Relationship between ovarian cysts and infertility: what surgery and when?

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The relationship between ovarian cysts and infertility is a subject of debate, mainly because it is difficult to determine the real impact of the cyst and its treatment on later fertility. For a long time it was hoped that surgical treatment could prevent potential complications (such as rupture or malignancy). For presumed benign ovarian tumors, fertility sparing should be the main concern. The goal of this survey of current knowledge on the subject is to thoroughly explore the potential relationship between cysts, their treatment, and infertility. Our study is based on a review of the literature dealing with the epidemiology of ovarian cysts and the effects of their surgical management in relation to infertility. Analysis of the epidemiologic data, drawn mainly from comparative studies and cohorts, shows that the role of cysts in infertility is controversial and that the effects of surgical treatment are often more harmful than the cyst itself to the ovarian reserve. Surgery does not seem to improve pregnancy rates. When a surgical option is nonetheless chosen, a conservative laparoscopic approach is more suitable. Besides excision, sclerotherapy and plasma vaporization are promising, offering a greater preservation of the ovarian parenchyma, especially in endometriomas. These techniques must be better defined. The context of the infertility is essential, and surgeons and specialists in reproductive medicine should decide management jointly. (Fertil Steril® 2014;101:608–14. ©2014 by American Society for Reproductive Medicine.)

Key Words: Ovarian cyst, endometrioma, mature teratoma cyst, infertility, ART, IVF, ovarian reserve, cystectomy

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An ovarian cyst is a common discovery in women of reproductive age generally as well as in those undergoing work-ups for infertility. Surgical management by laparoscopic cystectomy is often the rule, to prevent such potential complications as rupture or malignancy, while optimizing preservation of fertility (1). The impact of the cyst on folliculogenesis depends on the nature, size, and number of cysts. Most women consider it essential that their physicians provide them with clear information on the consequences on subsequent fertility of cysts and their management (2). It is not, however, always easy to determine the cyst's relationship to a woman's infertility, which can have many causes. Further treatment can result in a nontrivial reduction in ovarian reserve. The management of ovarian cysts in an infertile woman raises two questions: 1) Do these cysts impair the prognosis of assisted reproductive technologies (ART)? and 2) How does treatment of a cyst affect these results? These two questions obviously depend on various factors, including the size, number, and histologic type of cysts. The roles of therapeutic abstention, aspiration, vaporization, and cystectomy will be discussed in this review of the literature.

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MATERIALS AND METHODS

This literature review was conducted by consulting the Medline database for articles published from January 2000 through August 2013. The articles were selected by combining the following key words: ovarian cyst, endometrioma, mature teratoma cyst, infertility, ART, IVF, ovarian reserve, surgery, cystectomy, aspiration. Our selection gave priority to meta-analyses, literature reviews, randomized controlled trials, and cohort studies. The level of evidence (LE) scale proposes by the Oxford Centre for Evidence-Based Medicine (www.cebm.net) was used to classify the selected articles.

IMPACT OF OVARIAN CYSTS ON FERTILITY

Endometrioma

Endometriosis affects up to 10% of women of reproductive age (LE1) (3–5). At least one endometrioma is

found in 20%–40% of patients with endometriosis (6, 7) and is often associated with a more severe form of endometriosis (LE2). Despite the lack of evidence of a causal relation between endometriosis and infertility, many studies have examined the impact of endometrioma on fertility. Thus, a recent study compared the results of ovarian biopsies of a healthy ovary and those of the contralateral ovary in 11 women with an endometrioma of size <4 cm; it found significantly decreased follicular density in the endometrioma group (6.3/mm^3 vs. 25.1/mm^3; P=.0002; LE4) (8). These data confirmed the results of earlier studies on endometriomas measuring 5–6 cm compared with other ovarian cysts: The endometriomas were associated with decreased ovarian volume and reduced follicular density in the adjacent cortex (LE3) (9, 10). Histologic analysis of the cortex adjacent to the endometrioma and findings of extensive fibrosis might explain this result.

A recent prospective study compared ovarian reserve, based on antimüllerian hormone (AMH) and an antral follicle count (AFC), in patients with endometriomas >2 cm (without previous surgery) matched with patients of the same age with no ovarian cysts. Those with endometriomas had reduced AMH levels (2.81 vs. 4.20; P=.02) and AFC (9.73 vs. 14.7; P<.01; LE3) (11).

The impact of endometriomas on spontaneous ovulation was studied in a prospective cohort of 70 women with one or more endometriomas >10 mm in one of the two ovaries; the authors observed a significantly lower ovulation rate in ovaries with endometrioma compared with healthy ovaries (P=.002; LE3) (12). On the other hand, the presence of small endometriomas (<4 cm) does not appear to influence the results of ART (LE2) (13–18). These results confirm those of the earlier meta-analysis by Gupta et al., with a similar clinical pregnancy rate in the endometrioma group compared with the control group (odds ratio [OR] 1.07 [95% confidence interval (CI) 0.63–1.81]; LE1) (19).

A recent retrospective study investigating the effect of one or more endometriomas (>4 cm) on the ovarian response of 84 patients found that this mass did not affect the number or size of the cysts or the number of follicles retrieved (LE4) (20). These results seem to be consistent with those of Almog et al., who compared the results of IVF in 19 patients with bilateral endometriomas (LE4) (13). Although these results might be explained by a lack of power and selection bias, they also call into question the idea of a cutoff in the size of endometriomas before ART.

A recent retrospective study of women without surgery compared 39 women with bilateral endometriomas (2 cm on average) and 78 matched control subjects with none. Women with bilateral endometriomas had significantly fewer follicles >10 mm and >15 mm, compared with the control group (9.6 and 6.2 vs. 14.1 and 9.6, respectively; P<.001; LE4). However, although the quantitative response to ovarian stimulation appeared to be lower, quality was not impaired: The rates of top-quality embryos, pregnancies, and live births per cycle were similar in both groups (LE4) (21).

It thus appears that an isolated endometrioma can and should be ignored, especially if it is asymptomatic. It is quite difficult to determine accurately the responsibility between endometriomas and endometriosis regarding infertility (22, 23). Only symptomatic endometriomas should be treated. Moreover, it does not seem to be acceptable to propose a cystectomy to a young woman of reproductive age to prevent the future risk of malignant degeneration or torsion.

Dermoid Cysts

Dermoid cysts account for 70% of ovarian cysts in women <30 years of age and are bilateral in ~10%–20% of cases (LE1) (24–31). Although they grow 1.7–1.8 mm per year, their management remains controversial. Several series of expectant management of dermoid cysts estimate the prevalence of torsion at 3.5%–11% (LE2) (27, 32). Most malignant transformations occur when cyst size is >10 cm and usually in women older than 50 years (33–35).

A recent retrospective Korean case-control study found no significant differences in mean AMH levels between women with dermoid cysts (n = 48) and a control group after adjustment for age and body mass index (4.0 vs. 4.0; ns; LE4) (36). The average size of dermoid cysts in that series was 6.3 cm. A wait-and-see attitude seems to be reasonable for asymptomatic women, especially for moderate-sized dermoid cysts (4–6 cm), where the risk of secondary interventions is low.

IMPACT OF SURGERY FOR OVARIAN CYSTS ON FERTILITY

Endometrioma

Several series have studied the effect of surgical treatment for endometriomas on fertility. The meta-analysis by Raffi et al. reported seven prospective studies and randomized controlled trials published from 2009 to 2011 to investigate postoperative AMH levels (Table 1) (49). In all, 152 excisions were performed for endometriomas measuring at least 3–4 cm. The postoperative AMH level was significantly lower than the preoperative level (−1.13 [interquartile range −1.88 to −0.37]; P=.003), corresponding to a 30% decrease (LE1). A systematic review of 11 series confirmed the decline in ovarian reserve assessed postoperatively by AMH (50). Those authors did not pool the results owing to strong cohort heterogeneity, different study designs, different measurement techniques, and different numbers of measurements. Most studies, however, found a significant decrease in AMH levels, which was greater in women with bilateral endometriomas (LE1). This decrease in AMH level occurs early, in the 1st week after surgery, and seems to persist after 6–9 months (LE1) (50). Two prospective cohort studies have found a progressive depletion of AMH over successive measurements (LE3) (11, 47), thus contradicting the data from an earlier study that found a partial restoration of ovarian reserve 3 months after cyst excision (LE3) (37). The AFC also seems to be affected by this surgical treatment: A recent series found that AFC decreased >10% at 6 months of cystectomy for endometrioma compared with the preoperative count (LE3) (51). The impact of surgery on the ovarian reserve is greater for endometriomas >4 cm. A retrospective study found a significant decrease in the AFC, in the number of dominant follicles, and in the number of oocytes in women with endometriomas >4 cm compared