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The identification of ectopic "endometrial-like" tissue was first described by Sampson and Cullen in the 1920's (1). This initial finding fueled research into the complex pathology of endometriosis, in addition to treatment modalities that may be employed to reduce associated symptomatology, including pelvic pain and dysmenorrhea, as well as the suspected detrimental impact on fertility.

According to the most recent Center for Disease Control (CDC) report on Assisted Reproductive Technology (ART) statistics, six percent of all women seeking ART have been diagnosed with endometriosis. In total, almost 87,000 fresh cycles from non-donor oocytes are performed in the United States annually, in addition to over 15,000 frozen embryo transfers (2). Through the use of simple mathematical computation, the number of patients suffering from endometriosis and seeking in vitro fertilization (IVF) is approximately 6,120, not to mention those who have been labeled with the diagnosis of "male factor" or "unexplained infertility" and directed to IVF without completing the laparoscopic evaluation to investigate for a peritoneal factor.

Barnhart et al. performed a meta-analysis on twenty-two published studies, ultimately concluding that patients with endometriosis-associated infertility undergoing IVF have pregnancy rates that are almost half that of women undergoing IVF for other reasons (3). Aboulghar and colleagues supported these findings in a case-controlled study highlighting a detrimental impact of stage IV endometriosis on IVF outcome even after surgical intervention as compared to age-matched controls with tubal factor infertility (4). More recently, Kuivasari et al. conducted an observational study, reporting a significantly lower pregnancy rate among women with stage III/IV endometriosis (22.6%) compared to stage I/II (40%) or tubal factor infertility (36.6%) (5). These findings support further investigation into not only the pathophysiologic mechanisms of the disease, but means by which we as clinicians may impact this particular patient population in a beneficial manner.

With reductions in IVF success compared to controls, the question that is most perplexing is whether women with multiple IVF failures or sonographic evidence of an endometrioma would benefit from surgical therapy prior to controlled ovarian stimulation? Furthermore, would patients labeled with the diagnosis of "unexplained infertility" with an incomplete fertility evaluation and repeated IVF failures benefit from a laparoscopic evaluation and treatment of endometriosis if discovered? In order to address these issues, it is important to explore the potential benefits from an evidence-based perspective and critically appraise the available literature.

First, Surrey and Schoolcraft performed a retrospective analysis in patients with the primary diagnosis of endometriosis undergoing IVF, all of whom had surgical therapy for endometriosis in the preceding 60 months. Patients were subdivided into whether or not the surgical procedure occurred more or less than six months from transvaginal oocyte aspiration. Regression analyses revealed no correlation between implantation rates and the interval between surgical intervention for endometriosis and transvaginal oocyte aspiration. They concluded that any enhancement in reproductive function that is gained through surgery in spontaneous conception is most likely overcome by the greater impact of the implementation of IVF (6). This publication is contrasted to the recent findings of Littman et al. in
which the investigators cited a 76% conception rate following surgical intervention in patients with one or more IVF failures (7). Although these findings seem to promote laparoscopic intervention, several limitations must be taken into account including self-selection bias, the potential for physician encouragement, as well as the fact that some patients may undergo unnecessary surgical intervention without known benefit. Regardless, the authors certainly provoke thought into an area of much deserved attention.

A second issue that has been extensively debated in the literature focuses on the proper treatment of endometriomas in the context of controlled ovarian stimulation. Garcia-Velasco et al. in a retrospective, matched case-control trial reported that there were no differences in fertilization rates, embryos transferred, implantation, pregnancy or miscarriage rates between women that had undergone ovarian cystectomy and those with endometriomas in vivo. The study did, however, note a lower peak estradiol on the day of human chorionic gonadotropin administration, as well as a higher total follicle stimulating hormone (FSH) dose in postoperative patients (8). Although Marconi et al. did not find a similar reduction in peak estradiol postoperatively, they did report a significantly higher number of gonadotropin ampules required for ovarian stimulation in patients following excision of endometriomas (9). These studies may suggest a potential disadvantage of excising endometriomas. Suzuki et al. reported in a retrospective analysis that the number of oocytes retrieved from the ovary containing the endometrioma was similar to the ultrasonographically healthy ovary (10). Pabuccu et al. prospectively analyzed 171 patients with ovarian endometriomas and tubal factor infertility and reported that aspiration of endometriomas prior to controlled ovarian stimulation did not affect the number of metaphase II oocytes retrieved, the implantation or clinical pregnancy rates (11). Operative intervention for an asymptomatic endometrioma prior to controlled ovarian stimulation should be discouraged as there is no clear benefit toward improved outcome and the potential for operative complications, cycle delay, and a reduction in ovarian reserve certainly exist.

A third issue that deserves mention concerns patients suffering from endometriosis that desire oocyte donation. Some have proposed that the presence of endometriosis may adversely affect uterine receptivity, whether immunologically mediated or otherwise. An interesting case-control study performed by Diaz and colleagues was designed in order to determine whether the presence of endometriosis adversely affects the endometrium in oocyte recipients. Oocytes from a single donor were donated to recipients in one of two groups - stage III/IV endometriosis diagnosed via laparoscopy (staging according to the American Society for Reproductive Medicine) or those free of disease. The live birth rate was similar between the two groups supporting the claim that implantation is not adversely affected by the presence of endometriosis in oocyte recipients (12).

The literature is loaded with controversial statements supporting or refuting the implementation of surgical therapy for the treatment of endometriosis prior to controlled ovarian stimulation. The one problem that does exist is the difficulty in accepting conclusions on the basis of retrospective data and the limitations that exist within each study. An evidence-based approach is difficult to follow when prospective, randomized trials are lacking. Another way to approach such a dilemma is to examine it from a benefit/risk perspective. On the one hand, laparoscopy and the surgical management of endometriosis may have the potential to improve spontaneous conception as evidenced through meta-analysis (13). On the other hand, any surgical procedure possesses its own inherent risks not limited to but including hemorrhage, infection, injury to adjacent organs as well as thrombosis. Although these complications are rare, they must certainly be considered. In the context of IVF, surgical intervention would delay treatment cycles that could be successful. Furthermore, there does not seem to be substantial evidence from the literature to support operative treatment of endometriosis prior to IVF. In conclusion, the potential unproven benefit of surgical treatment of endometriosis prior to IVF
must be weighed against the disadvantages of the risks and complications of surgery, the delay of proven treatment in patients with advanced maternal age, and the potential for reductions in ovarian reserve in patients with large endometriomas.

REFERENCES


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