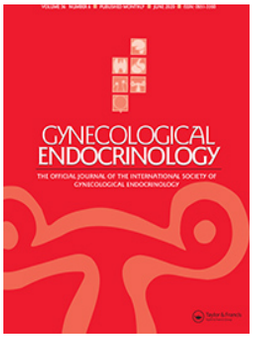

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EDITORIAL

Adenomyosis and fertility outcomes

Adenomyosis which is associated with dysmenorrhea, uterine bleeding disorders, chronic pelvic pain, and dyspareunia, may co-exist with leiomyomas, endometriosis and endometrial polyps. The prevalence might even be quite high in younger women with adenomyosis. Since adenomyiosis may be present in one-third of women with surgically treated endometriosis, those with endometriosis should always be carefully examined for image signs of adenomyosis. The prevalence of adenomyosis in a population of infertile women ranges between 7% and 27% [1].

Although 2D, 3D, and color or power Doppler ultrasound have been used to evaluate the type and extension of adenomyosis, there is no standard for the staging of the disease. Hence, no objective treatment algorithm has been proposed in clinical practice [2]. Six grayscale features on 2D ultrasound have been described as suggestive of adenomyosis. All possible combinations of two (15 possible permutations) and three variables (20 possible permutations) resulted in improved specificities but with low sensitivities. Additionally scores of 1–4 have been assigned for each of the five different conditions of adenomyosis, in order to determine the interobserver reproducibility of a new ultrasonographic mapping system to define the type and extension of uterine adenomyosis [2]. 3D-transvaginal ultrasound parameters, such as junctional zone (max) $>$ 8 mm, myometrial asymmetry, and hypoechoic striation, and sonoelastography (measuring tissue strain and stiffness) have been used to discriminate myometrium, myomas, and adenomyosis [3]. Four offline 3D transvaginal ultrasound features have been used to evaluate the junctional zone in all uterine walls. Typical magnetic resonance imaging parameters in the T2-weighted resonance would be another choice for the diagnosis [3]. Hysteroscopic and laparoscopic diagnostic parameters of adenomyosis have also been developed. The ultimate goal in all these different diagnostic tools would be the standardization of the imaging approach, reproducibility of the technique and better training of image interpreters for the correct diagnosis of myometrial disease.

Although reduced fertility outcomes seem to be linked to the presence and severity of adenomyosis, the evidence is based on cohort and case-control studies with inadequate power. Moreover, the lack of standardization on imaging criteria for defining adenomyosis and different types of adenomyosis will shadow interpretation of results [1]. As a matter of fact, the ideal clinical trial is designed only when groups of patients are compared in terms of their different treatments. The comparison of treatments can be biased if the groups differ by other characteristics. Once these can be identified, their effects on the cause-effect relation can be avoided. Confounding factors such as the lack of homogeneity among inclusion/exclusion criteria, false double blind, lack of post-surgery double blind, power of the study, sample characteristics, patients lost to follow-up, age homogeneity, lack of psychiatric and psychological patient evaluation, could unintentionally result in missing the real association between exposure and outcome [4]. Besides, in clinical trials that have looked at surgical interventions on adenomyosis and fertility outcomes, no sham surgery was reported that would neutralize biases such as the placebo effect. In this sense, there are no well-designed studies regarding adenomyosis and fertility outcomes that have taken most of these confounding factors into consideration.

The severity of adenomyosis is likely to be associated with an increasing chance of failed in vitro fertilization-embryo transfer that is independent of age and ovarian reserve. Briefly it is right to speculate that the higher number of visible ultrasonographic features translate into worse clinical impact through deeper and more extensive myometrial invasion [5]. It is worth mentioning that adenomyosis is a continuum without sharp demarcation in most cases. Therefore calculating the affected part of the uterus would be imprecise and difficult to standardize. In practical terms there is a significant impact on the chance of clinical pregnancy once the uterus contains four or more ultrasonic features of adenomyosis [5].

The most challenging surgical treatment option is conservative treatment with complete surgical removal of disease resulting in a pregnancy rate of 60%. In cases where only partial excision was possible, these results decreased to 47%. While the partial excision occurred in a greater proportion of women, poorer clinical outcomes were reported from women having more extensive disease. It should be known that none of these data are from randomized trials, but mostly from small and retrospective series [6]. Moreover, women over 40 years of age had a very low pregnancy rate after cytoreductive surgery. Thus, surgery may not be appropriate for women over 40. Surgery should only be considered for symptomatic women with repeated in vitro fertilization/intracytoplasmic sperm injection failure, after the transfer of high-quality embryos [1].

If women with adenomyosis undergo an in vitro fertilization treatment, couples should be counseled that there will be a significant reduction in clinical pregnancy and delivery rates (a clinical pregnancy rate of 41% vs 50% and of 26.8% vs 37.1% in women with and without adenomyosis, respectively). Miscarriage would occur in 32% women with adenomyosis and 14% in those without adenomyosis [6]. Clinical pregnancy, implantation, and ongoing pregnancy rates were significantly higher in women undergoing frozen embryo transfer after long-term GnRH-analog therapy compared to those not pretreated with GnRH-analog [1]. The beneficial effect of GnRH-analog for the treatment of adenomyosis might be due to the improved implantation window. Therefore, GnRH-analog pretreatment before natural conception or in vitro fertilization/intracytoplasmic sperm injection, and embryo transfer is suggested in women with adenomyosis.

Women with adenomyosis who are in their later reproductive years will have most likely reduced ovarian reserves. Immediate in vitro fertilization or intracytoplasmic sperm injection with oocyte retrieval in repetitive cycles should be performed for egg harvesting and freezing oocytes/embryos. Later frozen thawed embryos can be transferred after 3–6 months of GnRH-analog treatment. Women with normal ovarian reserves and adenomyosis may benefit from a fresh embryo transfer with or without 3 months of pretreatment with GnRH-analog.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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