

Endometriosis Bulletin

December 2017/ Issue-4



ENDOMETRIOSIS

AND ADENOMYOSIS SOCIETY ENDOACADEMY MEETINGS IV

MANAGEMENT OF ENDOMETRIOMA 2018

28 January 2018 - Sunday, Divan Hotel Gaziantep CHAIRS: Prof. Turan Cetin M.D. Assoc. Prof Baris Mulayim M.D.

PREFACE

Dear Colleagues,

We are with you with the fourth issue of our bulletin. Although we have encouraging improvements on our side during the last 3 months, unfortunately, by the decision of Board of EEL league -due to political issues-, 4th European League Congress that was thought to be hosted by our Society and was to be held in Antalya, Turkey in 2018 will be held in Vien, Austria. Prof Engin ORAL will be the scientific secretary of this Congress. In the following days, we will inform you –our collegues- on the improvements.

With the support of local authors, we will organize one-day meeting on "endometrioma" in Gaziantep on January 28th, 2018. We will discuss all updated-information on endometriosis in detail. You may find the info on this meeting in this bulletin and also on our website.

We have participated in two activities; one was "Eker I Run" in Bursa on October 8th and the other one was in 39th Vodafone Istanbul marathon in Istanbul on 12th December. With these activities we wanted to draw public attention to "endometriosis" and "pelvic pain". You may find the details of these activities on our website (www.endometriozis.org).

We have also started to give information under the title of "chocolate cyst", in this section, a group of experts are giving information and aiming to shed light on most-wondered questions by public.

With the wish of better and more successful news in the first issue of the Bulletin in 2018...

With Regards,

Board Members of Endometriosis & Adenomyosis Society

Board Members of Endometriosis&Adenomyosis Society 2017



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Endometriosis e-bulletin is prepared by Turkish Endometriosis & Adenomyosis Society. If there will be subjects, which you would like to be includedin the bulletin or comments/questions that you would like to add, please contact us via drtanerusta@gmail.com or drenginoral@gmail.com .

Table of Contents



Selected Articles

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B News from Our Society

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News from The World of Endometriosis

Social Media

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Ing Version

Umit Inceboz, Prof, M.D. Fitnat Topbas, M.D. in

A SELECTED ARTICLES

1- Value of ultrasound shear wave elastography in the diagnosis of adenomyosis.

Acar S, Millar E, Mitkova M, Mitkov V. Ultrasound. 2016 Nov;24(4):205-213. Epub 2016 Oct 12.

Abstract



Background

The aim of the study was to assess the accuracy of ultrasound shear wave elastography in the diagnosis of adenomyosis.

Methods

One hundred and fifty three patients were examined. Ninety-seven patients were with suspected adenomyosis and 56 patients were with unremarkable myometrium. Adenomyosis was confirmed in 39 cases (A subgroup) and excluded in 14 cases (B subgroup) in the main group based on morphological examination. All patients underwent ultrasound examination using an Aixplorer (Supersonic Imagine, France) scanner with application of shear wave elastography during transvaginal scanning. Retrospective analysis of the elastography criteria against the findings from morphological/histological examination was performed.

Results

The following values of Young's modulus were found in subgroup A (adenomyosis): Emean – 72.7 (22.6–274.2) kPa (median, 5–95th percentiles), Emax – 94.8 (29.3–300.0) kPa, SD – 9.9 (2.6–26.3) kPa; in subgroup B (non adenomyosis) – 28.3 (12.7–59.5) kPa, 33.6 (16.0–80.8) kPa, 3.0 (1.4–15.6) kPa; in the control group – 24.4 (17.9–32.4) kPa, 29.8 (21.6–40.8) kPa, 2.3 (1.3–6.1) kPa, respectively (P<0.05 for all comparison with subgroup B and the control group). The Emean cut-off value for adenomyosis diagnosis was 34.6 kPa. The sensitivity, specificity, positive predictive value, negative predictive value and area under curve (AUC) were 89.7%, 92.9%, 97.2%, 76.5% and 0.907, respectively).

Conclusion

This study showed a significant increase of the myometrial stiffness estimated with shear wave elastography use in patients with adenomyosis.

2- Does surgery for deep infiltrating bowel endometriosis improve fertility? A systematic review.

Iversen ML, Seyer-Hansen M, Forman A. Acta Obstet Gynecol Scand. 2017 Jun;96(6):688-693.

Abstract

INTRODUCTION

Reduced fertility is a major concern in women with endometriosis. The influence of surgery of deep infiltrating endometriosis (DIE) affecting the bowel wall on fertility is controversial and the literature on this field is heterogeneous. In this review we addressed whether surgery for bowel DIE improves the spontaneous pregnancy rate, and the results of in vitro fertilization (IVF), and the potential risk of such surgery.

MATERIAL AND METHODS:

We conducted a literature search including the terms "deep", "deep infiltrating", "bowel", rectovaginal", "endometriosis", "fertility", "infertility" and "IVF" in PubMed.

RESULTS:

No randomized controlled studies were found. Other publications of relevance included four retrospective and three prospective observational studies. Moreover, one retrospective study compared results of IVF treatment with or without previous surgery for bowel DIE. All studies reported detailed data on surgical complications. The poor data quality precluded firm conclusions. The results indicate, however, the possibility that surgery for bowel DIE may improve the spontaneous pregnancy rate, and positive effects on IVF outcome cannot be excluded. Such surgery will be associated with risk of major complications.

CONCLUSION:

The lack of proper data precludes conclusions on the potential role for bowel DIE surgery to improve the spontaneous pregnancy rate and results of IVF treatment. Positive effects cannot be excluded, but the definite risk of major complications must be taken into account.

3- The effect of surgery for endometriomas on fertility. Jayaprakasan K, Becker C, Mittal M on behalf of RCOG Scientific Impact paper No:55. September 2017

1-Background

Endometriosis is an inflammatory condition characterised by the presence of tissue resembling endometrium in sites other than the uterine cavity.] It is estimated that 6-10% of women,1 mainly of reproductive age, are affected by the condition, with a reported higher prevalence in certain subgroups, such as those affected by infertility. Ovarian endometrioma(s) can be found in up to 17-44% of women with endometriosis and are often associated with the severe form of the disease.2,3 While the pathognomonic mechanisms of endometriosis per se remain elusive, it is widely believed that most endometriotic lesions develop from retrograde menstruation and are possibly associated with immune dysfunction, which can interfere with endometrial implant clearance.1 Endometriotic ovarian cysts (known as 'endometriomas') are mostly thought to occur through invagination of endometriotic tissue/cells through the ovarian serosa, for example, during remodelling of the ovarian cortex after ovulation.4 The presence of an endometrioma can often present a clinical dilemma during the course of fertility treatment. For example, there can be uncertainty regarding the decision to operate or to manage conservatively, balancing the potential detrimental effect of surgery on the ovarian reserve against the potential benefit that may be gained. Current guidelines often rely on the evidence from either small and/or retrospective controlled studies. In particular, for assisted reproductive treatment (ART) some of the referenced studies were conducted in the 1980s and 1990s. Since then, in vitro fertilisation (IVF) success rates have significantly improved due to changes in stimulation protocols and available drugs, as well as the introduction of laboratory techniques such as intracytoplasmic sperm injection and blastocyst culture.

This Scientific Impact Paper will review the current evidence for management of endometriomas within the context of infertility treatment.

2-Endometriomas and infertility

Fecundity rates may be reduced in women with endometriosis, potentially related to the severity of the disease (revised American Society for Reproductive Medicine [rASRM] classification).5 The presence of ovarian endometriomas is usually associated with rASRM staging of moderate or severe disease.2 A number of theories for endometriosis-related infertility have been proposed, including chronic inflammation, tuboperitoneal anatomic distortion and reduced endometrial receptivity, leading to compromised oocyte and embryo quality, and ovarian reserve, but the precise mechanism has yet to be determined.6

3-Potential mechanisms for endometrioma-associated infertility

3.1 Chronic inflammation

Endometriosis is associated with dysregulation of the immune system.6 Peritoneal fluid from women with endometriosis has been found to contain increased numbers of immune cells, including macrophages, and mast, natural killer and T cells, as well as elevated levels of growth factors, chemokines and cytokines.7–9 The enhanced inflammatory state can affect the quality of the oocytes and impair ovarian function, resulting in defective folliculogenesis and fertilisation.10 As endometriomas and peritoneal disease often occur concomitantly and might be pathogenically linked, it is difficult to establish which of these inflammatory clinical presentations of endometriosis affects fertility.

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3.2 Oocyte and embryo quality

Endometriomas and associated pelvic endometriosis may affect oocyte and embryo quality adversely. While embryo development in women with endometriosis is slower compared to women with tubal disease,11 women with moderate-to-severe disease receiving eggs from a donor without endometriosis have been shown to have similar pregnancy rates to other egg recipients.12 An altered follicular environment, represented by elevated concentrations of progesterone and interleukin-6 and decreased concentration of vascular endothelial growth factor, may be responsible for alterations within the oocyte, leading to impaired fertilisation capacity of the oocytes and reduced embryo quality with low implantation potential.13

3.3 Ovarian reserve

The presence of ovarian endometriomas, especially if bilateral, can affect the ovarian reserve, impacting the ovarian response to gonadotrophins during ART. A histological studyl4 reported a significant reduction in the primordial follicle cohort in affected ovaries. Follicle depletion may be secondary to damage induced by the endometriosis-associated inflammatory reaction and by increased tissue oxidative stress leading to fibrosis.15 A group of potentially toxic agents, such as free iron, that can diffuse through the cyst wall of the endometrioma, as well as long-lasting mechanical stretching of ovarian cortex, can all have a detrimental impact on the ovarian reserve.16 Most importantly, however, is the negative effect of ovarian surgery on ovarian reserve, especially if performed repeatedly (see sections 4.1.2, 4.1.3 and 4.1.4)

4. Management options

While the options include expectant and surgical management, the recommended treatment should be guided by: the woman's symptoms; fertility prognostic factors, including age and ovarian reserve; previous treatment history with specific reference to past surgical interventions; nature of the cyst; and the wishes of the woman.17 Treatment of incidental disease in otherwise asymptomatic women is currently not recommended, as the development and natural progression of endometriomas is not well understood.

4.1 Spontaneous conception

4.1.1 Conservative management for spontaneous conception

Young women with regular menstrual cycles and an incidental finding of an ovarian endometrioma without suspicion of malignancy who wish to conceive should be encouraged to try natural conception before seeking fertility treatment.15 While the evidence of the impact of an endometrioma on spontaneous conception is limited, a prospective observational study18 (n = 244) reported a 43% spontaneous pregnancy rate during the 6-month followup period in the presence of unilateral endometriomas of varying sizes (diameter 5.3 _ 1.7 cm [mean _ SD]). The study also reported similar ovulation rates in the affected ovary to the healthy ovary (49.7% versus 50.3%), not influenced by the laterality of the endometriomas, their number and size, or by the presence of deep endometriosis diagnosed by ultrasound. This finding contradicted previously reported data in a smaller prospective study (n = 70),19 of reduced ovulation in the affected ovary (31% versus 69%). For women with a naturally or abnormally reduced ovarian reserve, conservative management for fertility should be weighed against the potential benefits of surgery or fertility treatment.

4.1.2 Surgical treatment for spontaneous conception

There is controversy regarding the surgical management of endometriomas in women undergoing treatment for infertility. While surgical treatment may improve spontaneous pregnancy rates by restoring the pelvic anatomy, it remains unclear as to whether surgical intervention on the ovary itself is beneficial as it may not reverse the inflammatory and biomolecular changes shown to influence fertilisation and implantation.20 Furthermore, there are concerns regarding the safety of surgical treatments, with a reported reduction in the ovarian reserve21,22 and the small added risk of requiring an oophorectomy. In contrast, concerns have been raised about the effect of an endometrioma on oocyte quantity and quality. This conflict suggests that management should be individualised and based upon clinical factors, including pain symptoms, size of the cysts and concerns over potential malignancy. Consideration should be given to surgical treatment being undertaken by a gynaecologist with specific expertise in endometriosis and fertility, in order to minimise the impact on the ovarian reserve and provide a holistic assessment regarding future fertility management. When performing surgery, ovarian endometriomas are best managed by performing a cystectomy, as opposed to drainage and coagulation, which is associated with an overall lower recurrence risk and higher spontaneous postoperative pregnancy rate, particularly if the cyst is 3 cm or more in diameter. Hart et al.23 summarised two randomised controlled trials (RCTs) which showed a beneficial effect of excisional surgery over drainage or ablation of an endometrioma in achieving a spontaneous pregnancy in subfertile women (OR 5.24, 95% Cl 1.92–14.27; n = 88; two trials). However, this can lead to a significant reduction in the number of ovarian follicles, especially in women who have undergone previous ovarian surgery, and therefore, ovarian reserve, reflected by a sustained decrease in anti-M€ullerian hormone (AMH) levels. While data from observational controlled studies24,25 investigating ovarian endometrioma drainage and ablation using energy with minimal thermal spread, such as CO2 laser or plasma energy, indicated good results; in terms of a satisfactory fertility outcome, reduced ovarian damage and reduced recurrence risks, RCTs are needed to be able to draw definitive conclusions.

4.1.3 Effect of endometriomas on IVF outcome

Evidence of the impact of an endometrioma on ovarian response during IVF is equivocal. Systematic reviews of controlled studies have reported similar ovarian responses in women with endometriosis to controls with no evidence of endometriosis,26 and in women with a unilateral ovarian endometrioma compared to contralateral normal ovaries.27 While most studies included in the latter systematic review evaluated women with small endometriomas, two studies28-30 reported on the potential detrimental effect of the size of the endometrioma on ovarian response especially when this was 3 cm or more in diameter. In one systematic review, 31 ovarian responsewas lower, with a lower number of oocytes retrieved (mean difference –0.23; 95% Cl 0.37–0.1) and a higher cancellation rate (OR 2.83; 95% Cl 1.32–6.06) in women with an endometrioma, although the total stimulation dosage of gonadotrophin used was comparable. However, live birth (OR 0.98; 95% CI 0.71–1.36), pregnancy (OR 1.17; 95% CI 0.87–1.58) and miscarriage rates (OR 1.7; 95% CI 0.86–3.35) following IVF were similar in women with an endometrioma compared to women with no endometriosis.32 When compared to women with peritoneal endometriosis in the absence of an endometrioma, IVF outcomes (live birth, pregnancy, miscarriage and cycle cancellation rates, and mean number of oocytes retrieved) were similar in women with an endometrioma. No data on adverse events, such as bleeding, infection or pain, were reported in these studies. Basal follicle stimulating hormone levels were higher in women with an endometrioma compared with women with no evidence of endometriosis (three studies; n = 491), however, the antral follicle count was similar between the two groups (two studies; n = 433). Although equivocal, most studies33,34 report that the observed reduced ovarian response, especially in the presence of larger endometriomas, is related to an overall reduced ovarian reserve in women with an endometrioma.

In contrast, an adverse impact of endometriomas and endometriosis on oocyte quality has been suggested by Simon et al.,35 who reported on data from an oocyte donation programme in which women with endometriosis were shown to have the same chance of implantation and pregnancy as other oocyte recipients, when the oocytes came from donors without known endometriosis. However, the implantation rates were reduced in healthy recipients when the oocytes came from donors of the mometriosis, suggesting the condition had a negative effect on oocyte quality. Nevertheless, as reviewed by the European Society of Human Reproduction and Embryology (ESHRE) guideline for the management of endometriosis,17 no such differences have been demonstrated in large databases that include more recent IVF cycles, such as the Human Fertilisation and Embryology Authority and the Society for Assisted Reproductive Technology.

4.1.4 Surgical treatment prior to IVF

Surgical treatment of endometriomas prior to IVF is widely practised,36 although debatable on its effect and need. A systematic review32 (five controlled studies; n = 655) reported similar live birth (OR 0.9; 95% CI 0.63-1.28), clinical pregnancy (OR 0.97; 95% CI 0.78–1.2) and miscarriage rates (OR 1.32; 95% CI 0.66–2.65) following IVF treatment in women with surgically-treated endometriomas compared to those with intact endometriomas. While the number of oocytes retrieved and the cancellation rates were comparable, women with a surgically-treated endometrioma had a lower antral follicle count and required higher doses of gonadotrophins for ovarian stimulation. Interestingly, women who had undergone surgical management for a unilateral endometrioma had a lower number of oocytes retrieved from the surgically-treated ovary (mean difference -2.59; 95% CI -4.13 to -1.05) when compared with the contralateral normal ovary, indicating a reduction in the ovarian reserve following surgical intervention, as has been reported in several other studies.22,31,37 The potential physiological compensation by the normal ovary for the compromised ovary, in conjunction with the higher follicle stimulating hormone doses required for ovarian stimulation, may account for the similar IVF outcomes noted in women who have undergone surgical treatments for their endometriomas.32 A Cochrane review38 incorporating two small RCTs has reported similar pregnancy rates for surgical (cystectomy or aspiration) and expectant management. While no differences in pregnancy rates have been shown between a cystectomy and aspiration of an endometrioma, a cystectomy is associated with a lower ovarian response following controlled stimulation, with a lower number of mature oocytes retrieved, raising concern about the potential adverse influence of a cystectomy on ovarian reserve. In contrast, a meta-analysis32 incorporating three controlled studies (including non-RCT studies) reported similar ovarian responses and pregnancy rates following IVF in women with an endometrioma surgically managed with a cystectomy compared to transvaginal aspiration prior to IVF treatment. Based on the available evidence, the ESHRE guideline group17 concluded that a cystectomy for an endometrioma larger than 3 cm, prior to undergoing IVF treatment, does not improve pregnancy rates. However, surgery prior to ART can be considered for the management of endometriosis-associated pain, for increasing the accessibility of the follicles during oocyte retrieval procedures, or to ameliorate any concern for malignancy. Despite the lack of evidence of the clear benefit of surgical treatment for the management of an endometrioma on pregnancy rates, and the various potential drawbacks and risks, conservative management in women with an endometrioma undergoing IVF treatment has been questioned. The presence of an endometrioma may theoretically interfere with ovarian responsiveness to controlled stimulation and oocyte competence, as well as pose potential risk and technical difficulties during oocyte retrieval, including the associated risks to injury to adjacent organs due to altered pelvic anatomy with the presence of adhesions, infection and abscess formation, follicular fluid contamination with endometrioma content, progression of endometriosis, further growth and rupture of the endometrioma, missed occult malignancy and cancer development in later life. A systematic review27 evaluating the potential risks of conservative management in women with a known endometrioma undergoing IVF concluded that there was insufficient evidence on the risks of reduced ovarian responsiveness and reduced oocyte competence.

Furthermore, surgery for an endometrioma may potentially reduce ovarian reserve, as evidenced by a decrease in the AMH levels22 and subsequent responsiveness to gonadotrophin stimulation.39 While the risk of technical difficulties during oocyte retrieval is low, based on very limited reports, there are no data to suggest that surgery for an endometrioma will prevent adhesion reformation and facilitate oocyte retrieval effectively. While the available data exclude a clinically relevant effect of IVF on progression of pelvic endometriosis and ovarian endometriomas, the risks of infection from an endometrioma (0–1.9%) and follicular fluid contamination (2.8–6.1%) are very small, and unable to justify surgery for the presence of an endometrioma prior to IVF treatment. The risk of missing an occult malignancy in an endometrioma is extremely low and in the absence of any suspicious radiological features, surgery is not warranted. Although rare, the risk of developing ovarian cancer later in life can be a serious concern, with the lifetime probability increasing from 1% to 2% in the presence of an endometrioma.40 However, in the context of IVF treatment, delaying surgery for a few months or years, until the treatment has been completed or following delivery, would usually be a reasonable course of action unless there are other immediate concerns.

The ESHRE guideline group17 discussed the importance of women being appropriately counselled about the risk of reduced ovarian function following surgical intervention and even the possible risk of an oophorectomy. The decision to proceed with surgery for an endometrioma should be carefully considered, including the various prognostic factors that can influence the success of an ART cycle, such as the age of the woman, ovarian reserve status, unilaterality or bilaterality of the disease, number and size of the cysts, symptoms, presence or absence of suspicious radiological features, extent of extraovarian disease and history of previous ovarian surgery.41 Asymptomatic women, women of advanced reproductive age, those with reduced ovarian reserve, bilateral endometriomas or a history of prior ovarian surgery may benefit from proceeding directly with IVF, as surgery may further compromise ovarian function and delay the start of treatment. Surgery may be considered first line in highly symptomatic women, those with an intact ovarian reserve, unilateral and large cysts, and should be considered for cysts with suspicious radiological and clinical features. Endometriomas may be associated with extraovarian disease, including intestinal disease and deeply infiltrating endometriosis. Reproductive outcomes have not been shown to be improved by the excision of deeply infiltrating endometriosis, with surgical excision of endometriotic nodules providing symptomatic benefit albeit potentially exposing the woman to significant surgical risks, to which the women should be appropriately counselled.17

5. Opinion

• Endometriomas are associated with reduced monthly fecundity rates, although a direct causal relationship has not been well established.

• Repeated or extensive ovarian surgery has a detrimental impact on ovarian reserve and this should be considered when deciding on treatment and specifically, further surgery. The theoretical benefit of performing surgery to improve pelvic anatomy and accessibility is plausible, but has not been supported with substantive scientific evidence.

• Until robust evidence from large RCTs incorporating modern treatment modalities is available, many uncertainties will remain on the optimal treatment of an endometrioma. Meanwhile, management decisions should be based on individual circumstances, such as patient choice, age, ovarian reserve and associated symptoms.

4- Pelvic Physiotherapy

Source: http://www.pelvicphysiotherapy.com/manual-therapy/

Pelvic Floor Manual Therapy



Pelvic Floor Manual Therapy is a clinical approach utilizing skilled, specific hands-on mobilizing techniques to diagnose and treat soft tissues. This is for the purpose of:

Modulating pain Increasing range of motion Reducing or eliminating soft tissue inflammation Inducing relaxation Improving tissue repair Improving tissue extensibility Improving stability Facilitating movement Improving function

The pelvic floor is susceptible to negative tension and holding patterns for many reasons. Posture, poor seating, holding patterns, emotional holding due to stress, childbirth damage, history of constipation or any bowel disorders or history of urinary tract infections. There may be no history of any of the above but just a genetically tight pelvic floor. These can all lead to a tension build up in the pelvic floor. Strengthening an already tense or tight pelvic floor can be counterproductive and can increase rather than relieve symptoms or can mean that regular pelvic floor exercises just don't work.

HOW DOES PELVIC FLOOR MANUAL THERAPY HELP?

Pelvic floor manual therapy is a series of internal and external soft tissue release techniques to address unwanted tension in the pelvic floor muscles and fascia. There should be a sense of relief having had the pelvic floor mobilised that results either immediately or over time in an increased range of movement in the muscles. This in turn should result in an increased ability to either contract or release muscles improving timing in the muscles and pelvic organ position.

Pelvic floor manual therapy is used for stress incontinence, pelvic organ prolapse, urinary urgency, urge incontinence, bowel disorders, chronic pelvic pain and sexual disorders. There may be some discomfort at the time of mobilization in the same way that one would feel it with back or neck mobilisation but there should not be any post treatment soreness.

Techniques

Myofascial trigger point therapy to the pelvic floor Dry needling to the pelvic floor Myofascial trigger point therapy to the pelvis,

trunk and abdomen

Dry needling to the pelvis, trunk and abdomen Connective tissue manipulation to the external perineal tissue, abdomen and pelvis



Trigger Points

Pelvic Floor Manual Therapy techniques for the pelvic floor include stretching and trigger point treatment where a muscle is tense.





A short or tense muscle is identified by internal examination and then stretched centrally along the bulk of the attachment bone which uncomfortable. muscle or at the to is often more A trigger point will often refer pain elsewhere in the pelvic floor or to the hips or rectum or may just be painful on the spot. Once held for a few seconds the pain eases and the therapist moves on to the next point. There are also nerves in the pelvic floor and they can be mobilised along their pathways. There is often external tension in the pelvis and abdomen linked to internal restriction, this is known as a connective tissue restriction. This can be successfully released through pelvic floor manual therapy externally on the identified areas. Pelvic Floor Manual therapy should not be so painful that the patient reacts by tensing up. The pelvic floor muscles should not be sore after manual therapy. The contractility of the pelvic floor can be seen to change on realtime ultrasound following a session of manual therapy.

5-Does preoperative antimüllerian hormone level influence postoperative pregnancy rate in women undergoing surgery for severe endometriosis?

Does preoperative antimüllerian hormone level influence postoperative pregnancy rate in women undergoing surgery for severe endometriosis? Stochino-Loi E, Darwish B, Mircea O, Touleimat S, Millochau JC, Abo C, Angioni S, Roman H. Fertil Steril. 2017 Mar;107(3):707-713.e3. doi: 10.1016

The association between endometriosis and infertility has been routinely studied in the literature, although multiple mechanisms and accurate management of infertility are still debated. Infertility may be related to various events, such as distorted pelvic anatomy that impairs oocyte release or pickup, inflammatory cytokines, growth and angiogenic factors, and aberrantly expressed genes. Women with advanced stages of endometriosis may present with decreased ovarian reserve, low oocyte and embryo quality, and poor implantation. As many as 30%–50% of women with endometriosis may have various degrees of infertility. The spontaneous fertility rate in women with advanced stages of endometriosis can be as low as 2%–10%.

Endometriosis lesions may involve various organs, such as ovaries, posterior Douglas cul-de-sac, bowel, bladder, or ureters. Choosing the best treatment for endometriosis in young patients with pregnancy intention may be challenging because it should provide both a high pregnancy rate and significant improvement in pelvic complaints, as well as efficient prevention of further complications related to endometriosis spread. A primary surgical approach has been proposed on the basis of improving spontaneous fertility in patients with advanced endometriosis as well as lowering the risk of various complications during pregnancy. Furthermore, in women with deep endometriosis infiltrating the bowel, recent studies have suggested a potential fertility benefit for postoperative assisted reproductive technology (ART) results. However, in daily practice, surgery in advanced endometriosis is frequently refuted due to a presumed risk of complications or negative impact on ovarian reserve.

Antimüllerian hormone (AMH) is a reliable independentmarker of ovarian reserve in the ovarian cycle, while oral contraception and GnRH agonists have little impact on blood level. AMH is produced by the granulosa cells of the ovaries and is expressed by small antral follicles. Levels surge at the time of puberty to approximately 5–8 ng/mL but then gradually decline throughout reproductive life until they become undetectable by menopause. Therefore, AMH levels are considered valuable indicators of ovarian reserve. Various studies in the literature have investigated the impact of surgical management of ovarian endometriomas on AMH level before and after surgery (16–18). However, no study has assessed the relationship between preoperative AMH level and postoperative pregnancy rate in women managed for advanced stages of endometriosis.

The aim of our retrospective study was to investigate whether surgery for severe endometriosis may be proposed in women with low ovarian reserve with good fertilityoutcomes. To achieve this goal, we compared postoperative pregnancy rate in women with low and normal AMH level, managed for stage 3 and 4 endometriosis.

METHODS

Women included in this present study were managed from June 2010 to May 2015 in the Department of Gynecology of Rouen University Hospital, for stage 3 and 4 endometriosis responsible for either infertility or pelvic pain. These women had either deep infiltrating endometriosis or ovarian endometriomas measuring over 3 cm (women with only superficial endometriosis and hydrosalpinx were not included). All patients had expressed pregnancy intention before surgery and benefited from pre- and postoperative assessment of AMH, with a minimum 12-month follow-up. Preoperative assessment of AMH was performed 1–12 weeks before surgery to accomplish systematic evaluation of ovarian reserve in patients with severe endometriosis and postoperative pregnancy intention. As the AMH test costs 40 Euros on average and is not reimbursed by the French Social Security, patients were able to opt out of the test. AMH assessment was performed postoperatively 2 months after the arrest of medical therapy in women with pregnancy intention to evaluate their fertility status before deciding on conception mode. Thus, it was routinely associated with FHS and LH assessment (day 3 of ovarian cycle), E2 (days 3 and 12) and P (day 23), antral follicle count, spermogram, and hysterosalpingography.

Patients were prospectively enrolled in the CIRENDO database (the North-West Inter-Regional Female Cohort for Patients with Endometriosis), a prospective cohort financed by the G4 Group (the University Hospitals of Rouen, Lille, Amiens, and Caen, France) and coordinated by the corresponding author of the present study (H.R.). Information was obtained from surgical and histological records and from self-questionnaires completed before surgery. Data recording, patient contact, and follow-up were carried out by a clinical research technician. Postoperative follow-up was based on data from the aforementioned questionnaires completed at 1, 3, and 5 years after surgery. Prospective data recording and analysis were approved by the French authorities Commission Nationale de l'Informatique et des Libertes: the French data protection commission; and Comite Consultatif pour le Traitement de l'Information en matiere de Recherche dans le domaine de la Sante: the advisory committee on information technology in health care research.

Endometriomas were exclusively managed by plasma energy ablation. Bowel lesions were treated by shaving, disc excision, or segmental resection. Urinary tract lesions were managed by resection of bladder, advanced ureterolysis requiring JJ stent, ureteral resection followed by end-to-end anastomosis, or ureterocystostomy. All the procedures were fully recorded in mpeg format.

Patients were enrolled in two groups according to preoperative AMH level: women with AMH R 2 ng/mL were assigned to group A, and those with AMH < 2 ng/mL to group B. We recorded the time from surgery to first pregnancy as well as pregnancy outcomes: delivery, miscarriage, ectopic pregnancy, or on-going pregnancies of over 12 weeks' gestation. For each pregnancy we recorded conception mode: spontaneous or with ART.

Statistical analysis was performed using Stata 11.0 software (StataCorpLP). Univariate analysis compared characteristics, clinical history, baseline complaints, intraoperative data, and postoperative outcomes of women enrolled in the two groups. Fisher's exact test was used to compare qualitative variables, and Student's t-test and Mann-Whitney tests were used to compare continuous variables. Kaplan-Meier curves were built to estimate the probability of nonpregnancy according to postoperative time and were compared using the log-rank test. Cox's model was used to estimate independent hazard ratios for the probability of live births according to various variables. P<.05 was considered statistically significant.

Supplementary analysis was performed after dividing women with AMH < 2 ng/mL in two groups: low AMH (1–1.99 ng/mL) and very low AMH level (<1 ng/mL). The study was approved by the Institutional Review Board.

RESULTS

The CIRENDO database was searched for postoperative pregnancy intention and AFRs score >15 and resulted in a series of 397 consecutive women. After thorough review of recorded data and surgical reports, 184 (46.3%) and 13 (3.3%) women, respectively, were excluded because their pre- and postoperative AMH levels were either not assessed or not available and because of hydrosalpinx and absence of deep endometriosis or endometrioma measuring more than 3 cm. In addition, 20 women were lost to follow-up (5%) because they had changed address, phone number, or e-mail address.

Thus, 180 patients were definitively enrolled in the study: 134 women (74.5%) in group A (normal AMH level) and 46 women (25.5%) in group B (low AMH level; Supplemental Fig. 1). Preoperative AMH level was 4.3± 2.1 ng/mL in group A versus 1 0.5 ng/mL in group B (P<.001). After surgery, postoperative AMH levels were, respectively, 3.4 ±2.5 ng/mL and 1.2 0.9 ng/mL (P =.001). Table 1 presents patient characteristics, medical history, obstetrical antecedents, and related pain symptoms, such as dysmenorrhea, dyspareunia, and digestive complaints. Among these 180 women, 135 (75.4%) had been attempting pregnancy for more than 1 year before surgery: 99 (74.4%) in group A and 36 (78.2%) in group B (P=.38).

Table 2 presents intraoperative findings: operative time, operative route, American Fertility Society revised score, main surgical procedures, and fertility outcomes. Ovarian endometrioma ablation using plasma energy was performed in 145 patients (80.6%). Pregnancy was achieved by 134 (74.4%) patients, and conception was spontaneous in 74 of them (55.2%). The rate of pregnancy in groups A and B was, respectively, 74.6% (100 patients) and 73.9% (34 women; P=.52), while spontaneous conception represented 54% (54 women) and 58.8% (20 women; P=.17). These values were comparable to the pregnancy rate observed in 184 women recorded in the database and excluded due to the lack of AMH assessment (129 pregnancies, 70.1%; P=.65).

Pregnancy rates in women with normal and low AMH level were, respectively, 74.6% and 73.9%, resulting in a difference of 0.7%, with a 95% confidence interval [CI] of - 14%; 15.4%. Delivery rates in women with normal and low AMH were, respectively, 72% and 73.5%, with a 95% CI of the difference of -16%; 13%.

Kaplan-Meier curves of the probability of pregnancy were close during the whole period of follow-up, thus their comparison did not reach statistical significance (Fig. 1). The probability of pregnancy at 12, 24, and 36 months after surgery in groups A and B was, respectively, 65% (95% Cl, 55%–75%), 77% (95% Cl, 86%–68%), and 83% (95% Cl, 90%–75) versus 50% (95% Cl, 69%–34%), 77% (95% Cl, 90%–61%), and 83% (95% Cl, 94%–68%; P=.19).

The results of multivariate analysis using Cox's model are presented in Table 3. Independent impact of preoperative AMH level on the probability of live birth was not statistically significant after adjustment for several variables with clinical interest: women's age, antecedents of ovarian cystectomy, ablation of ovarian endometriomas, documented preoperative infertility, and colorectal surgery for endometriosis.

Supplemental Tables 1 and 2 present comparisons of women with normal, low, and very low AMH levels. There was a significantly inverse relationship between AMH level and women's age or antecedents of miscarriage. Patients with very low AMH could have presented with more severe disease, as the operative time and their rate of transitory colostoma were significantly higher. In addition, there was a tendency towards more frequent use of colorectal resection in women with very low AMH. However, the

pregnancy rate was not statistically different among the three groups of women, nor was the probability of pregnancy at 12 and 24 months, respectively, 59.5% (95% CI, 49.3%–70%) and 77.4% (95% CI, 68%–85.4%); 57.1% (95% CI, 34%–83%) and 78.6% (95% CI, 55.2%–94.8%); and 46.7% (95% CI, 25.6%–73.7%) and 73.3% (95% CI, 50.4%–91.7%).

DISCUSSION

To our knowledge, this is the first study to assess the postoperative pregnancy rate in patients managed for stage 3 and 4 endometriosis based on preoperative AMH level. Our study demonstrated that preoperative AMH level did not significantly impact the probability of postoperative pregnancy rate when spontaneous conception and conception after ART were considered together. Even though our study wa sunable to reach the high level of evidence specific to randomized trials, it provides convincing arguments to support the use of surgery in young patients with severe symptomatic endometriosis and pregnancy intention who have a preoperative AMH level below the inferior threshold of normal values.

The main strength of our study was the prospective collection of data and careful follow-up performed by a dedicated clinical researcher, leading to a low rate of patients lost to follow-up. Furthermore, the fact that surgery was performed in a single expert center represents a major strength as it allows reliable measurement of the impact of surgical management when guided by special care to preserve fertility. Another strength of our study was its undivided focus on severe forms of the disease, mainly involving women in whom surgeons might postpone surgery owing to fear of a potential negative impact of extended surgery on the patient's fertility.

Nonetheless, our study has several weaknesses. The retrospective design reduces the level of evidence of our data. Preoperative assessment of AMH level was not performed in all patients, as some women opted out of the AMH test due to its cost and others did not fully understand the reason for performing the test. Thus, women with no further pregnancy intention were likely not to accept the cost of the test. In other patients, the results were either missing or had not been recorded in their medical chart. In some women, low and very low preoperative AMH levels could have impacted their postoperative pregnancy intention; hence they might have stopped their postoperative medical treatment and were thus missing from our study. However, it is our opinion that their number may be rather small, with little impact on our results. Another limitation of our study is related to the small number of patients with low preoperative AMH values, resulting in a large 95% CI and low statistical power to detect differences between the two groups. The 95% CI of the hazard ratio suggests that increasing the sample size may have led to the decrease in the live-birth rate in the low AMH group, down to 60% of that observed in the normal AMH group.

Our statistical analysis employed the Cox model as live birth is a time-dependent variable. Thus, the model estimated the effect of several variables upon the time delay for live birth to occur. When compared with the logistic regression model, Cox's model is a more accurate statistical tool because estimation of the probability of live birth takes into account right censored data represented by women who accomplished a follow-up period without achieving a live birth. AMH level was used as a categorical dummy variable instead of a continuous variable to estimate distinct probabilities of live birth for each category: normal, low, and very low AMH level.

Different studies have shown that low AMH level is associated with a reduction in pregnancy rate in ART. More specifically, low AMH values were associated with poor response of ovaries to hyperstimulation, resulting in lower rates of pregnancies after ART. Conversely, it appears that the relationship of AMH level and spontaneous conception rate is disputable, as women with low AMH attained satisfactory spontaneous pregnancy rates. These latter results have led us to believe that in women with low AMH, restoring the capacity of spontaneous conception may be an interesting alternative

to primary ART.

Recent guidelines do not recommend surgery for deep infiltrating endometriosis in infertile women with the single aim of improving ART results. However, data in the literature suggest that surgery for deep infiltrating endometriosis may enhance spontaneous conception, as 25%-35% of infertile women could become pregnant after surgery. It is our belief that surgical management should not be definitively contraindicated in women with low AMH levels, as spontaneous conception could compensate for the poor response to hyperstimulation for IVF. Despite the opposing opinions of numerous colleagues, there are no existing guidelines or consistent evidence to support the mandatory referral of women with pregnancy intention to ART instead of surgery, especially when the surgeon takes special care to preserve fertility.

The potential negative impact of surgery for ovarian endometriomas on ovarian reserve has been demonstrated. As far back as 2009, our team reported data on ovarian tissue loss after cystectomy and definitively introduced a new ablative technique using plasma energy, with the single aim of preserving fertility. Hence, we are aware of the risk of impairing ovarian reserve in patients managed for ovarian endometrioma, regardless of their preoperative AMH level. Even though ablation using plasma energy is followed by a temporary decrease in AMH level, pregnancy rates in our various studies were rather high, and most of them resulted in spontaneous conception. Theseobservations led to the present study, in which we attempted to estimate whether performing surgery in women with low and very low AMH might or might not impair their postoperative fertility, when compared with women with normal AMH level. Despite postoperative changes occurring in AMH level, the pregnancy rate observed in our series was satisfactory and independent of preoperative AMH level.

One may wonder whether our high postoperative pregnancy rate could be explained by the inclusion of only 75% of presumed infertile women. Nevertheless, even though one in four women had not attempted to conceive before surgery, it was likely that their fertility might have been negatively impacted by endometriosis. Despite little attempt to conceive preoperatively, a diagnosis of deep endometriosis and its strong relationship with infertility risk could prompt a woman's decision to expedite conception and pregnancy. Indeed, the probability of spontaneous pregnancy was low in these women with stage 3 or 4 endometriosis and either deep localizations or endometriomas measuring over 3 cm, as well as digestive tract involvement and Douglas pouch obliteration recorded in more than 70% and 49% of cases, respectively. Among women with no presumed infertility were young patients who had been attempting to conceive for less than 1 year and who were referred to our department owing to complaints related to pain. When these young patients are referred to other facilities, they are automatically scheduled for primary IVF and are thus indirectly recorded as infertile. It is therefore likely that the rates of infertile women are underestimated in series of patients managed by primary surgery when compared with those receiving primary ART.

Our results suggest that overall postoperative pregnancy rate is not closely associated with preoperative AMH level in women managed for stage 3 and 4 endometriosis andwith a mean age of 30 years. As three in four women achieved pregnancy after surgery, either spontaneously or after ART, surgical management of severe endometriosis in young women with low ovarian reserve appears to be followed by good fertility outcomes.

6-NICE Guideline Algorithma

www.nice.org.uk/guidance

Suspect endometriosis (including in young women aged 17 and under) with 1 or more of:

- chronic pelvic pain
- · period-related pain (dysmenorrhoea) affecting daily activities and quality of life
- · deep pain during or after sexual intercourse
- · period-related or cyclical gastrointestinal symptoms, in particular, painful bowel movements
- · period-related or cyclical urinary symptoms, in particular, blood in the urine or pain passing urine
- infertility in association with 1 or more of the above.

Assess women's individual information and support needs

Take into account their circumstances, symptoms, priorities, desire for fertility, aspects of daily living, work and study, cultural background, and their physical, psychosexual and emotional needs.

Also:

First presentation

- discuss keeping a pain and symptom diary
- · offer an abdominal and pelvic examination to identify abdominal masses and pelvic signs
- consider an ultrasound scan (see page 2).



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B NEWS FROM OUR SOCIETY

As a part of the endoacademia meetings with the support of our lecturers in the region we will organize a meeting on 'Endometrioma' in Gaziantep on January, 28 2018. We are going to share in detail the up-to-date information on endometrioma. You can find further information on our website. We are going to keep conducting these regional meetings in other cities.



ENDOMETRIOSIS AND ADENOMYOSIS SOCIETY ENDOACADEMY MEETINGS IV

MANAGEMENT OF ENDOMETRIOMA 2018

28 January 2018 - Sunday, Divan Hotel Gaziantep

PROGRAM DETAILS

09:00 - 10.00	Registration
10:00 - 11:30	1. Session: ENDOMETRIOMA – General Chairman: Ozcan Balati Ali Irfan Kutlar
10:00 - 10:15	Symptomatology of Endometrioma <i>Koray Elter</i>
10:15 - 10:30	Which is more harmful; operating on endometrioma or leaving it in its place? Gurkan Uncu
10:30 - 10:45	How should the approach be to endometrioma in infertile women? <i>Hulusi Zeyneloglu</i>
10:45 - 11:00	The relationship between endometrioma and cancer: Should we be frightened? <i>Mete Gurol Ugur</i>
11:00 - 11:15	The association between endometrioma, ovarian cancer and adenomyosis <i>Ahmet Kale</i>
11:15 - 11:30	Discussion
11:30 - 12:00	Coffee break 🖆

ENDOMETRIOSIS AND ADENOMYOSIS SOCIETY ENDOACADEMY MEETINGS IV

MANAGEMENT OF ENDOMETRIOMA 2018

28 January 2018 - Sunday, Divan Hotel Gaziantep

PROGRAM DETAILS

12:00 - 13:30	2. Session: ENDOMETRIOMA – CURRENT TREATMENT Chairmen: Hakan Kiran Yilmaz Atay
12:00 - 12:15	Approaching to endometrioma in adolescence Baris Mulayim
12:15 - 12:30	How can we improve endometrioma surgery? <i>Taner Usta</i>
12:30 - 12:45	In medical treatment of endometrioma: oral contraceptives? Progesterone? GnRH? <i>Engin Oral</i>
12:45 - 13:00	In difficult cases how should the operative treatment of endometrioma proceed? Yucel Karaman
13:00 - 13:15	Management of recurring endometiroma cases
	M. Turan Cetin
13:15 - 13:30	Discussion
13:30 - 14:30	Lunch
14:30 - 14:40	Mother and baby health in pregnancy Exeltis
14:40 - 16:00	3. Session: INTERACTIVE CASE DISCUSSION ON ENDOMETRIOMA Moderator: <i>Engin Oral</i>
Panelists:	Yucel Karaman, Gurkan Uncu, M. Turan Cetin, Hulusi Zeyneloglu, Koray Elter, Taner Usta, Ahmet Kale, Baris Mulayim, Mete Gurol Ugur
15:50 - 16:00	Discussion
16:00	Closing remarks

ACTIVITIES

Board Meeting of The Society of Endometriosis and Adenomyosis (September, 24 2017)



On September, 24 2017 Society board meeting has taken place. Future acitivities have been planned and responsibilities have been distributed among the members.





Endometriosis 2017 From Diagnosis to Medical and Surgical Management:

A Stocktaking International Experts' Meeting, 14-16 September 2017, Italy

Prof. Engin Oral, MD., Assoc. Prof. Ercan Bastu, MD., and Cihan Kaya, MD. have participated in and represented our society in the Endometriosis 2017 From Diagnosis to Medical and Surgical Management: A Stocktaking International Experts' Meeting in Napels, Italy. They have benefited from the experiences, and management and operative techniques of their colleagues and leading experts in the field. You may find further information on the meeting under the following link. http://www.endometriosis2017.com





TURKISH REPUBLIC MINISTERY OF HEALTH DEPARTMENT OF CHILDREN, ADOLESCENCE, WOMEN AND REPRODUCTIVE HEALTH'S INFORMATIONAL MEETING

On November, 30 2017 as the Endometriosis and Adenomyosis Society we gave a talk to 200 general practitioners on the subject of 'Endometriosis – Chronic Pelvic Pain – Dysmenorrhea' in the employee's educational meeting organized by Turkish Republic Ministery of Health Department of Children, Adolescence, Women and Reproductive Health. The talk was given by Prof. Banu Kumbak Aygün, MD

We have emphasized on the importance of severe mensturation pain and its connection with endometriosis. We also laid stress on the fact that increasing public awareness on endometriosis will help to reduce the time for diagnosis. With exchange of questions and answers the meeting was very productive

4.EKER I RUN





Vodafone 39th Istanbul Marathon

We ran to raise awareness on endometriosis in Istanbul Marathon! Fitnat Topbas, MD., and Goknur Topcu, MD. ran in the 39. Vodafone Istanbul Marathon to represent our society and to raise awareness in endometriosis. During the marathon, we answered questions raised by other participants and we did raise awareness on the subject.



6. Asian Endometriosis and International Minimal Invasive Surgery Congress

In this congress which took place in Iran between 22 and 24th of November 2017 Prof. Engin Oral, MD., and Kutay Biberoglu, MD. represented our country and out society. They both gave presentations and moderated panels.











© NEWS FROM THE WORLD OF ENDOMETRIOSIS

EFA Medical Conference 2017 "Breast, Ovary and Endometriosis"

October 28, 2017 - Lotte New York Palace Hotel

On October 28th in New York Endometriosis Foundation of America (EFA) organised a congress on breast cancer, ovarian and endometriosis cancer. In this congress organized by the founder of EFA Tamer Seçkin, MD Serda Bulun, MD. gave a presentation. For further details; https://www.endofound.org/medicalconference



4. EMEL Conference on Endometriosis and Uterine Disorders

In this congress which took place in Iran between 22 and 24th of November 2017 Prof. Engin Oral, MD., and Kutay Biberoğlu, MD. represented our country and out society. They both gave presentations and moderated panels. http://endometriosisuae.com/4thEMEL



ENDODUBAI 2018

You can also find further details about the congress on endometriosis which will take place beginning of February and which is organized by United Arab Emirates under the following link. https://endo-dubai.ae You can find further information on the congress organized by United Arab Emirates Endometriosis Society which will take place between February 22 and 23rd 2018 in Dubai.



Endo Dubai is quickly becoming a reference in minimally invasive gynecological surgery providing a forum of the highest standard for scientific, clinical and social exchange.

With a mix of expert panels, tutorials, hands-on sessions and opportunities for networking, Endo Dubai will

SEUD 2018

SEUD congress 4th will be held in Florence, Italy on 26-28th April, 2018 http://seud.org



D SOCIAL MEDIA



Endometriosis and Adenomyosis Society's special website for healthcare providers (www.endometriozisdernegi.com)

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 has been 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: Mart2017 Makale özetleri

Hazırlayan Prof. Dr. F. F. Verit

Publication Summaries on Endometriosis

On our website's main page endometriozisdernegi.com you can find publications on endometriosis monthly selected and summarized by Prof. Fatma Ferda Verit, MD. You can find the most up-to-date publications on endometriosis under the following link:

nttp://www.endometriozisdernegi.com/ makaleler



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 an 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 of charge website and designed the give accurate information to the patients.

http://www.endometriozisdernegi.com/en



You can follow us on social media!