Antral follicle count as a predictor of ovarian responsiveness in women with endometriomas or with a history of surgery for endometriomas

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Objective: To evaluate the accuracy of antral follicular count (AFC) in predicting ovarian responsiveness in ovaries with endometriomas or with a past history of surgical excision of endometriomas.
Design: Retrospective review.
Setting: Academic hospital.
Patient(s): Eighty-three women for a total of 166 gonads.
Intervention(s): None.
Main Outcome Measure(s): Total number of developing follicles.
Result(s): The ovaries were characterized as four groups: [1] unoperated gonads without endometriomas (n = 42, control group), [2] unoperated gonads with endometriomas (n = 46), [3] operated gonads without endometriomas (n = 55), and [4] operated gonads with endometriomas (n = 23). The analyses subsequently considered all ovaries with endometriomas (groups 2 + 4, n = 69) and all operated ovaries (groups 3 + 4, n = 78). The capacity of AFC to predict low response (≤2 follicles) or hyperresponsiveness (≥7 follicles) was evaluated using receiver operating characteristic curves. We used a linear regression model to calculate the adjusted B coefficients. The adjusted B coefficients in unaffected ovaries, in all ovaries with endometriomas, and in all operated ovaries were 0.55 (95% confidence interval [CI], 0.07–1.03), 0.76 (95% CI, 0.54–0.98), and 0.51 (95% CI, 0.26–0.76), respectively. The area under the curve (AUC) for the prediction of low response was 0.83 (95% CI, 0.68–0.99), 0.83 (95% CI, 0.73–0.93), and 0.74 (95% CI, 0.63–0.85), respectively. The AUC for the prediction of hyperresponse was 0.84 (95% CI, 0.70–0.97), 0.74 (95% CI, 0.63–0.85), and 0.77 (0.60–0.94), respectively.
Conclusion(s): The accuracy of AFC for predicting ovarian response is similar in unaffected ovaries, ovaries with endometriomas and ovaries with a history of surgery for endometriomas. (Fertil Steril® 2015;103:1544–50. ©2015 by American Society for Reproductive Medicine.)
Key Words: AFC, controlled ovarian hyperstimulation, endometrioma

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The impact of ovarian endometriomas and their surgical removal on the ovarian reserve is still a debated issue. There is consistent biological evidence suggesting a detrimental effect of these cysts on the ovarian reserve (1–3). Potential mechanisms of damage include the diffusion of toxic substances from the endometrioma to the ovarian tissue (2) and the burn-out effect of damage consequent to an enhanced recruitment of primordial follicles and consequent accelerated exhaustion of the ovarian reserve (3). This latter mechanism is strongly supported by two recent contributions that documented a lower number of primordial follicles and an increased proportion of activated and atretic follicles in ovaries with endometriomas (1, 3). In contrast, available clinical data have failed to document a relevant impact. In women with unilateral endometriomas, ovarian responsiveness to hyperstimulation does not differ between the two gonads, and ovarian reserve appears to be only modestly affected in women with bilateral cysts (4–6).

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Laparoscopic stripping has been shown to damage the ovarian reserve by most but not all investigators (7–9). Moreover, recent preliminary evidence suggests that alternative surgical techniques such as laser vaporization, partial cystectomy, or surgical suture may cause less or no damage (10–16).

Not surprisingly, this controversial scenario has had a clinical impact, and physicians frequently to have deal with a high degree of uncertainty. The decision to operate depends on several clinical factors and sonographic findings (17–20). A neglected but potentially relevant issue is the measurement of the ovarian reserve in ovaries with endometriomas or with a history of surgery for endometriomas. A clear knowledge of the remnant ovarian reserve of an affected or previously operated ovary may influence therapeutic decisions.

Unfortunately, the evaluation of ovarian reserve in women with current or past ovarian endometriomas is challenging. In most cases, these cysts are unilateral, thus hampering the validity of hormone assessments such as serum follicle-stimulating hormone (FSH) or inhibin because the contralateral gonad may properly compensate for the reduced function of the affected one. The validity of antimüllerian hormone (AMH) is also debatable because the relative contribution of the affected and intact ovaries cannot be definitely discriminated. The accuracy of serum AMH is also questionable in women with bilateral cysts because it cannot be excluded that endometriomas may affect ovarian reserve differently in the same patient. At present, sonographic assessment of antral follicle count (AFC) is the only means of obtaining independent data on the ovarian reserve of an ovary. A huge amount of literature has validated the use of AFC as a surrogate measurement of ovarian reserve (21–24). However, to the best of our knowledge, even though AFC in ovaries with current or past endometriomas has been used repeatedly in research studies (10–13, 15, 16, 25–29), this tool has never been validated. Of note, based on the currently accepted recommendations, AFC should not be assessed in women with ovarian endometriosis or previous ovarian surgery (30).

Our study focused on women undergoing in vitro fertilization (IVF) to validate the use of AFC in ovaries with current or past endometriomas. Ovarian responsiveness to hyperstimulation is actually considered the best noninvasive surrogate measurement of ovarian reserve (31). The correlation of AFC and ovarian responsiveness in ovaries with current or past endometriomas may thus provide valuable information on the accuracy of AFC in this context.

MATERIALS AND METHODS

Our retrospective study at the Infertility Unit of the Department of Obstetrics and Gynecology of the Fondazione Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy, reviewed the clinical charts of women who underwent IVF cycles between January 2011 and March 2013. The inclusion criteria were as follows: [1] previous surgery for ovarian endometriomas and/or sonographic diagnosis of endometriomas at the time of the cycle, [2] availability of a pre-IVF assessment of AFC between days 2 and 4 of a spontaneous menstrual cycle, and [3] age ≤ 42 years. The exclusion criteria included [1] past history of ovarian surgery for nonendometrial lesions, [2] diagnosis of nonendometrial cysts at the time of IVF cycle, and [3] pre-IVF hormone treatment (progestins, estroprogestins, or gonadotropin-releasing hormone analogs). The women could be enrolled for only one cycle. Women who are referred to our unit are routinely asked to provide informed consent for their clinical data to be used for research purposes, and those who had refused consent were excluded from our study. The local institutional review board approved the study protocol.

Our analyses focused on the relationship between AFC and the total number of developing follicles per ovary. Specifically, four different groups of gonads were initially considered: [1] unoperated ovaries without endometriomas (control group), [2] unoperated ovaries with endometriomas, [3] operated ovaries without endometriomas, and [4] operated ovaries with endometriomas. The analyses subsequently considered all ovaries with endometriomas together (groups $2 + 4$), all ovaries with endometriomas with a mean diameter >20 mm (subgroup of the latter), and all operated ovaries (groups $3 + 4$).

During the study period, AFC was assessed based on the current available recommendations (30). Briefly, all identifiable antral follicles 2–10 mm in diameter were recorded. The diagnosis of endometrial cysts was performed by transvaginal ultrasound and had to be documented on at least two occasions and at least two menstrual cycles apart. More specifically, ovarian endometrioma was defined as a round-shaped cystic mass with a minimum diameter of 10 mm, with thick walls, regular margins, homogeneous low echogenic fluid content with scattered internal echoes, and without papillary proliferations (32). Women with atypical lesions were excluded, such as cysts whose sonographic appearance was compatible with but not distinctly identifiable as endometriosis. The diameter of the endometriomas was calculated as the mean of three perpendicular diameters. All sonographic evaluations were performed by four physicians who have had a long-term specialization in reproductive medicine, all of whom attended an internal meeting in 2010 to discuss the new recommended modality to assess AFC. In our unit, women with a history of surgery for ovarian endometriosis are routinely asked to provide documentation of the intervention; only those with a histologically confirmed diagnosis of endometriomas were included in the study.

During the IVF cycle, the patients selected for IVF were monitored and managed according to standardized clinical protocols, as reported elsewhere (33). Briefly, the patients underwent a transvaginal ultrasound in the early proliferative phase of the cycle preceding the initiation of ovarian hyperstimulation. The AFC assessment was systematically recorded at this time and again on day 3 of the following menstrual cycle if the woman received a flare-up protocol or a protocol with gonadotropin-releasing hormone antagonists (if two AFC assessments were available, the latter one was used for the analysis). The regimen used and the dose of gonadotropins were determined on an individual basis according to the age, day-3 serum FSH value, serum AMH value, and AFC. During