

Conservative treatment versus surgical excision of ovarian dermoid cysts: Impact on ovarian stimulation and IVF cycle success

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Abstract

Objective: To analyze outcomes of IVF treatment among women diagnosed with an ovarian dermoid cyst (DC).

Methods: Retrospective analysis of women with an ovarian DC who underwent IVF with fresh blastocyst transfer at a single center in New York from January 2010 to March 2018. Outcomes were compared between women with conservative treatment and those with surgical excision of the DC. Multivariate logistic regression was used to assess associations between variables and the presence of a DC during treatment.

Results: Overall, 119 women with a DC were included. No differences were found in demographic characteristics, controlled ovarian hyperstimulation parameters, and IVF outcomes between women with an intact DC (n=65, 54.6%) and those who underwent cystectomy (n=54, 45.4%) (all $P < 0.05$). Similarly, there was no difference in anti-Müllerian hormone and basal antral follicle count among women with a DC (respectively, $\beta = -0.1$, $P = 0.8$, and $\beta = -1.0$, $P = 0.28$) or resected DC (respectively, $\beta = 0.9$, $P = 0.07$, and $\beta = 1.5$, $P = 0.08$) as compared with control women with no DC (n=352).

Conclusion: Ovarian reserve, embryo implantation and IVF success rates were not lower in the presence of an ovarian DC. Surgical therapy, if indicated, can be safely postponed until family planning goals have been achieved.

KEYWORDS

Cystic teratoma; Dermoid cyst; In vitro fertilization; Ovarian cystectomy; Ovarian reserve; Ovarian surgery; Ovarian tumor

1 | INTRODUCTION

Cystic teratomas, commonly referred to ovarian dermoid cysts (DCs), are benign germ cell tumors that derive from totipotential cells of the ectoderm, mesoderm, and endoderm.¹ Thus, the interior structures of DC have varying tissue composition, including hair, bone, primitive or mature teeth, cartilage, nerve, and sebaceous materials.² These types of tumor are the most common neoplasms observed among women during their reproductive lifespan, with a reported incidence of 10%–25%.³

Typically, cystic teratomas are diagnosed by pelvic ultrasound and are identified by their characteristic appearance: namely, a cystic adnexal unilocular mass known as a “Rokitansky nodule” or a dermoid plug; a dermoid mesh caused by hyper-echogenic structures; or a linear demarcation caused by fat fluid or hair levels.^{4,5} Although most DC cases are asymptomatic and require no treatment, a growing number of practitioners agree that a teratoma of 5 cm or larger should be removed to diminish ovarian torsion or to prevent malignancy, which has been described to occur in 1.7% of all cases.^{6,7}

Management of DC in adolescents and women of reproductive age requires important clinical supervision. Because DC treatment might impact fertility, it remains uncertain whether surgical removal of a DC is necessary. Surgical excision of an ovarian DC may complicate future infertility or the ability to conceive because the normal ovarian cortex might be resected, affecting basal ovarian reserve or leading to risk of pelvic adhesion formation.^{8,9} Furthermore, for women who seek assisted reproduction technology (ART) treatment to achieve pregnancy, surgical removal of DC can create potential complications at the time of vaginal oocyte retrieval. Of greatest concern are spillage of the cyst contents and subsequent peritonitis, and the increased technical difficulty encountered during oocyte retrieval.^{10,11}

Few studies have evaluated ART treatment outcomes among women diagnosed with an ovarian DC. Based solely on basal antral follicle count (AFC) measurements, Yan et al.¹² reported that DC excision may significantly reduce ovarian reserve; by contrast, Kim Yi et al.¹³ showed that anti-Müllerian hormone (AMH) levels were similar for women before surgical excision of an ovarian DC and a control population matched for age and body mass index (BMI). Other studies have shown that ovarian response to controlled ovarian stimulation during IVF is not significantly affected by the presence of a DC.^{12,14} Nevertheless, in a modern IVF setting, the optimal treatment for women with a DC requires additional research with greater statistical power to understand whether the presence of the DC compromises ovarian response and cycle outcomes.

The primary aim of the present study was therefore to compare ovarian reserve, response to stimulation, and IVF cycle success among women with an intact ovarian DC, women with a history of resected DC, and a matched control group. A secondary aim was to analyze the potential consequences of DC removal before undergoing ART treatment.

2 | MATERIALS AND METHODS

2.1 | Study design and population

In a retrospective study, data were analyzed from women with an ovarian DC who completed an IVF cycle with a fresh blastocyst transfer at a single center in New York, USA, from January 1, 2010, to March 31, 2018. This analysis was approved by an Institutional Review Board (WIRB PRO NUM: 20161791; Study number: 1167398). Patient information was de-identified before data analysis; patient consent was not needed for the purposes of this study.

The study women were diagnosed with a DC by transvaginal ultrasound examination up to 12 months before ART treatment by the observation of one or more of the following characteristics: a heterogenic intra-ovarian mass or cyst; a Rokitansky nodule; the presence of a dermoid mesh with internal echoes or calcifications; or a complex mass with linear demarcations (Fig. 1). The largest diameter (in cm) of the DC was recorded as the cyst size. Surgical management of the cysts was discussed with each patient if indicated before ART treatment. Serum AMH was measured during the first consultation and, in cases of resection, reassessed after surgery before IVF stimulation was started.

2.2 | Controlled ovarian hyperstimulation and laboratory procedures

The controlled ovarian stimulation protocol^{15,16} used for each woman was selected at the discretion of the treating physician. Vaginal oocyte retrieval was performed by using transvaginal ultrasound guidance 36 hours after oocyte maturation was triggered. Oocytes were fertilized by conventional insemination or intracytoplasmic sperm injection approximately 4 hours after retrieval. All embryos were cultured up to blastocyst stage as described previously.¹⁷ Day-5 embryos were transferred in a fresh cycle with luteal support by vaginal and/or intramuscular progesterone. The total number of embryos transferred was done in accordance with ASRM practice committee guidelines.¹⁸

2.3 | Outcome measures

The primary outcome was live birth, considered as the delivery of a live-born neonate after 24 gestational weeks. The secondary outcomes were clinical pregnancy, confirmed by the sonographic evidence of fetal cardiac activity; implantation rate, calculated as the number of detectable gestational sacs divided by the number of embryos transferred; and clinical pregnancy loss, defined as a pregnancy loss occurring after the presence of a heart beat on an ultrasound.

For the main analysis, study women were segregated according the presence or prior excision of an ovarian DC. A control group of women with no DC or history of DC was created by using a 3:1 propensity score matching for age, BMI (calculated as weight in kilograms divided by the square of height in meters), and year of treatment.

A sub-analysis was also performed based on surgical excision of the ovarian DC. The following three groups were compared: a propensity score-matched control group; women with history of resected DC before ART; and those with an intact DC during ART.

2.4 | Statistical methods

Statistical analyses were performed by using SAS version 9.4 (SAS Institute, College State, TX, USA). The results were expressed as mean \pm SD or number (percentage). Descriptive data were compared by unpaired two-sided Student *t* test. A *P* value of less than 0.05 was considered significant.

Multivariate logistic regression analysis was used to assess the relationship between a resected DC or intact DC and IVF outcomes, and to assess the correlation between the ovarian reserve markers levels (AMH and basal AFC) and the presence or resection of a DC after adjusting for age. Complex multivariate logistic regression analysis controlling for age, BMI, AMH, DC size, endometrial ultrasound thickness at transfer, and number of embryos transferred was also performed to model the relationship between the presence or absence of a DC and IVF outcomes. Odds ratios (ORs) with 95% confidence interval (CI) and corresponding *P* values were reported. For

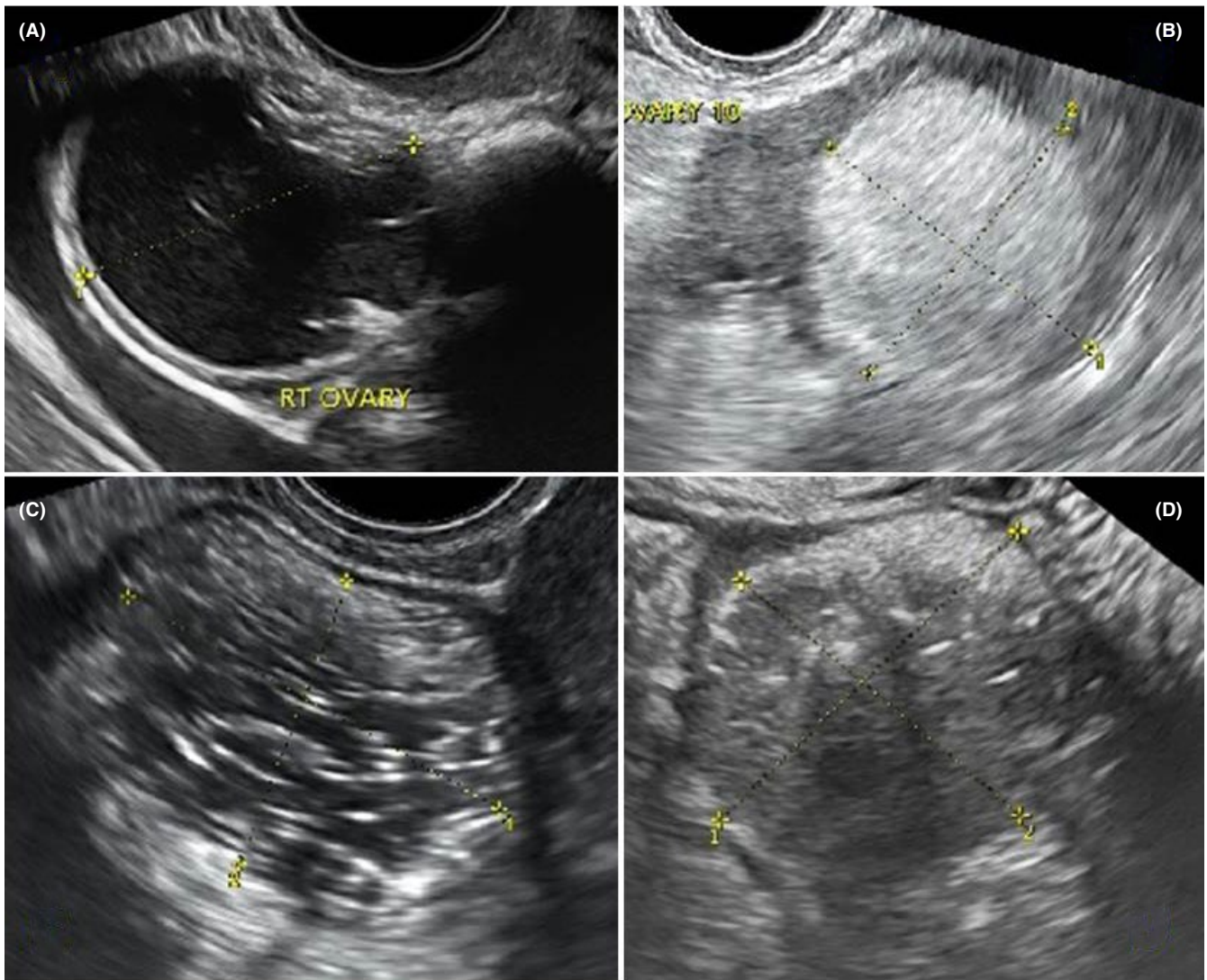


FIGURE 1 Different ultrasonographic features of a dermoid cyst. (A) Cystic adnexal unilocular mass with a “Rokitansky Nodule” on the superior margin. (B) Finely delimited dermoid plug and dermoid mesh created by different echogenic structures. (C & D) Adnexal masses with mixed echogenicity, dermoid mesh sign, multiple calcifications and posterior acoustic shadowing.

the main analysis, a sample size of 120 patients per group was calculated to have an 80% power to detect a 15% difference in live birth rate ($\alpha=0.05$).

3 | RESULTS

3.1 | Main analysis

During the study period, 119 women were diagnosed with a DC and included in the analysis. The control group of propensity score-matched women consisted of 352 women. No significant difference were observed in demographic characteristics, ovarian reserve metrics, or stimulation metrics such as cumulative gonadotropin use, days of stimulation, number of eggs retrieved, blastulation rate, and number of transferred and cryopreserved embryos between the two groups (Table 1). No complications during vaginal oocyte retrieval were observed among the study women.

In terms of IVF outcomes, there were no differences in implantation rate (40.3% vs 13.1%, $P=0.45$), clinical pregnancy rate (87.5% vs 80.2%, $P=0.25$), live birth rate (75.0% vs 67.1%, $P=0.3$), clinical pregnancy loss (12.5% vs 13.1%), and multiple pregnancy rate (16.6% vs 20.3%) between the women with a DC and the control group (Table 1).

In a logistic regression analysis controlling for age, AMH, BMI, DC size, endometrial thickness at embryo transfer, and number of embryos transferred, there was no association between the presence of a DC and the odds of impaired IVF outcomes: implantation rate (OR, 1.56; 95% CI, 0.32–7.57; $P=0.58$), clinical pregnancy rate (OR, 2.52; 95% CI, 0.05–113.46; $P=0.63$), live birth (OR, 1.30; 95% CI, 0.09–18.56; $P=0.84$), clinical pregnancy loss (OR, 0.76; 95% CI, 0.05–10.85; $P=0.84$), and multiple pregnancy (OR, 0.64; 95% CI, 0.007–58.93; $P=0.46$) (data not shown).

In a multivariate linear regression analysis adjusted for age and BMI, the women’s AMH levels ($\beta=-1.07$, $P=0.25$) and basal AFC

TABLE 1 Demographic characteristics, laboratory data, and clinical outcomes by the presence or absence of a dermoid cyst.^a

Characteristic/outcome	Patients without DC (n=352)	Patients with DC (n=119)	OR (95% CI)	P value
Maternal characteristics				
Age	36.04 ± 4.80	35.93 ± 4.91		0.83
BMI	24.55 ± 5.12	24.14 ± 4.91		0.49
Laboratory data				
Estradiol at hCG, pg/mL	2085 ± 1093	2070 ± 1162		0.89
Progesterone at hCG, ng/mL	0.87 ± 0.46	0.95 ± 0.55		0.18
Baseline FSH, IU/mL	6.73 ± 4.04	6.74 ± 4.10		0.98
Baseline LH, mIU/mL	4.13 ± 2.65	4.39 ± 2.67		0.43
AMH, ng/mL	2.19 ± 2.27	2.66 ± 3.84		0.35
Basal AFC	10.63 ± 6.43	9.41 ± 6.82		0.11
Cycle characteristics				
Day of hCG administration	12.01 ± 1.69	12.28 ± 1.83		0.14
Stimulation duration, d	9.00 ± 1.60	9.20 ± 1.83		0.14
Endometrial thickness at hCG, mm	10.15 ± 2.12	9.99 ± 2.08		0.49
Gonadotropin cumulative dose, IU	3644 ± 1433	3839 ± 1515		0.2
Endometrial thickness at transfer, mm	10.52 ± 7.91	10.27 ± 2.83		0.68
Cycle outcomes				
Oocytes retrieved	14.21 ± 8.90	15.10 ± 11.47		0.47
Mature (MII) oocytes	11.75 ± 8.19	13.15 ± 10.94		0.22
Fertilized oocytes	8.35 ± 6.35	9.40 ± 8.29		0.23
Blastocyst formation	4.91 ± 4.54	5.53 ± 5.82		0.31
Embryos transferred	1.33 ± 1.10	1.31 ± 0.98		0.89
Embryos cryopreserved	2.27 ± 3.67	2.87 ± 4.10		0.15
Cancellation rate	65/352 (18.4)	26/119 (21.8)	0.70 (0.33–1.88)	0.59
Best embryos used at ET	165/236 (69.9)	51/78 (65.3)	0.81 (0.47–1.99)	0.45
Implantation rate	152/352 (43.1)	48/119 (40.3)	0.80 (0.58–1.35)	0.58
Clinical pregnancy rate	122/152 (80.2)	42/48 (87.5)	1.72 (0.66–4.42)	0.25
Live birth rate	102/152 (67.1)	36/48 (75.0)	1.47 (0.70–3.06)	0.30
Clinical pregnancy loss	20/152 (13.1)	6/48 (12.5)	0.94 (0.35–2.5)	0.90
Multiple pregnancy rate	31/152 (20.3)	8/48 (16.6)	0.78 (0.33–1.83)	0.57

Abbreviations: AFC, antral follicle count; AMH, anti-Müllerian hormone; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); CI, confidence interval; ET, embryo transfer; FSH, follicle-stimulating hormone; hCG, human chorionic gonadotropin; LH, luteinizing hormone; MII, metaphase II.

^aValues are given as mean ± SD or number/total number (percentage) unless stated otherwise.

($\beta = -1.48$, $P = 0.32$) were not associated with the presence of a DC during ART treatment (data not shown).

3.2 | Sub-analysis

Of the 119 patients with a DC in the 12 months before ART, 65 (54.6%) were identified to have an intact DC during the IVF cycle, and 54 (45.4%) underwent cystectomy before ART. There was a significant difference in the recorded cyst size between those with an active DC and those with a resected DC (1.9 ± 1.6 cm vs 4.1 ± 2.3 cm, $P < 0.001$). No other differences in baseline demographic characteristics, ovarian stimulation parameters, or embryologic laboratory parameters were observed (Table 2). The implantation rate, clinical pregnancy rate,

ongoing pregnancy rate, pregnancy rate, and pregnancy loss rate were similar between the two groups (Table 2).

After controlling for age, BMI, AMH, DC size, endometrial thickness at embryo transfer, number of blastocysts transferred, and cyst size, there was no association between the presence of an intact DC during IVF versus a resected DC and the odds of implantation (OR, 1.31; 95% CI, 0.37–4.64; $P = 0.67$), clinical pregnancy (OR, 0.97; 95% CI, 0.14–6.36; $P = 0.91$) live birth (OR, 1.74; 95% CI, 0.35–8.53; $P = 0.49$), clinical pregnancy loss (OR, 0.57; 95% CI, 0.11–2.80; $P = 0.63$), multiple pregnancy (OR, 0.61; 95% CI, 0.06–5.85; $P = 0.51$), or cycle cancellation (OR 0.85; 95% CI, 0.35–2.07; $P = 0.72$). After adjusting for age and BMI, the women's AMH levels and basal AFC were not significantly associated with the presence of an intact DC during IVF treatment (respectively,

TABLE 2 Demographic characteristics, laboratory data, and clinical outcomes of the study women by the absence of a cyst, surgical cyst resection, or presence of an intact dermoid cyst.^a

Characteristic/outcome	No dermoid cyst (n=352)	Resected dermoid cyst (n=54)	Intact dermoid cyst (n=65)	P value
Maternal				
Age	36.04 ± 4.80	36.38 ± 5.03	35.57 ± 4.82	0.64
BMI	24.55 ± 5.12	25.11 ± 5.35	23.44 ± 4.49	0.22
Laboratory data				
Estradiol at hCG, pg/mL	2085 ± 1093	2032 ± 989	2101 ± 1296	0.93
Progesterone at hCG, ng/mL	0.87 ± 0.46	0.99 ± 0.61	0.91 ± 0.49	0.25
Baseline FSH, IU/mL	6.73 ± 4.04	7.02 ± 3.59	6.52 ± 4.49	0.84
Baseline LH, mIU/mL	4.13 ± 2.65	4.83 ± 2.68	4.05 ± 2.65	0.28
AMH, ng/mL	2.19 ± 2.27	3.19 ± 4.85	2.16 ± 2.52	0.17
Basal AFC	10.63 ± 6.43	9.24 ± 6.60	9.54 ± 7.03	0.27
Dermoid cyst size, cm	—	4.10 ± 2.30	1.97 ± 1.80	<0.001
Day of hCG trigger	12.01 ± 1.69	12.14 ± 1.52	12.40 ± 2.05	0.24
Stimulation duration, d	9.00 ± 1.60	9.13 ± 1.50	9.30 ± 2.00	0.24
Gonadotropin cumulative dose, IU	3644 ± 1433	3731 ± 1563	3929 ± 1480	0.34
Endometrial thickness at embryo transfer, mm	10.52 ± 7.91	10.35 ± 2.82	10.21 ± 2.87	0.96
Cycle outcomes				
Oocytes retrieved	14.21 ± 8.90	15.13 ± 6.99	15.07 ± 14.26	0.71
Mature (MII) oocytes	11.75 ± 8.19	13.10 ± 6.34	13.19 ± 13.74	0.37
Fertilization rate, %	68.0 ± 25.8	69.3 ± 26.4	71.7 ± 24.6	0.66
Fertilized oocytes	8.35 ± 6.35	9.15 ± 5.31	9.61 ± 10.19	0.36
Blastocysts	4.91 ± 4.54	5.69 ± 4.67	5.40 ± 6.67	0.49
Embryo transfer count	1.33 ± 1.10	1.31 ± 0.99	1.32 ± 0.98	0.99
Cryopreserved embryos count	2.27 ± 3.67	2.81 ± 3.35	2.91 ± 4.68	0.36
Cancelled cycles	65/352 (18.4)	13/54 (24.0)	13/65 (20.0)	0.61
Best embryos used at transfer	165/236 (69.9)	26/35 (74.2)	25/43 (58.1)	0.23
Implantation rate	152/236 (64.4)	23/35 (65.7)	25/65 (38.4)	0.77
Clinical pregnancy rate	122/236 (51.6)	19/35 (54.2)	23/65 (35.3)	0.36
Ongoing pregnancy rate	102/236 (43.2)	15/35 (42.8)	21/65 (32.3)	0.21
Clinical loss	20/152 (13.1)	4/23 (17.3)	2/25 (8.0)	0.62
Multiple pregnancy	31/152 (20.3)	3/23 (13.0)	5/25 (20.0)	0.70

Abbreviations: AFC, antral follicle count; AMH, anti-Müllerian hormone; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); CI, confidence interval; ET, embryo transfer; FSH, follicle-stimulating hormone; hCG, human chorionic gonadotropin; LH, luteinizing hormone; MII, metaphase II.

^aValues are given as mean ± SD or number/total number (percentage) unless stated otherwise.

$\beta = -0.1$, $P = 0.8$, and $\beta = -1.0$, $P = 0.28$), or a resected DC (respectively, $\beta = 0.9$, $P = 0.07$, and $\beta = 1.5$) as compared with no DC (Table 3).

4 | DISCUSSION

Ovarian cysts are commonly diagnosed among women of reproductive age, especially during ART consultation. Surgical procedures may delay the progress of reproductive care and might increase the economic burden and anxiety for affected women. As a result,

reproductive endocrinology and infertility specialists are advised to consider conservative treatments for DC when appropriate as a first-line approach to patient care. The present study found that the presence of an ovarian DC did not adversely affect COH response or compromise IVF outcomes among women undergoing ART treatment. In addition, women who underwent ART treatment with an intact DC were shown to have ovarian reserves comparable to those of control women without a DC.

The ovarian stimulation and cycle parameters, including serum estradiol on day of human chorionic gonadotropin (hCG) trigger, oocytes

TABLE 3 Multivariate analysis of AMH and basal AFC adjusted for age and BMI.

Study group	No. of women	AMH, ng/mL			Basal AFC		
		Mean	B-estimate	P value	Mean	B-estimate	P value
No DC	352	2.19 ± 2.27	Ref.		10.63 ± 6.43	Ref.	
Intact DC	54	2.16 ± 2.52	-0.1	0.8	9.54 ± 7.03	-1.0	0.28
Resected DC	65	3.19 ± 4.85	0.9	0.07	9.24 ± 6.60	1.5	0.08

Abbreviations: AFC, antral follicle count; AMH, anti-Müllerian hormone; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); DC, dermoid cyst.

retrieved, number of blastocysts, and embryos cryopreserved, were similar between women diagnosed with a DC and control women without a DC (all $P>0.05$). Furthermore, after controlling for factors correlated with ovarian reserve, such as age and BMI,¹⁹ no decrease in AMH or basal AFC was observed for the DC cohort as compared with the control cohort.

The present findings are consistent with those of Caspi et al.²⁰ and Rodriguez-Purata et al.,¹⁴ who demonstrated that serum estradiol concentrations on the day of hCG administration, mean number of oocytes retrieved, and IVF outcomes were not altered by the presence of a DC. Those studies have contributed to expanding the current knowledge base for DC treatment in an IVF setting. However, because DCs are diagnosed within less than 1% of infertile women, those studies remain inconclusive owing to their small sample sizes and underpowered evaluation.^{14,20} By contrast, the present study included a larger sample of women who were diagnosed with DC and undergoing ART treatment and was powered appropriately to detect clinical relevance.

Nevertheless, clinicians planning ART treatment for women diagnosed with a DC must decide whether to perform surgery for cyst resection before COH. The present sub-analysis found that women with an intact DC during COH had similar ovarian stimulation outcomes as compared with those with a history of surgical resection. Outcomes, including estradiol on day of hCG, oocytes retrieved, blastocyst count, number of embryos cryopreserved, and cycle cancellation rates, were similar even when compared with a matched control group (all $P>0.05$).

The present results are comparable with the findings in a large cohort reported by Yan et al.,¹² who found no difference in the mean number of retrieved oocytes, embryos transferred, or total dose of gonadotropins used between women with a surgically excised DC and those with an intact DC. Yan et al. also reported a significant difference in basal AFC after surgery, suggesting a detrimental effect of the intervention on ovarian reserve; however, they did not report AMH levels, a factor that might affect the generalizability of the results. In the present study, by contrast, the unadjusted analysis comparing intact DC, surgically excised DC, and control groups found no differences in AMH ($P=0.17$) or basal AFC ($P=0.2$). After adjustment for age and BMI, there was no association between AMH or basal AFC values and the presence of an intact cyst ($P=0.8$ and $P=0.28$, respectively) or a resected DC ($P=0.07$ and $P=0.08$, respectively) as compared with a control group of women with no DC.

Regarding IVF outcomes, the present study found no differences between women with and without a DC. After adjusting for potential cofounders, no association was observed between the presence of a DC and implantation rate, clinical pregnancy rate, live

birth, clinical pregnancy rate, and multiple pregnancy (all $P>0.05$). Similarly, no differences were found in these outcomes in the sub-analysis of women with surgical resection of the DC before ART therapy and those with an intact DC after adjusting for multiple cofounders (all $P<0.05$). The present results are comparable with previously published data.^{12,14,20}

Ultimately, one of the major concerns for performing COH and vaginal oocyte retrievals for women with an intact DC is the possibility of puncturing the cyst and spillage of the contents, leading to chemical peritonitis or difficult retrieval.¹⁰ In the present study, none of the women experienced any of these complications.

The study has limitations that must be taken into account. The retrospective study design can be subject to selection bias. Some of the study women attended the study clinic after treatment at a different fertility or gynecologic clinic, where they had surgery before undergoing ART. Owing to the retrospective nature of the analysis, it was not possible to retrieve all surgical, pre-operative, and post-operative ovarian reserve markers and/or AMH levels relative to the date of surgery. The lack of data on surgical techniques and ovary tissue insult performed during procedures before ART might have influenced cycle outcomes, thereby reducing the generalizability of the findings.

In summary, the presence or removal of an ovarian DC did not influence AMH levels or basal AFC. In addition, the analysis showed that the response to controlled ovarian stimulation, embryo implantation, and IVF outcomes were similar for women with an ovarian DC and matched control women. A DC should not be considered an obstacle for women undergoing ovulation induction and IVF treatment. Conservative DC therapy can be considered appropriate for women with a DC, as long as clinicians are vigilant during IVF and avoid puncturing the cyst at time of vaginal oocyte retrieval.

In our community of microsurgeons, who use meticulous laparoscopic and robotic techniques with high-power magnification and minimal cautery, there does not seem to be a downside to surgical removal of cysts. However, women can be reassured that the presence of a DC is not a barrier to ART success. Surgical therapy for the cyst, if indicated, can be safely postponed until the women has achieved her goals for family planning.

AUTHOR CONTRIBUTIONS

CHN, ABC, KG, TM, and BS conceived and designed the study. ABC, JL, KG, TM, and CHN analyzed the data. CHN, ABC, JL, KG, TM, and

BS wrote and revised the manuscript. All authors participated in reading, revising, and approving the final manuscript.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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