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 $\geq$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 $\pm$ 3.8 and 32 $\pm$ 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 ($\geq$2 ng/mL), low (1–1.99 ng/mL), and very low ($<$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

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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;■:■–■. ©2016 by American Society for Reproductive Medicine.)
Key Words: AMH, antimüllerian hormone, endometriosis, fertility, endometrioma, deep endometriosis, plasma energy

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The 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), E_2 (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,

disc excision, or segmental resection. Urinary tract lesions were managed by resection of bladder, advanced ureterolysis requiring JJ stent, ureteral resection followed by end-to-end anastomosis, or ureterocystostomy. All the procedures were fully recorded in mpeg format.

Patients were enrolled in two groups according to preoperative AMH level: women with AMH $\geq$ 2 ng/mL were assigned to group A, and those with AMH $<$ 2 ng/mL to group B. We recorded the time from surgery to first pregnancy as well as pregnancy outcomes: delivery, miscarriage, ectopic pregnancy, or on-going pregnancies of over 12 weeks' gestation. For each pregnancy we recorded conception mode: spontaneous or with ART.

Statistical analysis was performed using Stata 11.0 software (StataCorpLP). Univariate analysis compared characteristics, clinical history, baseline complaints, intraoperative data, and postoperative outcomes of women enrolled in the two groups. Fisher's exact test was used to compare qualitative variables, and Student's *t*-test and Mann-Whitney tests were used to compare continuous variables. Kaplan-Meier curves were built to estimate the probability of nonpregnancy according to postoperative time and were compared using the log-rank test. Cox's model was used to estimate independent hazard ratios for the probability of live births according to various variables. $P<.05$ was considered statistically significant.

Supplementary analysis was performed after dividing women with AMH $<$ 2 ng/mL in two groups: low AMH (1–1.99 ng/mL) and very low AMH level ($<$1 ng/mL). The study was approved by the Institutional Review Board.

RESULTS

The CIRENDO database was searched for postoperative pregnancy intention and AFRs score $>$15 and resulted in a series of 397 consecutive women. After thorough review of recorded data and surgical reports, 184 (46.3%) and 13 (3.3%) women, respectively, were excluded because their pre- and postoperative AMH levels were either not assessed or not available and because of hydrosalpinx and absence of deep endometriosis or endometrioma measuring more than 3 cm. In addition, 20 women were lost to follow-up (5%) because they had changed address, phone number, or e-mail address.

Thus, 180 patients were definitively enrolled in the study: 134 women (74.5%) in group A (normal AMH level) and 46 women (25.5%) in group B (low AMH level; Supplemental Fig. 1). Preoperative AMH level was 4.3 $\pm$ 2.1 ng/mL in group A versus 1 $\pm$ 0.5 ng/mL in group B ($P<.001$). After surgery, postoperative AMH levels were, respectively, 3.4 $\pm$ 2.5 ng/mL and 1.2 $\pm$ 0.9 ng/mL ($P=.001$).

Table 1 presents patient characteristics, medical history, obstetrical antecedents, and related pain symptoms, such as dysmenorrhea, dyspareunia, and digestive complaints. Among these 180 women, 135 (75.4%) had been attempting pregnancy for more than 1 year before surgery: 99 (74.4%) in group A and 36 (78.2%) in group B ($P=.38$).

Table 2 presents intraoperative findings: operative time, operative route, American Fertility Society revised score, main surgical procedures, and fertility outcomes. Ovarian endometrioma ablation using plasma energy was performed in 145 patients (80.6%). Pregnancy was achieved by 134 (74.4%) patients, and conception was spontaneous in 74 of them (55.2%). The rate of pregnancy in groups A and B was, respectively, 74.6% (100 patients) and 73.9% (34 women; $P=.52$), while spontaneous conception represented 54% (54 women) and 58.8% (20 women; $P=.17$). These values were comparable to the pregnancy rate observed in 184 women recorded in the database and excluded due to the lack of AMH assessment (129 pregnancies, 70.1%; $P=.65$).

Pregnancy rates in women with normal and low AMH level were, respectively, 74.6% and 73.9%, resulting in a difference of 0.7%, with a 95% confidence interval [CI] of $-$14%; 15.4%. Delivery rates in women with normal and low AMH were, respectively, 72% and 73.5%, with a 95% CI of the difference of $-$16%; 13%.

Kaplan-Meier curves of the probability of pregnancy were close during the whole period of follow-up, thus their comparison did not reach statistical significance (Fig. 1). The probability of pregnancy at 12, 24, and 36 months after surgery in groups A and B was, respectively, 65% (95% 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%; $P=.19$).

The results of multivariate analysis using Cox's model are presented in Table 3. Independent impact of preoperative AMH level on the probability of live birth was not statistically significant after adjustment for several variables with clinical interest: women's age, antecedents of ovarian cystectomy, ablation of ovarian endometriomas, documented preoperative infertility, and colorectal surgery for endometriosis.

Supplemental Tables 1 and 2 present comparisons of women with normal, low, and very low AMH levels. There was a significantly inverse relationship between AMH level and women's age or antecedents of miscarriage. Patients with very low AMH could have presented with more severe disease, as the operative time and their rate of transitory colostoma were significantly higher. In addition, there was a tendency towards more frequent use of colorectal resection in women with very low AMH. However, the pregnancy rate was not statistically different among the three groups of women, nor was the probability of pregnancy 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%).

DISCUSSION

To our knowledge, this is the first study to assess the postoperative pregnancy rate in patients managed for stage 3 and 4 endometriosis based on preoperative AMH level. Our study demonstrated that preoperative AMH level did not significantly impact the probability of postoperative pregnancy rate when spontaneous conception and conception after ART were considered together. Even though our study was

TABLE 1

Patient characteristics, medical history, and major pain symptoms related to endometriosis in women with normal and low AMH level.

Variable	Whole sample (n = 180)	AMH ≥ 2 ng/mL (n = 134)	AMH < 2 ng/mL (n = 46)	*P*
Patient antecedents				
Age, y	30.5 ± 4.1	30 ± 3.8	32 ± 4.6	.004
Antecedents of gynecological surgery	83 (46.6)	59 (44.3)	24 (53.3)	.19
Justification for previous surgeries				
Pelvic pain	51 (28.3)	38 (28.4)	13 (28.3)	.57
Infertility	19 (10.6)	12 (9)	7 (15.2)	.18
Ovarian cysts	10 (5.6)	6 (4.5)	4 (8.7)	.23
Endometriosis	43 (24)	32 (23.9)	11 (24.4)	.54
Other reasons	57 (31.7)	46 (34.3)	11 (23.9)	.2
Cystectomy				
Right ovary	22 (12.2)	15 (11.2)	7 (15.9)	.6
Left ovary	38 (21.3)	30 (22.4)	8 (18.2)	.6
Oophorectomy	1 (0.6)	0	1 (2.2)	.25
Adhesiolysis	16 (8.9)	12 (9)	4 (8.7)	.63
Right salpingectomy	3 (1.7)	2 (1.5)	1 (2.2)	.58
Left salpingectomy	4 (2.2)	2 (1.5)	2 (4.4)	.26
More than 12 mo of unsuccessful spontaneous conception	135 (75.4)	99 (74.4)	36 (78.2)	.38
Obstetrical antecedents				
Pregnancy	60 (33.3)	42 (31.3)	18 (39.1)	.21
Miscarriage	20 (11)	9 (6.7)	11 (23.9)	.005
Vaginal delivery	18 (10)	14 (10.4)	4 (8.6)	1
Cesarean section	12 (7.1)	10 (7.4)	2 (4.3)	.73
Ectopic pregnancies	6 (3.5)	5 (3.7)	1 (2.2)	1
Voluntary pregnancy interruption	4 (2.2)	4 (3)	0	.6
Principal pain symptoms related to pelvic endometriosis				
Dysmenorrhea	178 (98.9)	134 (100)	44 (95.6)	.06
Biberoglou and Behrman dysmenorrhea score	1.9 ± 0.74	1.9 ± 0.73	1.65 ± 0.7	.008
Intensity of dysmenorrhea (VAS score)	8.1 ± 1.7	8.1 ± 1.5	7.8 ± 1.9	.45
Cyclic symptoms associated with dysmenorrhea				
Defecation pain	110 (61.1)	90 (67.2)	20 (43.5)	.004
Rectorrhagia	23 (12.8)	16 (12)	7 (15.2)	.37
Constipation	72 (40.2)	56 (42.1)	16 (34.8)	.24
Diarrhea	84 (46.9)	66 (49.6)	18 (39.1)	.14
Bloating	88 (49.1)	59 (44.4)	29 (63)	.02
Having had sexual intercourse during the last 12 mo	161 (94.1)	121 (93.8)	40 (95.2)	.54
Deep dyspareunia	130 (73.6)	100 (74.6)	30 (66.7)	.47
Biberoglou and Behrman deep dyspareunia score	1.2 ± 1.1	1.2 ± 1.1	1 ± 1.1	.25
Intensity of dyspareunia (VAS score)	4.9 ± 2.1	5 ± 2.2	4.7 ± 2.1	.48

Note: Values presented as mean ± SD or n (%), unless stated otherwise. VAS = visual analog scale.

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unable to reach the high level of evidence specific to randomized trials, it provides convincing arguments to support the use of surgery in young patients with severe symptomatic endometriosis and pregnancy intention who have a preoperative AMH level below the inferior threshold of normal values.

The main strength of our study was the prospective collection of data and careful follow-up performed by a dedicated clinical researcher, leading to a low rate of patients lost to follow-up. Furthermore, the fact that surgery was performed in a single expert center represents a major strength as it allows reliable measurement of the impact of surgical management when guided by special care to preserve fertility. Another strength of our study was its undivided focus on severe forms of the disease, mainly involving women in whom surgeons might postpone surgery owing to fear of a potential negative impact of extended surgery on the patient's fertility.

Nonetheless, our study has several weaknesses. The retrospective design reduces the level of evidence of our data. Preoperative assessment of AMH level was not performed in all patients, as some women opted out of the AMH test due to its cost and others did not fully understand the reason for performing the test. Thus, women with no further pregnancy intention were likely not to accept the cost of the test. In other patients the results were either missing or had not been recorded in their medical chart. In some women, low and very low preoperative AMH levels could have impacted their postoperative pregnancy intention; hence they might have stopped their postoperative medical treatment and were thus missing from our study. However, it is our opinion that their number may be rather small, with little impact on our results. Another limitation of our study is related to the small number of patients with low preoperative AMH values, resulting in a large 95% CI and low statistical power to detect differences between the two

TABLE 2

Intraoperative findings and fertility outcomes in women with normal and low AMH level.

Variable	Whole sample (n = 180)	AMH ≥ 2 ng/mL (n = 134)	AMH < 2 ng/mL (n = 46)	*P*
Intraoperative findings				
Operative time, min	182.3 ± 106.2	179.6 ± 100.7	189.3 ± 121.8	.59
Operative route				.72
Open surgery	0	0	0	
Laparoscopy	170 (94.4)	125 (93.3)	45 (97.8)	
Robotic assistance	4 (2.2)	4 (3)	0	
Laparoscopy followed by open route	6 (3.3)	5 (3.7)	1 (2.17)	
American Fertility Society revised score	67.8 ± 41.9	68.8 ± 42.9	68 ± 39.3	.98
Douglas pouch complete obliteration	86 (48.6)	64 (48.9)	22 (48.9)	.97
Ablation of ovarian endometriomas	145 (80.6)	108 (80.6)	37 (80.4)	.57
Adhesiolysis of adnexae	162 (91)	122 (92.4)	40 (87)	.2
Surgical procedures on digestive tract				
Rectal shaving	51 (28.3)	39 (29.1)	12 (26.1)	.42
Rectal disc excision	22 (12.2)	17 (12.7)	5 (10.9)	.49
Colorectal segmental resection	40 (22.2)	29 (21.6)	11 (23.9)	.45
Isolated sigmoid colon disc excision	4 (2.2)	4 (3)	0	.30
Isolated sigmoid colon resection	13 (7.2)	9 (6.7)	4 (8.7)	.43
Transverse colon disc excision	1 (0.6)	1 (0.7)	0	.74
Cecum resection	5 (2.8)	3 (2.2)	2 (4.3)	.38
Appendectomy	11 (6.1)	6 (4.5)	5 (10.9)	.12
Resection of small bowel	3 (1.7)	2 (1.5)	1 (2.2)	.6
Transitory stoma	28 (15.6)	21 (15.7)	7 (15.2)	.57
Surgical procedures on urinary tract				
Resection of the bladder	6 (3.3)	6 (4.5)	0	.16
Advanced ureterolysis requiring JJ stent	13 (7.2)	9 (6.7)	4 (8.7)	.43
Ureteral resection and ureterocystostomy	3 (1.7)	2 (1.5)	1 (2.2)	.59
Fertility outcomes				
Pregnant women	134 (74.4)	100 (74.6)	34 (73.9)	.53
Pregnancy evolution				.18
On-going pregnancy, > 12 wk	25 (18.6)	21 (21)	4 (11.8)	
Delivery	97 (72.4)	72 (72)	25 (73.5)	
Miscarriage	11 (8.2)	7 (7)	4 (11.8)	
Ectopic pregnancy	1 (0.7)	0	1 (2.9)	
Conception modality (n = 134)				.39
ART	60 (44.8)	46 (46)	14 (41.2)	
Spontaneous pregnancy	74 (55.2)	54 (54)	20 (58.8)	
Delayed surgery/conception, mo	19 ± 23.6	17.1 ± 19.1	24.4 ± 32.9	.15
Preoperative AMH, ng/mL	3.4 ± 2.3	4.3 ± 2.1	1 ± 0.5	< .001
Postoperative AMH, ng/mL	2.8 ± 2.4	3.4 ± 2.5	1.2 ± 0.9	.001

Note: Values presented as mean ± SD or n (%), unless stated otherwise.

Stochino-Loi. Preoperative AMH in severe endometriosis. Fertil Steril 2016.

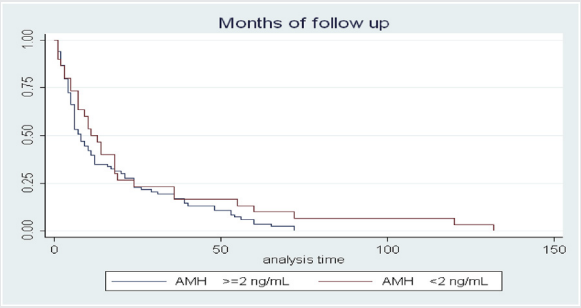
groups. The 95% CI of the hazard ratio suggests that increasing the sample size may have led to the decrease in the live-birth rate in the low AMH group, down to 60% of that observed in the normal AMH group.

Our statistical analysis employed the Cox model as live birth is a time-dependent variable. Thus, the model estimated the effect of several variables upon the time delay for live birth to occur. When compared with the logistic regression model, Cox's model is a more accurate statistical tool because estimation of the probability of live birth takes into account right censored data represented by women who accomplished a follow-up period without achieving a live birth. AMH level was used as a categorical dummy variable instead of a continuous variable to estimate distinct probabilities of live birth for each category: normal, low, and very low AMH level.

Different studies have shown that low AMH level is associated with a reduction in pregnancy rate in ART (20–22). More specifically, low AMH values were associated with poor response of ovaries to hyperstimulation, resulting in lower rates of pregnancies after ART (14, 23, 24). Conversely, it appears that the relationship of AMH level and spontaneous conception rate is disputable, as women with low AMH attained satisfactory spontaneous pregnancy rates (25, 26). These latter results have led us to believe that in women with low AMH, restoring the capacity of spontaneous conception may be an interesting alternative to primary ART (7).

Recent guidelines do not recommend surgery for deep infiltrating endometriosis in infertile women with the single aim of improving ART results (1). However, data in the literature suggest that surgery for deep infiltrating endometriosis may enhance spontaneous conception, as 25%–35% of infertile women could become pregnant after surgery (7). It is our belief that surgical management should not be definitively contraindicated in women with low AMH levels, as spontaneous conception could compensate for the poor response to hyperstimulation for IVF. Despite the opposing opinions of numerous colleagues, there are no existing guidelines or

FIGURE 1



Kaplan-Meier curves presenting the probability of postoperative pregnancy in women with normal (group A, *red line*) and low AMH (group B, *blue line*).

Stochino-Loi. Preoperative AMH in severe endometriosis. Fertil Steril 2016.

consistent evidence to support the mandatory referral of women with pregnancy intention to ART instead of surgery, especially when the surgeon takes special care to preserve fertility (7).

The potential negative impact of surgery for ovarian endometriomas on ovarian reserve has been demonstrated (1). As far back as 2009, our team reported data on ovarian tissue loss after cystectomy (27) and definitively introduced a new ablative technique using plasma energy, with the single aim of preserving fertility (19). Hence, we are aware of the risk of impairing ovarian reserve in patients managed for ovarian endometrioma, regardless of their preoperative AMH level. Even though ablation using plasma energy is followed by a temporary decrease in AMH level (17), pregnancy rates in our various studies were rather high, and most of them resulted in spontaneous conception (17, 19, 28). These observations led to the present study, in which we attempted to estimate whether performing surgery in women with low and very low AMH might or might not impair their postoperative fertility, when compared with women with normal AMH level. Despite postoperative changes occurring in AMH level, the pregnancy rate observed in our series was satisfactory and independent of preoperative AMH level.

One may wonder whether our high postoperative pregnancy rate could be explained by the inclusion of only 75% of presumed infertile women. Nevertheless, even though one in four women had not attempted to conceive before surgery, it was likely that their fertility might have been negatively impacted by endometriosis. Despite little attempt to conceive preoperatively, a diagnosis of deep endometriosis and its strong relationship with infertility risk could prompt a woman's decision to expedite conception and pregnancy. Indeed, the probability of spontaneous pregnancy was low in these women with stage 3 or 4 endometriosis and either deep localizations or endometriomas measuring over 3 cm, as well as digestive tract involvement and Douglas pouch obliteration recorded in more than 70% and 49% of cases, respectively. Among women with no presumed infertility were young patients who had been attempting to conceive for less than 1 year and who were referred to our department owing to complaints related to pain. When these young patients are referred to other facilities, they are automatically scheduled for primary IVF and are thus indirectly recorded as infertile. It is therefore likely that the rates of infertile women are underestimated in series of patients managed by primary surgery when compared with those receiving primary ART (19).

Our results suggest that overall postoperative pregnancy rate is not closely associated with preoperative AMH level in women managed for stage 3 and 4 endometriosis and

TABLE 3

Estimation of the probability of the rate of live births (Cox's multivariate model).

Risk factor	n (%)	Live births (%)	HR	HR 95% CI	*P*
AMH level, ng/mL					.95
≥2	134 (74.4)	72 (53.7)	1		
<2	46 (25.6)	25 (54.3)	0.98	0.6–1.5	
Age, y					.94
<38	167 (92.8)	91 (54.5)	1		
≥38	13 (7.2)	6 (46.1)	1.03	0.4–2.5	
Antecedent of ovarian cystectomy					.87
No	143 (79.4)	21 (60)	1		
Yes	37 (20.6)	76 (52.4)	0.96	0.6–1.6	
Antecedent of infertility					.84
No	45 (25)	27 (60)	1		
Yes	135 (75)	70 (51.8)	0.95	0.6–1.53	
Ablation of ovarian endometriomas					.83
No	35 (19.4)	76 (53.15)	1		
Yes	145 (80.6)	21 (56.8)	1.05	0.6–1.8	
Colorectal surgery					.88
No	66 (36.7)	39 (59.1)	1		
Yes	114 (63.3)	58 (50.9)	1.03	0.7–1.6	

Note: HR = hazard ratio.

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with a mean age of 30 years. As three in four women achieved pregnancy after surgery, either spontaneously or after ART, surgical management of severe endometriosis in young women with low ovarian reserve appears to be followed by good fertility outcomes.

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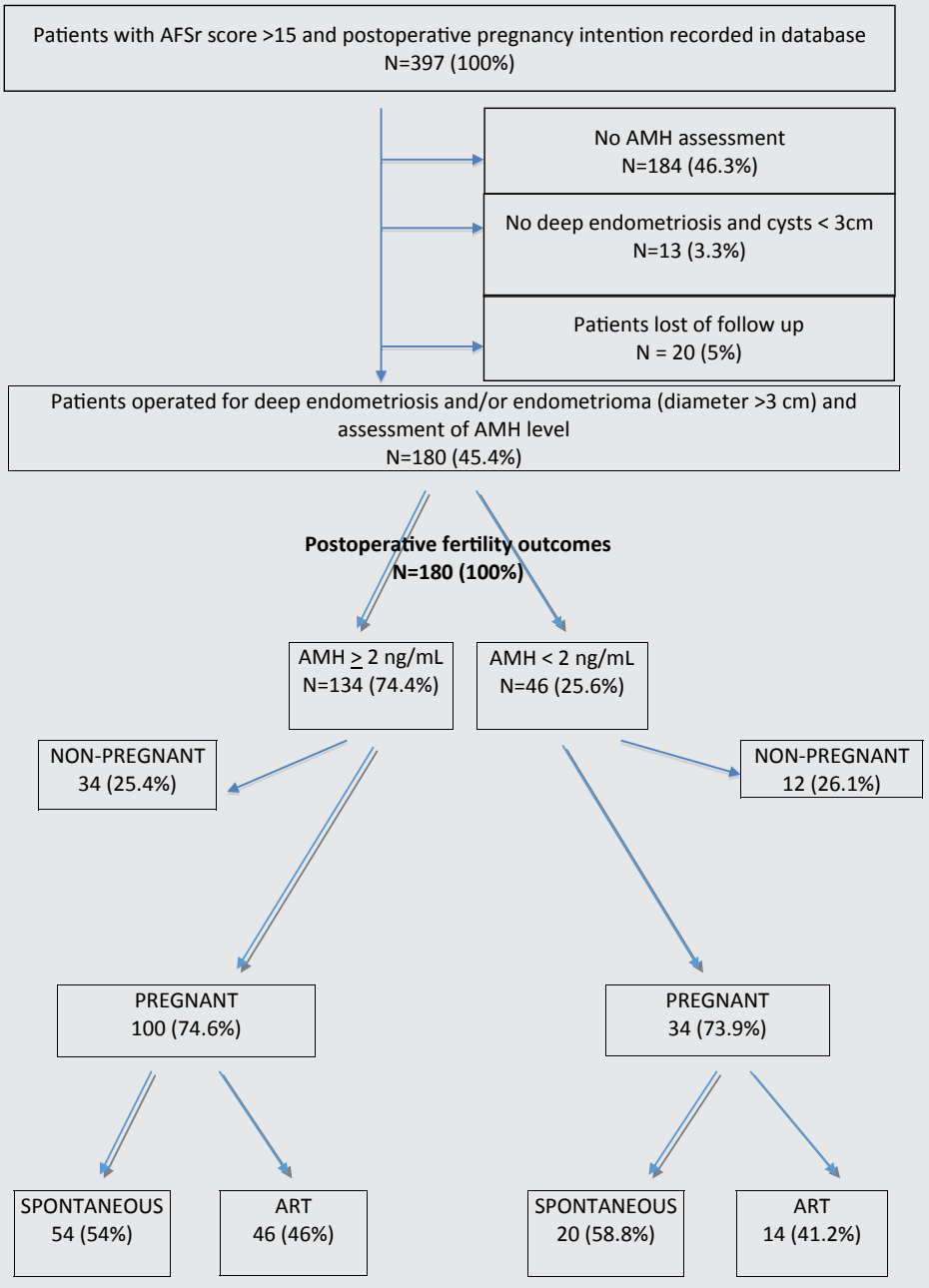
SUPPLEMENTAL FIGURE 1



Study flow chart.

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SUPPLEMENTAL TABLE 1

Patient antecedents and principal pain symptoms related to pelvic endometriosis in women with normal, low, and very low AMH level.

Variable	Whole sample (n = 180)	AMH ≥ 2 ng/mL (n = 134)	AMH 1–1.9 ng/mL (n = 24)	AMH < 1 ng/mL (n = 22)	*P*
Patient antecedents					
Age, y	30.5 ± 4.1	30 ± 3.8	31.2 ± 3.6	33.3 ± 5.14	.001
Antecedents of gynecological surgery	83 (46.6)	60 (45.1)	9 (39.1)	14 (63.6)	.20
Justification for previous surgeries					
Pelvic pain	51 (28.3)	38 (28.4)	6 (25)	7 (31.8)	.88
Infertility	19 (10.6)	11 (8.2)	3 (12.5)	5 (22.7)	.11
Ovarian cysts	10 (5.6)	7 (5.2)	1 (4.2)	2 (9.1)	.73
Endometriosis	43 (24)	32 (23.9)	6 (25)	5 (23.8)	.99
Other reasons	57 (31.7)	46 (34.3)	8 (33.3)	3 (13.6)	.15
Cystectomy					
Right ovary	23 (12.9)	15 (11.2)	7 (31.8)	1 (4.5)	.013
Left ovary	38 (21.3)	30 (22.4)	3 (13.6)	5 (22.7)	.64
Oophorectomy	1 (0.6)	0	0	1 (4.8)	.02
Adhesiolysis	16 (8.9)	12 (9)	4 (16.7)	0	.15
Right salpingectomy	3 (1.7)	2 (1.5)	0	1 (4.8)	.44
Left salpingectomy	4 (2.2)	2 (1.5)	1 (4.2)	1 (4.7)	.50
>12 mo of unsuccessful spontaneous conception	135 (75.4)	100 (75.2)	18 (75)	17 (77.3)	.98
Obstetrical antecedents					
Pregnancy	60 (33.3)	42 (31.3)	10 (41.6)	8 (36.3)	.56
Miscarriage	20 (11)	9 (6.7)	6 (25)	5 (22.7)	.005
Vaginal delivery	18 (10)	14 (10.4)	3 (12.5)	1 (4.5)	.7
Caesarean section	12 (7.1)	10 (7.4)	1 (4.2)	1 (4.5)	1
Ectopic pregnancies	6 (3.5)	5 (3.7)	0	1 (4.5)	.8
Voluntary pregnancy interruption	4 (2.2)	4 (3)	0	0	1
Principal pain symptoms related to pelvic endometriosis					
Dysmenorrhea	178 (98.9)	134 (100)	22 (91.7)	22 (100)	.001
Biberoglou and Behrman dysmenorrhea score	1.9 ± 0.74	1.9 ± 0.7	1.6 ± 0.7	1.7 ± 0.6	.01
Intensity of dysmenorrhea (VAS score)	8.06 ± 1.6	8.1 ± 1.5	7.7 ± 2.2	7.9 ± 1.5	.51
Cyclic symptoms associated with dysmenorrhea					
Defecation pain	110 (61.1)	89 (66.4)	15 (62.5)	6 (27.3)	.002
Rectorrhagie	23 (12.8)	16 (12)	3 (12.5)	4 (18.2)	.73
Constipation	72 (40.2)	56 (42 .1)	7 (29.2)	9 (40.9)	.49
Diarrhea	84 (46.9)	67 (50.4)	8 (33.3)	9 (40.9)	.25
Bloating	88 (49.2)	60 (45.1)	14 (58.3)	14 (63.6)	.17
Having had sexual intercourse during the last 12 mo	161 (94.1)	120 (93.7)	20 (95.2)	21 (95.4)	.93
Deep dyspareunia	130 (72.6)	102 (76.1)	15 (65.2)	13 (59.1)	.26
Biberoglou and Behrman deep dyspareunia score	1.18 ± 1.11	1.2 ± 1.11	1.04 ± 1.1	0.9 ± 1.1	.33
Intensity of dyspareunia (VAS score)	4.9 ± 2.2.1	5 ± 2.2	4.7 ± 2.08	4 ± 2	.26

Note: Values presented as mean ± SD or n (%), unless stated otherwise. VAS = visual analog scale.

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SUPPLEMENTAL TABLE 2

Intraoperative findings and fertility outcomes in women with normal, low, and very low AMH level.

Variable	Whole sample (n = 180)	AMH ≥ 2 ng/mL (n = 134)	AMH 1–1.9 ng/mL (n = 24)	AMH < 1 ng/mL (n = 22)	*P*
Intraoperative findings					
Operative time, min	182 ± 106.2	179 ± 100	140.6 ± 82.4	242 ± 137.6	.004
Operative route					.66
Open surgery	0	0	0	0	
Laparoscopy	170 (94.4)	125 (93.3)	24 (100)	21 (95.4)	
Robotic assistance	4 (2.2)	4 (3)	0	0	
Laparoscopy followed by open route	6 (3.3)	5 (3.7)	0	1 (4.5)	
American Fertility Society revised score	67.8 ± 41.9	68.8 ± 42.9	61 ± 41.2	77.7 ± 39.8	.39
Douglas pouch complete obliteration	86 (48.6)	64 (48.5)	10 (41.7)	12 (57.1)	.08
Ablation of ovarian endometriomas	145 (80.6)	108 (80.6)	19 (79.2)	18 (81.8)	.97
Adhesiolysis of adnexae	163 (91)	122 (91)	20 (83.3)	21 (95.5)	.14
Surgical procedures on digestive tract					
Rectal shaving	51 (28.3)	40 (29.8)	5 (20.8)	6 (27.3)	.66
Rectal disc excision	22 (12.2)	17 (12.7)	2 (8.3)	3 (13.6)	.81
Colorectal segmental resection	40 (22.2)	29 (12.6)	3 (12 .5)	8 (36.4)	.14
Isolated sigmoid colon disc excision	4 (2.2)	4 (3)	0	0	.49
Isolated sigmoid colon resection	13 (7.2)	8 (6)	3 (12.5)	2 (9)	.49
Transverse colon disc excision	1 (0.6)	1 (0.7)	0	0	.84
Cecum resection	5 (2.8)	3 (2.2)	0	2 (9)	.13
Appendectomy	11 (6.1)	6 (4.5)	3 (12.5)	2 (9)	.26
Resection of small bowel	3 (1.7)	2 (1.5)	1 (4.2)	0	.51
Transitory stoma	28 (15.6)	21 (15.7)	0	7 (31.8)	.012
Surgical procedures on urinary tract					
Resection of the bladder	6 (3.3)	6 (4.5)	0	0	.34
Advanced ureterolysis requiring JJ stent	13 (7.22)	8 (6)	2 (8.3)	3 (13.6)	.42
Ureteral resection and ureterocystostomy	3 (1.7)	2 (1.5)	0	1 (4.5)	.46
Fertility outcomes					
Pregnant women	134 (74.4)	100 (74.6)	19 (79.2)	15 (68.2)	.69
Pregnancy evolution					.07
Ongoing pregnancy > 12 wk	25 (18.6)	21 (21)	4 (21)	0	
Delivery	97 (72.4)	71 (72)	13 (68.4)	13 (86.7)	
Miscarriage	11 (8.2)	8 (8)	2 (10.5)	1 (6.7)	
Ectopic pregnancy	1 (0.7)	0	1 (4.2)	0	
Conception modality (n = 134)					.63
ART	60 (44.8)	46 (46)	9 (47.4)	5 (33.3)	
Spontaneous pregnancy	74 (55.2)	54 (54)	10 (52.6)	10 (66.7)	
Delayed surgery/ conception, mo	19 ± 23.6	17.1 ± 19.1	22.3 ± 33.4	26.9 ± 34.4	.29
Preoperative AMH, ng/mL	3.4 ± 2.3	4.3 ± 2.1	1.5 ± 0.30	0.5 ± 0.2	0
Postoperative AMH, ng/mL	2.8 ± 2.4	3.4 ± 2.4	1.35 ± 0.9	0.8 ± 0.9	0

Note: Values presented as mean ± SD or n (%), unless stated otherwise.

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