenapharm in then East Germany in the 1979 well before the boom of molecular biology of endometriosis and certainly before the advent of genomics or proteomics. Dienogest is effective in suppressing endometriosis-associated pain; however, it only alleviates symptoms, it does not reduce the volume of the endometriotic nodules (Leonardo-Pinto et al., 2017). While a new class of drug is now poised to get regulatory approval (i.e. gonadotropin-releasing hormone (GnRH) antagonists), it is far from innovative from the mechanism of action perspective even though it is structurally novel. GnRH antagonists still aims to modulate the hypothalamic–pituitary–gonadal (HPG) axis through a validated target, similarly to their agonist counterparts and, as such, may still share the same side-effects as GnRH agonists. Of course, GnRH antagonists can remove the ‘flare-up’ phenomenon, but their promise for more precise control of estrogen production could be undermined by the vast inter-individual variations. A search of ClinicalTrials.gov indicates that currently nine pharmaceutical companies are currently in the various stages of developing GnRH antagonists, making them the most coveted drug in reproductive medicine. Aside from GnRH antagonists, the research and development pipelines of all pharmaceutical companies seem to be trickling or are on the verge of drying up; several compounds in the Phase I stage appear to be congenitally ill-prepared to combat the fibroproliferative nature of endometriosis. No company is investing anything on drug research and development for adenomyosis, and so far all trials on non-hormonal drugs have apparently failed (Guo, 2014). Thus, it seems that in the next 5–8 years there will not be any truly revolutionary drug for patients with endometriosis or adenomyosis. This is a very serious problem.

What went wrong? Faced with such an abject failure, one could still pretend that all is well, continue business as usual, wait for divine revelation, and pray that some miracles will happen eventually. Conscientious and responsible investigators, however, may experience bouts of self-doubt, do some soul-searching, and then contemplate possible paradigm shifts. Realistically, questioning the very basic that we have espoused so dearly that might have shackled our minds and imagination would be an easy and rational first step.

Evolving definitions

Deceptively simple and straightforward, endometriosis has always been defined somewhat monolithically as ‘the presence of endometrial glands and stroma outside of the normal location’ (Beshay and Carr, 2012). However, this simple definition belies a kaleidoscopic variation in location, size, color, depth of invasion, presence or absence of adhesion, the proportion of epithelial/stromal cells, and even the presence or absence of these cell types, as in the well-documented phenomenon of ‘stromal endometriosis’ (i.e. lesions without glands) (Clement, 2007; Mai et al., 1997). On top of these variations, there is also a wild variation in symptomology and severity among patients. Dense fibrotic tissues are often present in and/or surrounding the lesions (Bonte et al., 2002; Clement, 2007; Cornillie et al., 1990; Guo et al., 2015; Itoga et al., 2003; Khare et al., 1996; Matsuzaaki et al., 1999; Nisolle and Donnez, 1997; Stovall et al., 1992), especially in deep endometriosis (Bonte et al., 2002; Cornillie et al., 1990; Khare et al., 1996; Nisolle and Donnez, 1997). The fibrosis may result in subsequent adhesion, anatomic distortion and pelvic pain (Nisolle and Donnez, 1997). In this sense, the proposed redefinition of endometriosis by Dr Vigano and the famed Italian team in their Opinion article recently published in Human Reproduction is quite fitting and in fact long overdue (Vigano et al., 2017). With remarkable prescience, Vigano et al. rightly point out that a redefinition should reorient current research efforts towards more effective therapies, help to develop more adequate animal models for endometriosis and improve patient care (Vigano et al., 2017). Their proposal is all the more admirable at a time when one notable fad is to seek consensus on just about everything, because the proposal invites people to ponder, to think, to muse, and to quest for innovation, which is unlikely to come from any consensus.

In fact, the proposed redefinition by Vigano et al. (2017) that endometriosis is ‘a fibrotic condition in which endometrial stroma and epithelium can be identified’ could go a bit further based on evidence unearthed in the last few years.
As we now know, endometriotic lesions, or ectopic endometrium for that matter, are fundamentally wounds undergoing repeated tissue injury and repair (ReTIAR) (Guo et al., 2015; Zhang et al., 2016a, 2016b) due mostly to cyclic bleeding (Brosens, 1997). Consequent to this ReTIAR, the endometriotic lesions, stimulated by transforming growth factor(TGF)-β1 secreted from activated platelets and other immune cells or by some neupeptides secreted from sensory nerve fibers, undergo epithelial–mesenchymal transition (EMT) and fibroblast-to-myofibroblast transdifferentiation(FMT), resulting in increased cellular contractility and collagen production, leading ultimately to fibrosis (Yan et al., 2017; Zhang et al., 2016a, 2016b). Prolonged exposure to activated platelets and/or immune cells also leads to increased expression of α-smooth muscle actin (α-SMA), as well as markers of differentiated smooth muscle cells(SMCs), by endometriotic stromal cells, which are likely to be responsible for the smooth muscle metaplasia (SMM) that is universally seen in endometriotic lesions (Itoga et al., 2003; Khare et al., 1996; Matsuzaki and Darcha, 2013; Mechsner et al., 2005). During disease progression endometriotic lesions also undergo epigenetic changes (Liu et al., 2017; Zhang et al., 2017a), resulting in epigenetic aberrations as reported years ago (Guo, 2009).

Remarkably, similar processes apparently also occur in adenometriotic lesions owing, perhaps in no small amount, to the shared defining feature of cyclic bleeding as in endometriotic lesions (Liu et al., 2016; Shen et al., 2016). In other words, fibrogenesis is an integral and intrinsic part of the progression of ectopic endometrium; fibrosis is not just the secondary event triggered by an insult (Walton et al., 2017) – rather it is an inescapable destiny for wounds that undergo ReTIAR. While many details, such as the source of myofibroblasts, still await more research, these processes essentially depict the natural history of endometriotic lesions, which so far can only be guesstimated very roughly by the color of lesions (Brosens, 1994; Harirchian et al., 2012; Nisolle et al., 1993; Redwine, 1987), and, to a much lesser extent, the depth of invasion (Brosens, 1994).

In light of these developments, endometriosis may be better defined as ‘a condition that started with the ectopic deposition of endometrial stroma and epithelium which undergo cyclic bleeding and thus repeated tissue injury and repair, resulting in gradual and progressive smooth muscle metaplasia and fibrogenesis’. One advantage of this definition is that it seems to cover all varieties of endometriosis and highlights the dynamic and progressive nature of endometriotic lesions. But more importantly, it essentially embodies the natural history of endometriotic lesions.

**Implications**

Arguably, knowing the natural history of endometriotic lesions holds the key to unlocking the enigma of the pathophysiology of endometriosis. Lesional fibrogenesis resulting from ReTIAR is essentially the Holy Grail of the natural history of ectopic endometrium.

The understanding of the natural history of ectopic endometrium should greatly empower endometriosis researchers. First, due to the shared commonality of cyclic bleeding, adenomyotic and endometriotic lesions can be investigated within the same framework (Liu et al., 2016; Shen et al., 2016). It has been long known that the two conditions often co-exist (Liet al., 2014; Leyendecker et al., 2015), and the two have been postulated to have the same origin (Leyendecker et al., 2002, 2009, 2015).

Second, it gives a global view of just how endometriotic lesions would develop and progress. This is important, since all too often we have seen a study that reports some molecular aberrations in endometriosis from painstakingly designed and meticulously executed experiments without knowing how the discovery fits in a global picture, much like a group of blind men groping and trying to figure out, in vain, what an elephant looks like. In addition, this global view could help to predict things that are otherwise difficult to find. Moreover, it may provide a framework to piece together seemingly unrelated findings, eventually weaving a complete tapestry of the pathophysiology of endometriosis.

Third, the natural history and the dynamic nature of several cell types involved in the process tell us that the cellular identity of lesions is simply not immutable. Rather, through interaction with other cells and mediators in their microenvironment, endometriotic cells may acquire a new morphology, new function, new phenotype and new identity, and collectively drive lesional fibrogenesis. The composition of cell types within a lesion may also change over time and this may explain why there are frequent conflicting reports in the literature because observations are often based on the use of mRNA or proteins extracted from a mixture of different cell types indiscriminately.

Fourth, through refocused research priorities, and perhaps also reallocation of resources, we can round up all perpetrators/suspects that are actively involved in promoting the lesional fibrogenesis, which can serve as potential drug targets. In the past, a great deal of efforts have been invested on hormonal and inflammation pathways without knowing what their roles are in lesional fibrogenesis. Since fibrosis is generally difficult to treat, let alone cure (Wynn, 2007), the fibrosis in endometriotic lesions is very likely to be chiefly responsible for the resistance to pharmacological treatment, especially in deep endometriosis (Koninckx et al., 2012). Conceivably, the low vascularization combined with the absence of steroid hormone receptors in the fibrotic tissues (Liu et al., 2017) are the major causes for the failure of the traditional hormonal drugs. As a corollary, any compound that does not have any anti-fibrotic capability may have little chance to succeed.

Sixth, by prudent choice of markers that represent various turning points in EMT, FMT, SMM and fibrogenesis it is possible to stage endometriosis by histology as has been shown in baboons (Zhang et al., 2016a, 2016b) and mice (Zhang et al., 2017a, 2017b). A good histology-based staging system should be useful not only for prognostic purposes but also to provide a basis for precision medicine. Seventh, by capitalizing on the advent of elastography, a novel imaging technique that can measure tissue stiffness, and on the intimate link between the extent of fibrosis and tissue stiffness, we can significantly improve our imaging diagnostic capability for endometriosis and adenomyosis, especially adenomyosis (Liu et al., 2018) and deep endometriosis. It is also possible that, due to the correlation between lesional stiffness and hormonal receptor expression levels, results from elastographic imaging could be used to help choose the best treatment modality for deep endometriosis and/or adenomyosis (Liu et al., 2018).
Eighth, seeing thorough the lens of this natural history of endometriosis, we can now understand why many clinical trials on endometriosis foundered. Despite enormous resources and toil invested, these trials are a parade of intrigue, surprise and disappointment, especially those trials on non-hormonal drugs (Guo and Evers, 2013; Guo, 2014). Surprisingly, there has been no open discussion on why and how these trials went bust, raising the prospect that many missteps and mistakes made in these failed trials would be repeated in future trials. With our current knowledge of the natural history of endometriotic lesions, it is easy to see that many, seemingly promising, preclinical studies that led to the launch of clinical trials (such as trials on infliximab and ERB-041) used rodent or nonhuman primate models of endometriosis that did not fully recapitulate human endometriosis in general and fibrosis in particular. The only study that used a right baboon model, which is the closest to human condition, did get the right results (Barrier et al., 2004). However, data interpretation in this study was in error: treatment with etanercept, a TNF neutralization agent, did reduce the amount of active lesions effectively, but it had no effect whatsoever on more advanced lesions. The latter observation is very likely replicated in the infliximab trial (Konincx et al., 2008), leading to its demise.

Lastly, knowing the stage of progression can help us design far better studies to identify biomarkers for endometriosis, which so far has been a debacle (Nisenblat et al., 2016a, 2016b). The information on the developmental stage of lesions should help boost the signal-to-noise ratio within the data, and perhaps also help to identify biomarkers for early-stage endometriosis.

Time for change
Dr Vigano and her associates are to be commended for their perceptive insight, timely proposal and for being the first to propose a change. In the face of innovation drought and all the debacles it is the right thing to do since ‘old ways will not open new doors’. Starting with a new definition, especially with the understanding of the natural history of ectopic endometrium, there is a hope that things will turn around. It may be a much-needed antidote to keep us sane and sober, since ‘doing the same thing over and over again and expecting different results’ are said to qualify for insanity.

PROGRESS IN THE DIAGNOSIS AND MANAGEMENT OF ADOLESCENT ENDOMETRIOSIS: AN OPINION.


Abstract
Increasing evidence indicates that early onset endometriosis (EOE), starting around menarche or early adolescence, may have an origin different from the adult variant, originating from neonatal uterine bleeding (NUB).

This implies seeding of naïve endometrial progenitor cells into the pelvic cavity with NUB; these can then activate around the larche. It has its own pathophysiology, symptomatology and risk factors, warranting critical management re-evaluation. It can also be progressive, endangering future reproductive capacity.

This variant seems to be characterized by the presence of ovarian endometrioma. Today, the diagnosis of endometriosis in young patients is often delayed for years; if rapidly progressive, it can severely affect pelvic organs, even in the absence of serious symptoms.

Given the predicament, great attention must be paid to symptomatology that is often non-specific, justifying a search for new, simple, non-invasive markers of increased risk. Better use of modern imaging techniques will aid considerably in screening for the presence of EOE. Traditional laparoscopy should be limited to cases in which imaging gives rise to suspicion of severity and a stepwise, minimally invasive approach should be used, followed by medical treatment to prevent recurrence. In conclusion, EOE represents a condition necessitating early diagnosis and stepwise management, including medical treatment.
Endometriosis is a chronic, estrogen-dependent disease and characterized by the implantation of endometrial glands and stroma deep and haphazardly into the outside the uterine cavity. It affects an estimated 10% of the female population of reproductive age and results in obvious reduction in health-related quality of life.

Unfortunately, there is no a consistent theory for the etiology of endometriosis. Furthermore, the endometriosis is hard to diagnose in early stage and the treatment methods are limited. Importantly, emerging evidence has investigated that there is a close relationship between endometriosis and autophagy. However, autophagy is a friend or foe in endometriosis is puzzling, the precise mechanism underlying autophagy in endometriosis has not been fully elucidated yet.

Here, we provide an integrated view on the acquired findings of the connections between endometriosis and autophagy. We also discuss which may contribute to the abnormal level of autophagy in endometriosis.

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**IS SHIFTING TO A PROGESTIN WORTHWHILE WHEN ESTROGEN-PROGESTINS ARE INEFFICACIOUS FOR ENDOMETRIOSIS-ASSOCIATED PAIN?**

**Abstract**

The purpose of this study was to assess the proportion of patients satisfied with their treatment after a change from a low-dose oral contraceptive (OC) to norethisterone acetate (NETA) because of inefficacy of OC on pain symptoms. To this end, prospective, self-controlled study was conducted on 153 women using OC as a treatment for endometriosis and with persistence of one or more moderate or severe pain symptoms. At baseline and during 12 months after a shift from OC to oral NETA, 2.5 mg/d, pelvic pain was measured by means of a 0- to 10-point numerical rating scale and a multidimensional categorical rating scale.

Variations in health-related quality of life, psychological status, and sexual function were also evaluated with validated scales. At the end of the study period, participants indicated the degree of satisfaction with their treatment according to a 5-degree scale from very satisfied to very dissatisfied. A total of 28 women dropped out of the study, the main reason was intolerable side effects (n = 15). At 12-month assessment, 70% of participants were very satisfied or satisfied with NETA treatment (intention-to-treat analysis). Statistically significant improvements were observed in health-related quality of life, psychological status, and sexual function.

At per-protocol analysis, almost half of the patients (58/125) reported suboptimal drug tolerability. However, complaints were not severe enough to cause dissatisfaction, drug discontinuation, or request for surgery.

These encouraging results could be used to counsel women with symptomatic endometriosis not responding to OC and to inform their decisions on modifications of disease management.
THE ISOLATED OVARIAN ENDOMETRIOMA: A HISTORY BETWEEN MYTH AND REALITY.

Abstract

STUDY OBJECTIVE: To assess the association between ovarian endometriomas detectable at transvaginal ultrasound (TVS) and other specific extra-ovarian lesions including adhesions, deep infiltrating endometriosis, and adenomyosis.

DESIGN: Retrospective observational study (Canadian Task Force classification II-2).

SETTING: Two university hospitals.

PATIENTS: 255 symptomatic women with at least one ovarian endometrioma found on ultrasound after presentation with pain or irregular menstruation.

INTERVENTIONS: Patients underwent TVS followed by either medical or surgical treatment.

MEASUREMENTS AND MAIN RESULTS: Two hundred and fifty-five women, aged 20 to 40 years, underwent TVS and were found to have at least one endometrioma with a diameter > 20 mm. Associated sonographic signs of pelvic endometriosis (adhesions, deep infiltrating endometriosis, and adenomyosis) were recorded, and a subgroup of patients (n = 50) underwent laparoscopic surgery within 3 months of TVS. Mean endometrioma diameter was 40.0 ± 18.1 mm, and bilateral endometriomas were observed in 65 patients (25.5%). Transvaginal ultrasound showed posterior rectal deep infiltrating endometriosis in 55 patients (21.5%) and a thickening of at least one uterosacral ligament in 93 patients (36.4%). One hundred eighty-six patients (73%) had adhesions, and 134 patients (53%) showed signs of myometrial adenomyosis on TVS. Thirty-eight patients (15%) exhibited only a single isolated endometrioma with a mobile ovary and no other signs of pelvic endometriosis/adenomyosis at TVS.

CONCLUSION: Ovarian endometriomas are indicators for pelvic endometriosis and are rarely isolated. Particularly, left endometriomas were found to be associated with rectal deep infiltrating endometriosis and left uterosacral ligament localization, and bilateral endometriomas correlated with adhesions and pouch of Douglas obliteration while no correlation was found between endometrioma size and deep infiltrating endometriosis. Determining appropriate management, whether clinical or surgical, is critical for ovarian endometriomas and concomitant adhesions, endometriosis, and adenomyosis in patients desiring future fertility.
Abstract

BACKGROUND: Chronic pelvic pain affects ∼15% of women, and presents a challenging problem for gynecologists due to its complex etiology involving multiple comorbidities. Thus, an interdisciplinary approach has been proposed for chronic pelvic pain, where these multifactorial comorbidities can be addressed by different interventions at a single integrated center. Moreover, while cross-sectional studies can provide some insight into the association between these comorbidities and chronic pelvic pain severity, prospective longitudinal cohorts can identify comorbidities associated with changes in chronic pelvic pain severity over time.

OBJECTIVE: We sought to describe trends and factors associated with chronic pelvic pain severity over a 1-year prospective cohort at an interdisciplinary center, with a focus on the role of comorbidities and controlling for baseline pain, demographic factors, and treatment effects.

STUDY DESIGN: This was a prospective 1-year cohort study at an interdisciplinary tertiary referral center for pelvic pain and endometriosis, which provides minimally invasive surgery, medical management, pain education, physiotherapy, and psychological therapies. Exclusion criteria included menopause or age >50 years. Sample size was 296 (57% response rate at 1 year; 296/525). Primary outcome was chronic pelvic pain severity at 1 year on an 11-point numeric rating scale (0-10), which was categorized for ordinal regression (none-mild 0-3, moderate 4-6, severe 7-10). Secondary outcomes included functional quality of life and health utilization. Baseline comorbidities were endometriosis, irritable bowel syndrome, painful bladder syndrome, abdominal wall pain, pelvic floor myalgia, and validated questionnaires for depression, anxiety, and catastrophizing. Multivariable ordinal regression was used to identify baseline comorbidities associated with the primary outcome at 1 year.

RESULTS: Chronic pelvic pain severity decreased by a median 2 points from baseline to 1 year (6/10-4/10, P < .001). There was also an improvement in functional quality of life (42-36% on the pain subscale of the Endometriosis Health Profile-30, P < .001), and a reduction in subjects requiring a physician visit (73-36%, P < .001) or emergency visit (24-11%, P < .001) in the last 3 months. On multivariable ordinal regression for the primary outcome, chronic pelvic pain severity at 1 year was independently associated with a higher score on the Pain Catastrophizing Scale at baseline (odds ratio, 1.10; 95% confidence interval, 1.00-1.21, P = .04), controlling for baseline pain, treatment effects (surgery), age, and referral status.

CONCLUSION: Improvements in chronic pelvic pain severity, quality of life, and health care utilization were observed in a 1-year cohort in an interdisciplinary setting. Higher pain catastrophizing at baseline was associated with greater chronic pelvic pain severity at 1 year. Consideration should be given to stratifying pelvic pain patients by catastrophizing level (rumination, magnification, helplessness) in research studies and in clinical practice.
Abstract

**BACKGROUND:** Laparoscopic stripping is the gold-standard treatment for ovarian endometriosis. The choice of hemostasis method might affect ovarian reserve.

**OBJECTIVES:** To determine whether bipolar electrocoagulation is more detrimental to ovarian reserve than non-thermal hemostasis methods.

**SEARCH STRATEGY:** Entry terms associated with the MeSH terms “endometrioma,” “laparoscopy,” and “ovarian reserve” were used to search databases for articles published up to April 3, 2017, in English, Spanish, Portuguese, French, and Italian.

**SELECTION CRITERIA:** Randomized controlled trials comparing the 3-month postoperative serum anti-Müllerian hormone (AMH) level in premenopausal women undergoing laparoscopic stripping with bipolar hemostasis or non-thermal hemostasis methods were selected.

**DATA COLLECTION AND ANALYSIS:** Data were extracted by two independent reviewers and a meta-analysis was performed.

**MAIN RESULTS:** Three studies met the inclusion criteria; overall, 105 patients underwent surgery with bipolar electrocoagulation and 105 patients underwent surgery with an alternative hemostasis method. The AMH level 3 months after surgery was decreased in the bipolar electrocoagulation group (mean difference -0.79 ng/mL, 95% confidence interval -1.19 to -0.39).

**CONCLUSIONS:** Bipolar electrocoagulation negatively impacts ovarian reserve and should be avoided, especially for patients with reproductive goals.
Abstract

Study question: What does this document on the surgical treatment of endometriosis jointly prepared by the European Society for Gynecological Endoscopy (ESGE), ESHRE, and the World Endometriosis Society (WES) provide?

Summary answer: This document provides recommendations covering technical aspects of different methods of surgery for endometriomas in women of reproductive age.

What is already known: Endometriomas (ovarian endometriotic cysts) are a commonly diagnosed form of endometriosis, owing to the relative ease and accuracy of ultrasound diagnosis. They frequently present a clinical dilemma as to whether and how to treat them when found during imaging or incidentally during surgery. Previously published guidelines have provided recommendations based on the best available evidence, but without technical details on the management of endometriosis.

Study design, size and duration: A working group of ESGE, ESHRE and WES collaborated on writing recommendations on the practical aspects of endometrioma surgery.

Participants/materials, setting and methods: This document focused on endometrioma surgery. Further documents in this series will provide recommendations for surgery of deep and peritoneal endometriosis.

Main results and the role of chance: The document presents general recommendations for surgery of endometrioma and specific recommendations for cystectomy, ablation by laser or by plasma energy, electrocoagulation and a combination of these techniques applied together or with an interval between them.

Limitations and reasons for caution: Owing to the limited evidence available, recommendations are mostly based on clinical expertise.

Wider implications of the findings: These recommendations complement previous guidelines on the management of endometriosis.

Study funding/competing interests: The meetings of the working group were funded by ESGE, ESHRE and WES. CB declares to be a member of the independent data monitoring committee for a clinical study by ObsEva and receiving research grants from Bayer, Roche Diagnostics, MDNA Life Sciences and Volition. ES received honoraria for provision of training to healthcare professionals from Ethicon, Olympus and Gedeon Richter. The other authors declare that they have no conflict of interest.
Dear colleagues,

We, as the Turkish Endometriosis and Adenomyosis Society, would like to invite you to the 1st Chronic Pelvic Pain Symposium that will take place on 20-21 April 2018 in Istanbul. This symposium is not only going to be on endometriosis, inflammatory bowel disease (IBD) or interstitial cystitis but also on many topics which were not discussed before and they will all be delivered by experienced national and international lecturers. During our meeting, Horace Roman from France will operate on a sacral nerve endometriosis case on live stream. Our international lecturers are mentioned briefly below:

Michael Hibner/The USA: Has started the first fellowship program on Chronic Pelvic Pain in the United States. He is the first man to execute transgluteal pudendal nerve release in America after getting educated in Europe. He has also carried out the first KPA courses at the AAGL.

Horace Roman/France: He is mainly working on Deep Infiltretive Endometriosis in France. He has a great deal of experience on pelvic nerve endometriosis. During our meeting, he will be joining us with video conference and also with a live surgery on pelvic nerve endometriosis.

Alysson Zanatta/Brazil: She is on the neuropelviology working group. Alysson was trained by Marc Possover and has articles on pelvic nerves. She is currently working in the Endometriosis Center of Brazil.

Vito Chiantera/Italy: He is also on the neuropelviology working group and was trained by Marc Possover. His articles can be found on deep infiltrative endometriosis and oncology. He has a lot of experience on pelvic anatomy and pelvic surgery.

Gökhan Kılıç/The USA: He is on the neuropelviology working group as well. He is experienced in pelvic floor and pelvic pain. He is also famous for his robotic surgery techniques.

Paolo Vercellini/Italy: He is a well-known researcher who has published many articles on endometriosis. He will be presenting his lecture by a video conference.

Only 110 participants will be accepted to our symposium so hurry up to sign up

Turkish Endometriosis & Adenomyosis Society
APRIL 20TH, 2018 - FRIDAY / 20 NİSAN 2018 - CUMA

16:15 - 17:50 SESSION 5: Neuropevelology-1 / OTURUM 5: Nöropelvıolojı-1
Chairs / Oturum Başkanları: Yakınl Karaman, Berna Haliloluoglu Peker

16:15 - 16:35 Anatomy of Pelvic Autonomic Nerves
Pelvik Otonom Sinir Anatomisi
Alysson Zanatta

16:35 - 16:55 Anatomy of Pelvic Somatic Nerves
Pelvik Somatik Sinir Anatomisi
Vito Chiontera

16:55 - 17:15 Nerves Sparring Surgeries: Feasibility, Techniques and Effectiveness
Sinir Karşıyayır Cerrahisi: Uygulanabilirliği, Teknikleri ve Etkinliği
Alysson Zanatta

17:15 - 17:35 Management of Endometriosis: Toward Value-Based Cost Effective, Affordable Care
Endometriozıs Yönetimi: Maliyet Hasıla, Karşılanabilir Bakıma Doğru
Paolo Vercellini

17:35 - 17:50 Discussion / Tartışma

APRIL 21ST, 2018 - SATURDAY / 21 NİSAN 2018 - CUMARTESİ

09:30 - 11:00 SESSION 6: Neuropevelology-2 / OTURUM 6: Nöropelvıolojı-2
Chairs / Oturum Başkanları: Funda Gündüz Uğurçam, Teğda Korescan

09:30 - 09:50 Neuroprotective Pelvic Pain - Imaging, Genitoferoral, Obturator, Femoral Nöropatik Pelvik Ağrı - İddme bilateral, Genitoferoral, Obturator, Femoral Michael Hildner

09:50 - 10:10 Laparoscopic Implantation of Neural Electrode: Techniques and Clinical Applications
Nöral Elektrotün Laparoskopik İmplantasyonu: Teknikleri ve Klinik Uygulanması
Vito Chiontera

10:10 - 10:30 Robotics In Neuropevelogy
Nöropelvıolojide Robot
Gökhan Kılıç

10:30 - 10:50 On-offactive Fluids and Laparoscopic Pudendal Nerve Stimulation: A Prospective Study
Açık-Ampolwäwsan ve Laparoskopik Pudendal Sinir Stıımülasyonu: Prospektif Çalışma
Vito Chiontera

10:50 - 11:00 Discussion / Tartışma

11:00 - 11:30 Coffee Break / Kahve Mezesi

11:30 - 13:00 SESSION 7 / OTURUM 7
Chairs / Oturum Başkanları: Gül Köknel Tulu, Hale Göksever Çelik

11:30 - 11:50 Colorectal Causes of CPP
Kronik Pelvik Ağrımın Kolorektal Nedenleri
Hülya Hamazoğlu

11:50 - 12:10 Urological Causes of CPP
Kronik Pelvik Ağrımın Uroloji Nedenleri
Oktay Demirkesen

12:10 - 12:30 FTR Causes of CPP
Kronik Pelvik Ağrımın Romatizmal Nedenleri
Zeynep Güven

12:30 - 12:50 Neurological Evaluation of Chronic Pelvic Pain
Kronik Pelvik Ağrımın Nörolojik Değerlendirilmesi
Müge Koçoğlu

12:50 - 13:00 Discussion / Tartışma

13:00 - 14:00 LUNCH / ÖGLE YEMEĞİ

14:00 - 15:00 SESSION 8: CPP Case Discussion - Multidisciplinary Approach / OTURUM 8: KPA Vaka Tartışması - Multidisipliner Yaklaşıım

Debaters / Tartışmacılar: Ahmet Kale, Alysson Zanatta, Gül Köknel Tulu, Hülya Hamazoğlu, Michael Hildner, Gökhan Kılıç, Taner Usta, Tibet Erdogru, Zeynep Güven

15:00 - 15:30 Coffee Break / Kahve Arası

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APRIL 21ST, 2018 - SATURDAY / 21 NİSAN 2018 - CUMARTESİ

15:30 - 17:00 SESSION 9 / OTURUM 9
Chairs / Oturum Başkanları: Gürkan Uncu, Pınar Yalbaş Bahat

15:30 - 15:50 Nerve Blocks, Trigger Point Injections, and Botoks
Sinir Bloksları, Tektit Nokta Enjeksiyonları ve Botoks
Michael Hildner

15:50 - 16:10 Vascular Entrapment of Pelvic Nerves
Pelvik Sinirlerin Vasküler Tuzaklanması
Taner Usta

16:10 - 16:30 Pain After Mesh Procedures
Mesh Prosedürlerinden Sonra Ağrı
Gökhan Kılıç

16:30 - 16:50 Discussion / Tartışma

16:50 - 17:00 Closing the Symposium / Kapanış
As a part of the Endoacademia meetings we are going to organize a one-day meeting on April 1st, 2018 in Kayseri. With the support of our local colleagues we are going to talk in detail about the management of Endometrioma and share all the up-to-date information on this subject. For further details please visit our website. We are going to be organizing other meetings in different cities.
Program

Moderators:  Prof. Dr. M. Turan, M.D., Assoc. Prof. Baris Mulayim, M.D.
09:00-09:30 Registration and Welcoming Speech

09:30-11:30 1. SESSION: ENDOMETRIOMA – GENERAL
Chairmen: Prof. Dr. Engin Oral, M.D., Prof. Dr. Bulent Ozcelik, M.D.
09:30-09:50 Symptomatology of Endometrioma
   Asst. Prof. Semih Uludag, M.D.
09:50-10:10 Should endometrioma be operated in women with infertility problems? Or should we avoid it?
   Prof. Dr. Yilmaz Sahin, M.D.
10:10-10:30 The relationship between Endometrioma and Ovarian Cancer: Should we be afraid?
   Prof. Dr. Fatma Ferda Verit, M.D.
10:30-10:50 The association between Endometrioma, Deep Infiltrative Endometriosis (DIE) and Adenomyosis
   Prof. Dr. Yucel Karaman, M.D.
10:50-11:15 Discussion
11:15-11:30 Coffee Break

2. SESSION: ENDOMETRIOMA – CURRENT TREATMENT OPTIONS
11:30-13:20
Chairmen: Prof. Dr. Ercan Aygen, M.D., Assoc. Prof. Baris Mulayim, M.D.
11:30-11:50 Management of Endometrioma in Adolescence
   Prof. Dr. Umit Inceboz
   Prof. Dr. Engin Oral
12:10-12:30 How to operate on difficult Endometrioma cases?
   Assoc. Prof. Taner Usta
12:30-12:50 Management of Endometrioma in cases of recurrence
   Prof. Dr. M. Turan Cetin
12:50-13:00 Insulin resistance in PCOS and treatment with Inositol
   Prof. Dr. Faruk Buyru
13:00-13:20 Discussion
13:20-14:30 Lunch Break

3. SESSION INTERACTIVE ENDOMETRIOMA CASE DISCUSSIONS
14:30-15:45 Moderators:
   Prof. Dr. Gurkan Uncu
Panelists:
   Prof. Dr. Yucel Karaman, Prof. Dr. M. Turan Cetin, Prof. Dr. Engin Oral
   Prof. Dr. Yilmaz Sahin, Assoc. Prof. Taner Usta, Assist. Prof. Semih Uludag
   Prof. Dr. Umit Inceboz, Prof. Dr. Fatma Ferda Verit
15:45-16:00 Closing Speech

PARTICIPATION IS FREE OF CHARGE.
Prof. Umit Inceboz, M.D. is going to give a talk with the title ‘Chronic Pelvic Pain in Endometriosis and Other Organ Related Factors and Treatment’ in Antalya at the 3rd Sexual Health Congress organized by The Institute of Sexual Health (CISED). This subject will be discussed in detail also with the input of our colleagues from the field of psychiatry.

Use the following link for further information;
http://cised.org.tr/kongre2018/tr/program
As a part of the Endoacademia meetings with the support of our lecturers in the region we organized a one-day meeting on ‘Management of Endometrioma’ in Gaziantep on January, 28th, 2018. Our physicians shared in detail the up-to-date information on this subject. The meeting was broadcasted live on Facebook. You can find further information on our website. We are going to keep conducting these regional meetings in other cities.

| PROGRAM DETAILS |
|-----------------|----------------|
| 09:00 - 10:00   | Registration  |
| 10:00 - 11:30   | 1. Session: ENDOMETRIOMA – General  |
|                 | Chairman: Ocah Balatli Ali Irfan Kutlar |
| 10:00 - 10:15   | Symptomatology of Endometrioma  |
| 10:15 - 10:30   | Keray Elfer  |
| 10:30 - 10:45   | Which is more harmful: operating on endometrioma or leaving it in its place?  |
| 10:45 - 11:00   | Gurcan Uncu  |
| 11:00 - 11:15   | How should the approach be to endometrioma in infertile women?  |
| 11:15 - 11:30   | Halis Özyeneloglu  |
| 11:30 - 12:00   | 2. Session: ENDOMETRIOMA – CURRENT TREATMENT  |
| 12:00 - 12:15   | Discussion  |
| 12:15 - 12:30   | 2. Session: ENDOMETRIOMA – CURRENT TREATMENT  |
| 12:30 - 12:45   | Approaching to endometrioma in adolescence  |
| 12:45 - 13:00   | Baris Malyayim  |
| 13:00 - 13:15   | How can we improve endometrioma surgery?  |
| 13:15 - 13:30   | Tamer Usta  |
| 13:30 - 14:30   | In medical treatment of endometrioma: oral contraceptives? Progestersones?  |
| 14:30 - 14:40   | Prof. Dr. Engin Oral  |
| 14:40 - 16:00   | In difficult cases how should the operative treatment of endometrioma proceed?  |
| 15:00 - 16:00   | Prof. Dr. Verel Karaman  |
| 16:00 - 17:00   | Management of recurring endometrioma cases  |
| 17:00 - 18:00   | M. Turan Cetin  |
| 18:00 - 19:00   | Discussion  |
| 19:00 - 20:00   | 3. Session: INTERACTIVE CASE DISCUSSION ON ENDOMETRIOMA  |
| 20:00 - 21:00   | Moderator: Engin Oral  |
| 21:00 - 22:00   | Panelists: Yucel Kacsman, Gurcan Uncu, M. Turan Cetin, Halis Özyeneloglu, Keray Elfer, Tamer Usta, Ahmet Kale, Baris Malyayim, Mete Gurul Ugur  |
| 22:00 - 23:00   | Discussion  |
| 23:00 - 00:00   | Closing remarks  |
21-25 FEBRUARY 2018  CONGRESS ON MINIMALLY INVASIVE SURGERY IN GYNECOLOGY

At the congress on minimally invasive surgery in gynecology held in Istanbul on February, 21-25, 2018, physicians from our society discussed endometriosis and infertility with international colleagues.

10:30-12:00 Session on Endometriosis and Infertility
10:30-10:45 Endometriosis and infertility; a still mysterious relationship Cihat Unlu
10:45-11:00 Indications of surgery in infertile patients with endometriosis? Ludovico Muzii
11:00-11:15 Endometrioma, endometrioma surgery and ovarian reserve – a dangerous relationship Gurkan Uncu
11:15-11:30 Should infertile patients with deep infiltrative endometriosis be treated with surgery? Yucel Karaman
11:30-11:45 Optimal treatment of recurrent cases on endometrioma in infertile patients, is surgery an option? Engin Oral
12:00-12:45 Lunch Break

9-10 MARCH 2018  THE UNIVERSITY OF HEALTH SCIENCES 2nd PELVIC REHABILITATION CONGRESS

On March 9-10th, 2018 at the 2nd Pelvic Rehabilitation Congress held by The University of Health Sciences with physicians from the field of physical therapy and rehabilitation, physicians from our society organized a course on pelvic pain. Information on this subject is discussed with physicians from different specialties.

For further information
http://sbupelvikrehabilitasyonkongresi.org/bilimsel_program.php

15:10-17:00 COURSE (HALL 2)
Course on Pelvic Pain
Moderators: Ahmet KALE, Taner USTA
15:10-15:25 Neuroanatomy of the pelvis / Ahmet KALE
15:25-15:40 Gynecological problems that cause chronic pelvic pain / Naris MULAYIM
15:40-15:55 Neurological examination while diagnosing pelvic pain:
    Should it be part of the diagnosis? / Muge KOCAK
15:55-16:10 Algological management of pelvic pain / Gul KOKNEL TALU
16:10-16:25 Neuropelvological management of pelvic pain / Taner USTA
16:25-16:40 Discussion
16:40-17:10 Interactive case presentations – Panel
    Moderators: Taner USTA
    Discussions: Ahmet KALE, Gul KOKNEL, Baris MULAYIM, Muge KOCAK
At the symposium in Uludag between March 8-10th, 2018 physicians from our society organized a session where they discussed management of pain and infertility. You can find detailed information under the following link: http://infertilitendoskopi.org/

10:00-10:15 Coffee Break
Panel 1
Session of National Endometriosis and Adenomyosis Society
Endometriosis – Management of Pain/Infertility
Chairmen: Engin Oral, Gurkan Uncu
What does the Endometriosis NICE guideline tell us?
Pınar Bahat
10:15-11:45 Pediatric Endometriosis, Endometriosis in Adolescence
Engin Oral
Dangers of Endometrioma Surgery
Ercan Bastu
How Should We Manage Adenomyosis and Infertility?
Unit Sungurtekin
Medical Treatment of Deep Endometriosis
Ahmet Kale
26-28 APRIL 2018  SEUD 2018

This congress which took place in Singapore last year will take place this year in Florence, Italy on April 26-28, 2018.
http://seud.org

22-24 NOVEMBER 2018  EEC 2018

Our vice-president Prof. Engin Oral, MD. will participate in the 4th European Congress on Endometriosis in Vienna, Austria on November 22-24, 2018. He will be the secretary of somatic endometriosis at the congress.
Program details will soon be uploaded.
For detailed information http://www.eec2018.com
NEW WEBSITES

Our website has been renovated. You can reach all the webpages through the following link.

Endometriosis & Adenomyosis Society
(www.endometriozis.org)

Endometriosis & Adenomyosis Society’s Special Website for Healthcare Providers
Did you know that through our website you can reach monthly publications on endometriosis, 2014 Endometriosis Diagnosis and Management Guideline, related books, information on our society’s activities, and information on national and international conferences. Our website is prepared not only in Turkish, but also in English. Thus, we are more connected with the world of endometriosis. You can reach the English language website under the following link: http://www.endometriosisturkey.com

Endometriosis & Adenomyosis Society’s Website for Our Patients
(www.endometriozis.org)
One of the most important goals of our society is not only to reach our physicians but also to reach our patients and inform them on the series of activities organized by our society. One of these activities was to set up endometriozis.org. Here, our patients can have the access to the current health news, booklets on the subject, easy tests and videos. Our website is under constant revision. Endometriozis.org is a free website and designed the give accurate information to the patients.

www.endometriosisturkey.com
SUMMARIES OF ENDOMETRIOSIS RELATED ARTICLES

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


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