ORIGINAL ARTICLE: ENDOMETRIOSIS

Does preoperative antimüllerian hormone level influence postoperative pregnancy rate in women undergoing surgery for severe endometriosis?

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Objective: To compare postoperative pregnancy rates as they relate to presurgery antimüllerian hormone (AMH) level in patients with stage 3 and 4 endometriosis.

Design: Retrospective comparative study using data prospectively recorded in the North-West Inter-Regional Female Cohort for Patients with Endometriosis (CIRENDO) database.

Setting: University tertiary referral center.

Patient(s): One hundred eighty patients with stage 3 and 4 endometriosis and pregnancy intention, managed from June 2010 to March 2015, were divided into two groups according to their preoperative AMH levels: group A (AMH ≥ 2 ng/mL) and group B (AMH < 2 ng/mL).

Intervention(s): Surgical procedure involved ovarian endometrioma ablation by plasma energy along with resection of various localizations of the disease. Postoperative conception was either spontaneous or used assisted reproductive technology, depending on patient characteristics.

Main Outcome Measure(s): Patient characteristics, preoperative symptoms, infertility history, intraoperative findings, and probability of pregnancy were recorded and compared between the two groups.

Result(s): Among 180 women enrolled in the study, 134 (74.4%) were assigned to group A and 46 (25.6%) to group B. The women's ages were, respectively, 30 ± 3.8 and 32 ± 4.6 years. Pregnancy was achieved by 134 (74.4%) patients, and conception was spontaneous in 74 of them (55.2%). Pregnancy rates in groups A and B were, respectively, 74.6% (100 women) and 73.9% (34 women), while spontaneous conception represented 54% (54 women) and 58.8% (20 women). The probability of pregnancy at 12, 24, and 36 months after surgery in groups A and B was comparable, respectively, 65% (95% confidence interval [CI], 55%–75%), 77% (95% CI, 86%–68%), and 83% (95% CI, 90%–75%) versus 50% (95% CI, 69%–34%), 77% (95% CI, 90%–61%), and 83% (95% CI, 94%–68%). Supplementary analysis in women with normal (≥ 2 ng/mL), low (1–1.99 ng/mL), and very low (< 1 ng/mL) AMH level showed an inverse relationship between AMH level, age, and antecedents of miscarriage; however, postoperative pregnancy rates were comparable among the three groups at 12 and 24 months, respectively, 59.5% (95% CI, 49.3%–70%) and 77.4% (95% CI, 68%–85.4%); 57.1% (95% CI, 34%–83%) and 78.6% (95% CI, 55.2%–94.8%); and 46.7% (95% CI, 25.6%–73.7%) and 73.3% (95% CI, 50.4%–91.7%).

Conclusion(s): The probability of postoperative pregnancy was comparable between women with low and normal AMH level who were managed for stage 3 and 4 endometriosis and who were a mean age of 30 years. However, the small sample size might have been unable

Received September 5, 2016; revised December 7, 2016; accepted December 13, 2016.

E.S.-L. has nothing to disclose. B.D. has nothing to disclose. O.M. has nothing to disclose. S.T. has nothing to disclose. J.-C.M. has nothing to disclose. C.A. has nothing to disclose. S.A. has nothing to disclose. H.R. reports personal fees for participating in a symposium and a master class presenting his experience in the use of PlasmaJet.

The North-West Inter-Regional Female Cohort for Patients with Endometriosis is financed by the G4 Group (the University Hospitals of Rouen, Lille, Amiens, and Caen) and the ROUENDOMETRIOSE Association.

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Fertility and Sterility® Vol. ■, No. ■, ■ 2017 0015-0282/\$36.00

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http://dx.doi.org/10.1016/j.fertnstert.2016.12.013

VOL. ■ NO. ■ / ■ 2017

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to detect differences in pregnancy and live-birth rates between the two groups. As the majority of pregnancies were spontaneous, our results suggest that surgical management may be offered to young patients with severe endometriosis and reduced ovarian reserve with good fertility outcomes. (Fertil Steril® 2016; $\blacksquare : \blacksquare - \blacksquare$. ©2016 by American Society for Reproductive Medicine.)

Key Words: AMH, antimüllerian hormone, endometriosis, fertility, endometrioma, deep endometriosis, plasma energy

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he association between endometriosis and infertility has been routinely studied in the literature, although multiple mechanisms and accurate management of infertility are still debated (1). Infertility may be related to various events, such as distorted pelvic anatomy that impairs oocyte release or pickup, inflammatory cytokines, growth and angiogenic factors, and aberrantly expressed genes (2). Women with advanced stages of endometriosis may present with decreased ovarian reserve, low oocyte and embryo quality, and poor implantation (3). As many as 30%–50% of women with endometriosis may have various degrees of infertility (4). The spontaneous fertility rate in women with advanced stages of endometriosis can be as low as 2%–10% (5).

Endometriosis lesions may involve various organs, such as ovaries, posterior Douglas cul-de-sac, bowel, bladder, or ureters. Choosing the best treatment for endometriosis in young patients with pregnancy intention may be challenging because it should provide both a high pregnancy rate and significant improvement in pelvic complaints, as well as efficient prevention of further complications related to endometriosis spread (6). A primary surgical approach has been proposed (7) on the basis of improving spontaneous fertility in patients with advanced endometriosis (8, 9) as well as lowering the risk of various complications during pregnancy (10, 11). Furthermore, in women with deep endometriosis infiltrating the bowel, recent studies have suggested a potential fertility benefit for postoperative assisted reproductive technology (ART) results (12). However, in daily practice, surgery in advanced endometriosis is frequently refuted due to a presumed risk of complications or negative impact on ovarian reserve.

Antimüllerian hormone (AMH) is a reliable independent marker of ovarian reserve in the ovarian cycle, while oral contraception and GnRH agonists have little impact on blood level (13). AMH is produced by the granulosa cells of the ovaries and is expressed by small antral follicles (14). Levels surge at the time of puberty to approximately 5–8 ng/mL but then gradually decline throughout reproductive life until they become undetectable by menopause. Therefore, AMH levels are considered valuable indicators of ovarian reserve (15). Various studies in the literature have investigated the impact of surgical management of ovarian endometriomas on AMH level before and after surgery (16–18). However, no study has assessed the relationship between preoperative AMH level and postoperative pregnancy rate in women managed for advanced stages of endometriosis.

The aim of our retrospective study was to investigate whether surgery for severe endometriosis may be proposed in women with low ovarian reserve with good fertility outcomes. To achieve this goal, we compared postoperative pregnancy rate in women with low and normal AMH level, managed for stage 3 and 4 endometriosis.

METHODS

Women included in this present study were managed from June 2010 to May 2015 in the Department of Gynecology of Rouen University Hospital, for stage 3 and 4 endometriosis responsible for either infertility or pelvic pain. These women had either deep infiltrating endometriosis or ovarian endometriomas measuring over 3 cm (women with only superficial endometriosis and hydrosalpinx were not included). All patients had expressed pregnancy intention before surgery and benefited from pre- and postoperative assessment of AMH, with a minimum 12-month follow-up. Preoperative assessment of AMH was performed 1-12 weeks before surgery to accomplish systematic evaluation of ovarian reserve in patients with severe endometriosis and postoperative pregnancy intention. As the AMH test costs 40 Euros on average and is not reimbursed by the French Social Security, patients were able to opt out of the test. AMH assessment was performed postoperatively 2 months after the arrest of medical therapy in women with pregnancy intention to evaluate their fertility status before deciding on conception mode. Thus, it was routinely associated with FHS and LH assessment (day 3 of ovarian cycle), E2 (days 3 and 12) and P (day 23), antral follicle count, spermogram, and hysterosalpingography.

Patients were prospectively enrolled in the CIRENDO database (the North-West Inter-Regional Female Cohort for Patients with Endometriosis), a prospective cohort financed by the G4 Group (the University Hospitals of Rouen, Lille, Amiens, and Caen, France) and coordinated by the corresponding author of the present study (H.R.). Information was obtained from surgical and histological records and from self-questionnaires completed before surgery. Data recording, patient contact, and follow-up were carried out by a clinical research technician. Postoperative follow-up was based on data from the aforementioned questionnaires completed at 1, 3, and 5 years after surgery. Prospective data recording and analysis were approved by the French authorities Commission Nationale de l'Informatique et des Libertés: the French data protection commission; and Comité Consultatif pour le Traitement de l'Information en matière de Recherche dans le domaine de la Santé: the advisory committee on information technology in health care research.

Endometriomas were exclusively managed by plasma energy ablation (19). Bowel lesions were treated by shaving,

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