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Preoperative serum anti-Müllerian hormone level is a potential predictor of ovarian endometrioma severity and postoperative fertility

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ABSTRACT

Objective: To establish a model for predicting revised American Society of Reproductive Medicine (rASRM) scores before endometrioma surgery based on serum anti-Müllerian hormone (AMH) level and to identify factors that might reliably predict postoperative fertility of women diagnosed with endometrioma.
Study design: The study population was composed of 134 women with endometrioma, 58 with benign cyst, and 115 with non-ovarian lesion. Preoperative serum AMH level and clinical parameters were compared among three groups. Univariate correlation analyses and multivariate linear regression modeling with a stepwise method were performed for constructing an rASRM scores prediction model. Cox regression analysis was then used to identify predictive variables of spontaneous pregnancy following surgical treatment of endometrioma.
Results: Preoperative AMH level were significantly lower in the endometrioma group than in the other two groups ($p < 0.001$). Multivariate linear regression analysis revealed that age (β=-0.324, $p < 0.001$), rASRM scores (β=-0.298, $p < 0.001$) and serum CA125 level (β=-0.176, $p = 0.026$) independently and negatively correlated with serum AMH level. Cox regression analysis of women with endometrioma who underwent surgical resection indicated that older age (per five-year increase, HR: 0.517; 95% CI, 0.299–0.896) and higher serum AMH level (cut-off value: >3.68 ng/ml, HR: 2.383; 95% CI, 1.093–5.197) were independent predictors for postoperative fertility.
Conclusion: Patients with advanced staged endometriosis tended to have a lower serum AMH level while postoperative infertility was more likely to occur in older patients with a lower level of serum AMH. Thus, timely detection of AMH levels to assess the severity of ovarian endometriosis and possibility for postoperative pregnancy success is necessary to ensure that optimal medical treatment can be provided.

Introduction

Endometriosis is a gynecological disease characterized by development of endometrial tissue outside of the uterus that causes pain and infertility [1]. It is a relatively common condition that affects many women of reproductive age. Owing to the variability in clinical presentation and the fact that the only reliable diagnostic test is laparoscopy, the prevalence of endometriosis is difficult to determine. Population based studies report a prevalence of around 1.5% compared with 6–15% in hospital-based studies [2]. And the prevalence is even as high as 40% in subfertile women [3]. Endometriosis can extend to the ovaries, forming cysts or endometriomas. By space-occupying effects, local reactions, or both, these cysts can reduce the amount of functional ovarian tissue, which can be aggravated further by surgery [4]. An estimated 25–50% of women with infertility have endometriosis, and approximately 30–50% of women with endometriosis have infertility [5]. However, studies on the effects of endometriosis on ovarian reserve remain limited, even though assessing ovarian reserve is an important issue in infertility [6,7].

In recent years, laparoscopy has become the gold standard for the treatment of ovarian endometriotic cysts [8] and revised American Society of Reproductive Medicine (rASRM) scores is

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widely used to classify the severity of endometriosis postoperatively around the world [9]. However, prospective clinical studies confirm that surgery for endometriomas reduces ovarian reserve, particularly in women with bilateral disease, which has an adverse effect on fertility [10]. Moreover, clinical examination cannot provide a definitive diagnosis of endometriosis before surgery. While over 100 putative biomarkers for endometriosis have been proposed, a systematic review found that none are consistently clinically useful, and biomarkers such as cancer antigen 125 (CA125) lack specificity [11]. The endometrioma, when transvaginal ultrasonography [12] and magnetic resonance imaging (MRI) [13] can reliably be used to identify the disease, is an advanced stage when fertility is already impaired. Thus, for patients with indication of surgical intervention, given the high recurrence rates following endometrioma excision and the unequivocal detrimental effects of repeated surgeries on ovarian reserve, valid biomarkers that can predict the severity of ovarian endometrioma before surgery are needed for clinical reference, especially for patients whose fertility has been impaired by ovarian cysts, and for whom subsequent surgery may lead to permanent sterility and early menopause.

Serum anti-Müllerian hormone (AMH) has been identified as a typical hormone of reproductive age [14]. The levels of AMH are independent of the menstrual cycle and are not affected by the use of gonadotropin-releasing hormone (GnRH) agonists or oral contraceptives. It can also reflect the number of preantral follicles that comprise the oocyte pool. Therefore, measurement of serum AMH has been widely used to assess ovarian reserve and is currently measured frequently during the initial work-up for infertility [15–17]. Recently, AMH has been used in initial fertility work up and follow up studies on ovarian damage due to chemotherapy, ovarian surgery of diseases like endometrioma [18].

For this study, we attempted to establish a forecasting model for predicting rASRM scores before surgery based on serum AMH level and to identify factors that might reliably predict postoperative fertility for women diagnosed with endometrioma.

Materials and methods

Study population

We assessed a total of 307 patients undergoing surgery for adnexal mass in Fujian Provincial Maternity and Children's Hospital, Affiliated Hospital of Fujian Medical University, from January 2016 and January 2017 (Fig. 1). Imaging findings of adnexal mass with exclusion of ectopic pregnancy were primary reasons of admission for all patients. Ultrasound or MRI was performed on the patients upon admission. A decision to perform a surgery was made after careful evaluation and mainly in the following cases: (1) the diameter of ovarian endometrioma or adnexal mass ≥4 cm lasting for more than two menstrual periods; (2) complicated with infertility (male factors were evaluated by semen analysis and had been excluded); (3) severe dysmenorrhea with ineffective drug treatment.

The main study population comprised three groups based on pathologic confirmation after surgery: patients who were diagnosed with ovarian endometrioma; patients who had other benign ovarian cysts (teratoma, serous cystadenoma, mucinous cystadenoma, etc.); and patients who were diagnosed with non-ovarian lesions (uterine leiomyoma, tubal lesions, etc.). The inclusion criteria were: 25–40 years of age, with normal menstrual period and regular menstrual cycle. Exclusion criteria were the following: 1) premature ovarian failure, 2) confirmed polycystic ovary syndrome, 3) previous history of pelvic surgery, 4) endocrine disorder such as hyperprolactinemia or thyroid dysfunction, 5)

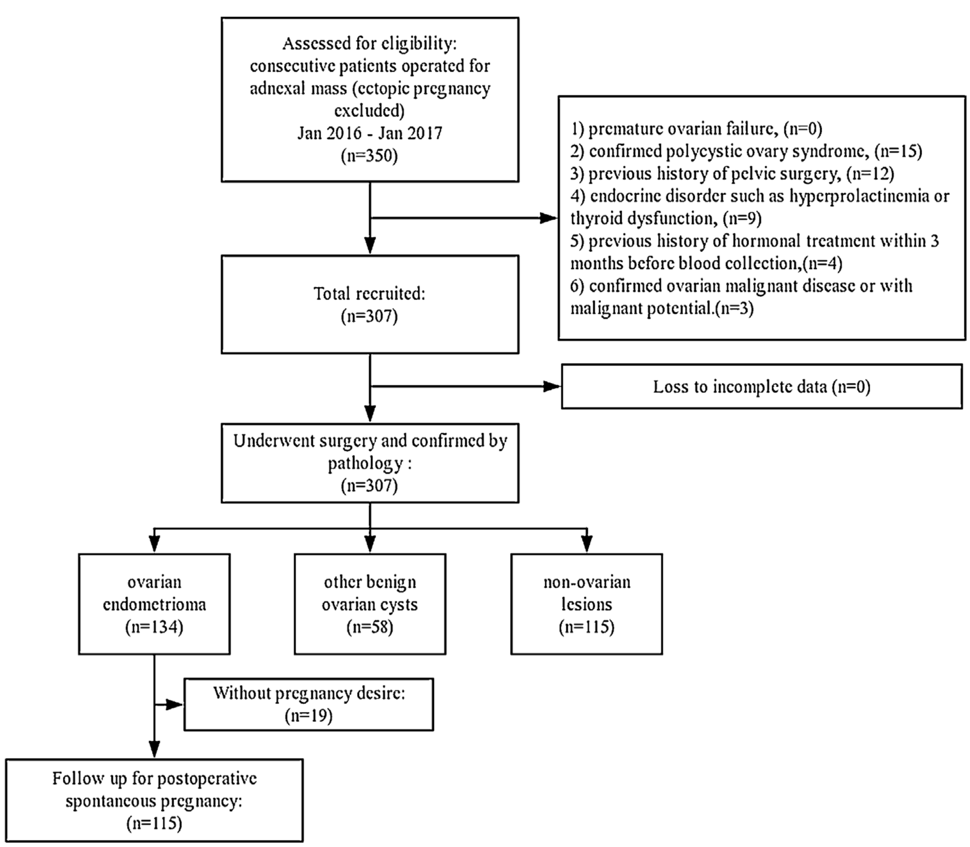

Fig. 1. Flow chart of the patients included.

previous history of hormonal treatment within 3 months before blood collection, 6) confirmed ovarian malignant disease or with malignant potential.

Surgeries were performed by two experienced surgeons (Xi XIie, Pengming SUN) and all the patients underwent complete surgical exploration for resection of endometrioma, other benign ovarian cysts and intraligamentous myoma, as well as for tubal plastic surgery or tubal resection. For surgeries in the group of women with endometrioma, cystectomies were performed with attempts of complete resection of all endometriosis lesions and restoration of normal pelvic anatomy. Among all patients with ovarian endometrioma, the rASRM scores and stage of endometriosis (stage I, II, III, or IV) were determined after surgery.

The present study was approved by the Research Ethics Committee of Fujian Provincial Maternity and Children Hospital, Affiliated Hospital of Fujian Medical University (NO. 2016038). All participants provided written informed consent for data collection.

Clinical and biochemical assessment

Demographic and clinical data were collected for all subjects including detailed medical history and body mass index (BMI)

Table 1
Baseline characteristics in patients with ovarian endometrioma, compared to those with other benign ovarian cyst and non-ovarian lesion.

	Ovarian endometrioma(n = 134)	Other benign cyst(n = 58)	Non-ovarian lesion(n = 115)	p
Age(year)	31.69 ± 4.11	30.66 ± 4.54	31.57 ± 4.72	0.325[a]
Menarche time(year)	14.13 ± 2.2	14.05 ± 1.46	14.22 ± 1.34	0.893[a]
Menstural cycle(day)	29.69 ± 2.49	30.33 ± 4.45	30.25 ± 3.42	0.303[a]
Menstrual period(day)	6.36 ± 1.90	6.09 ± 1.34	6.11 ± 1.41	0.398[a]
Gravidity	0.95 ± 1.22	1.36 ± 1.46	/	0.044[a]
Parity	0.37 ± 0.54	0.5 ± 0.78	/	0.235[a]
Infertility(%)	51(38.1%)	8(13.8%)	/	<0.001[b]
Primary infertility	34(25.4%)	5(8.6%)	/	
Secondary infertility	17(12.7%)	3(5.2%)	/	
Duration of infertility (year)	3.22 ± 2.72	1.25 ± 0.5	/	<0.001[c]
Dysmenorrhea(%)	83(61.9%)	6(10.3%)	/	<0.001[b]
Complicated with adenomyosis(%)	47(35.1%)	5(8.6%)	/	<0.001[b]
Diameter of cyst(cm)				
Total diameter	6.11 ± 3.40	5.66 ± 2.81	/	0.380[c]
Smaller than 4cm	3.04 ± 1.18	2.56 ± 0.97	/	
Greater than or equal to 4 cm	7.51 ± 3.15	6.79 ± 2.40	/	
With bilateral cysts	76(56.7%)	50(86.2%)	/	<0.001[b]
With unilateral cyst	58(43.3%)	8(13.8%)	/	
BMI(kg/m^2)	20.54 ± 2.63	21.19 ± 3.53	21.14 ± 2.46	0.153[a]
FSH(mIU/ml)	6.88 ± 1.15	7.27 ± 1.42	7.20 ± 0.92	0.028[a]
LH (mIU/ml)	4.19 ± 1.24	4.39 ± 1.34	4.09 ± 0.77	0.255[a]
E2(pg/ml)	61.11 ± 28.07	61.90 ± 19.76	58.53 ± 9.35	0.641[a]
TG(mmol/l)	0.78 ± 0.42	0.98 ± 0.82	0.92 ± 0.42	0.029[a]
TC(mmol/l)	4.46 ± 0.80	4.83 ± 0.10	4.52 ± 0.81	0.025[a]
HDL(mmol/l)	1.45 ± 0.37	1.50 ± 0.27	1.42 ± 0.26	0.271[a]
LDL(mmol/l)	2.43 ± 0.61	2.72 ± 0.89	2.52 ± 0.58	0.043[a]
CA 125(U/ml)	118.44	45.82	/	0.112[d]
CA 199(U/ml)	99.06	90.58	/	0.137[d]
AMH level(ng/ml)	3.78 ± 2.59	4.79 ± 3.43	5.42 ± 3.52	<0.001[a]

Data are expressed as mean ± standard deviation, median or number (percentage) of patients.
Abbreviations: BMI body mass index, FSH follicle stimulating hormone, LH luteinizing hormone, E2 estradiol, TG triglyceride, TC total cholesterol, HDL high density lipoprotein, LDL low density lipoprotein, CA125 cancer antigen 125, CA199 cancer antigen antigen 199, AMH anti-Müllerian hormone.
[a] Variance analysis.
[b] Chi-squared test.
[c] t-Test.
[d] Mann-Whitney U test.
/: Not Applicable.

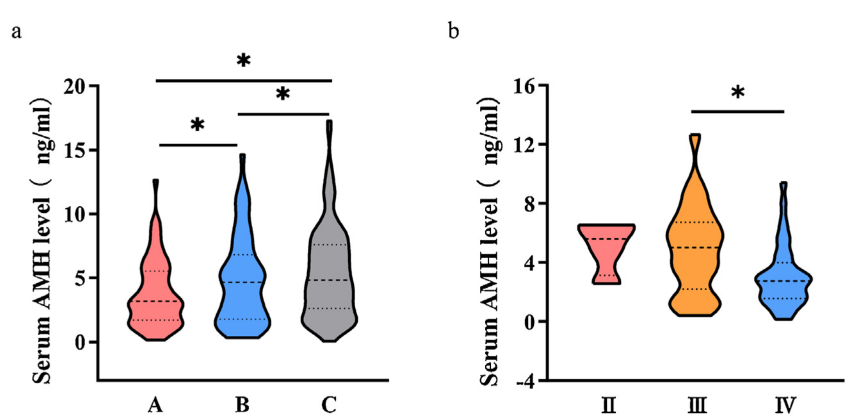

Fig. 2. Violin plot of serum AMH levels in study population.
a. Serum AMH levels in different groups. A: ovaraian endometrioma, B: other benign cyst, C: non-ovarian lesion.
b. Serum AMH levels in patients with different stages of endometriosis. *: $p < 0.05$.

measured after admission. The classification of stage of endometriosis was based on rASRM score system that divided women to different stages: Ⅰ(1–5 points), Ⅱ (6–15 points), Ⅲ (16–40 points), and Ⅳ (>40 points). All included patients underwent transvaginal ultrasonography preoperatively to examine the size and characteristics of their ovarian cysts. The mean diameter of each cyst was calculated by averaging the maximum diameter of cyst and its vertical diameter. When there were multiple cysts, the total cyst diameter was calculated by adding all cysts' mean diameters.

Serum AMH was quantitatively detected with an ELISA-based diagnostic kit for anti-Mullerian hormone (Kangrun Biotech, Guangzhou, China), strictly following the manufacturer's instructions. Based on the test kit and laboratory conditions, the reference range for AMH level is from 0.24 ng/ml to 11.78 ng/ml, and the median concentration is 3.58 ng/ml. Serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), cancer antigen 125 (CA125), cancer antigen 199 (CA199) levels and the concentrations of high density lipoprotein (HDL), low density lipoprotein (LDL), triglyceride (TG), and total cholesterol (TC) were detected with a chemiluminescent Architect® enzyme immunoassay from Abbott Laboratories (ARCHITECT CI16200, Abbott, USA) and related kits. The female sex hormones were detected on the 2nd to 3rd day of the menstrual cycle. And all the tests were taken before surgery.

Patient follow up

For patients with endometrioma, we evaluated the spontaneous pregnancy outcome of each patient for whom postoperative conception were desired by telephone or mail during a follow-up period of 24 months. The endpoint of cumulative spontaneous pregnancy was defined as conceived during the follow-up. Patients still not conceived naturally at the time of the last follow-up, or follow-up shedding of any cases for any reasons were defined as censored.

Statistical analysis

Statistical analysis was performed using SPSS software version 19.0 for Windows (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as the mean ± standard deviation. Differences in serum AMH level and clinical parameters between the groups were analyzed by the Mann-Whitney U test, Student's t-test, χ^2 test and one-way analysis of variance. For analyzing the

Table 2
Serum AMH levels in patients with ovarian lesions.

		Ovarian endometrioma(n = 134)	Other benign cyst(n = 58)	p[b]
Clinical features		**Serum AMH level(ng/ml)**		
Diameter of cyst	**<4cm**	4.58 ± 2.77	5.78 ± 4.20	0.218
	≥4cm	3.41 ± 2.43	4.45 ± 3.11	0.037
	p[a]	0.008	0.609	
Bilaterality	**Unilateral**	4.26 ± 2.79	4.41 ± 1.76	0.774
	Bilateral	3.15 ± 2.16	7.16 ± 3.44	0.037
	p[a]	0.014	0.035	
With or without infertility	**Infertility**	4.33 ± 2.86	5.38 ± 2.99	0.428
	Without infertility	3.44 ± 2.36	4.69 ± 3.53	0.013
	p[a]	0.035	0.515	
With or without dysmenorrhea	**Dymenorrhea**	3.72 ± 2.51	5.45 ± 4.83	0.168
	Non-dysmenorrhea	3.87 ± 2.72	4.71 ± 3.30	0.188
	p[a]	0.052	0.625	
Whether complicated with adenomyosis	**Adenomyosis**	3.26 ± 2.14	2.80 ± 1.68	0.647
	Non-adenomyosis	4.06 ± 2.77	4.98 ± 3.51	0.109
	p[a]	0.090	0.178	

Data are expressed as mean ± standard deviation of patients.
[a] differences between clinical features in each group.
[b] differences between two groups.

Table 3
Univariate correlations and multivariate regression analysis between serum AMH levels and demographic, clinical, biochemical parameters.

	Univariate correlations		Multivariate linear regression analysis	
	r	p	β	p
Age(year)	**−0.317**	**<0.001**	**−0.324**	**<0.001**
BMI(kg/m^2)	−0.088	0.309		
rASRM scores	**−0.363**	**<0.001**	**−0.298**	**<0.001**
Stage of endometriosis	**−0.331**	**<0.001**		
Diameter of cyst(cm)	**−0.191**	**0.027**		
Bilateral of ovarian cyst	**−0.165**	**0.020**		
FSH(mIU/ml)	0.097	0.264		
LH(mIU/ml)	0.086	0.324		
E2(pg/ml)	**−0.178**	**0.040**		
TG(mmol/l)	−0.057	0.519		
TC(mmol/l)	−0.003	0.972		
HDL(mmol/l)	0.091	0.308		
LDL(mmol/l)	0.058	0.535		
CA125(U/ml)	−0.133	0.130	**−0.176**	**0.026**
CA199(U/ml)	−0.116	0.222		

Bold values indicate p < 00.05.
Values that are not statistically significant are not present in the table.
r: correlation coefficient.
β: partial regression coefficient.

correlations between serum AMH levels and clinical parameters, correlation analyses were performed using Spearman's and Pearson's correlation methods. Multivariate linear regression modeling with a stepwise method was used for variables that showed statistically significant differences with the univariate analysis. The primary outcome measures for the study were the cumulative probability of spontaneous pregnancy during a follow-up period of 24 months. There were no secondary outcomes. The X-tile software (version: 3.6.1, Copyright Yale University 2003–2005) was applied to determine the optimal cutoff points for the AMH. The Kaplan-Meier method was used to measure the cumulative pregnancy incidence for patients with high and low serum AMH levels. The curves of the two groups were tested by using the log-rank test. Hazard ratios (HRs) of pregnancy incidence and the corresponding 95% confidence intervals (CIs) for candidate variables were estimated using Cox regression analysis. P values of <0.05 were considered statistically significant.

Results

Baseline characteristics of study population

In total, 307 patients were divided to 3 groups by pathologic confirmation. The age differences of the three groups were not statistically significant. All patients denied smoking. The menarche time and menstrual cycle were similar among three groups. The 58 patients with other benign ovarian cysts were as follows: 46 with mature cystic teratoma, 2 with mucinous cystadenoma, 5 with serous cystadenoma, 3 with ovarian simple cysts, and 2 with both serous mature cystic teratoma and serous cystadenoma. The demographic and clinical data are shown in Table 1. The preoperative AMH level was significantly lower in the endometrioma group (endometrioma group vs. other benign cysts group, $P = 0.04$; endometrioma group vs. non-ovarian lesions group, $P < 0.001$; other benign cysts group vs. non-ovarian lesions group, $P = 0.04$) (Fig. 2a).

Serum AMH level in patients with ovarian lesions

Patients with ovarian endometrioma and other benign ovarian cyst were divided into subgroups by the diameter of cysts, bilaterality, fertility, whether they had dysmenorrhea, and whether they were complicated with adenomyosis. The serum AMH level of each subgroup were shown in Table 2. In the endometrioma group, 4, 48 and 82 cases were stage II, III, and IV endometriosis, respectively. The preoperative level of AMH in stage IV patients was significantly lower than that of patients with stage II and III ($P < 0.05$) (Fig. 2b).

Univariate correlations and multivariate regression analysis

In the univariate analysis, **s**erum AMH levels were negatively correlated with age ($r = -0.317$, $p < 0.001$), rASRM scores ($r = -0.363$, $p < 0.001$), stage of endometriosis ($r = -0.331$, $p < 0.001$), diameter of the cyst ($r = 0.191$, $p = 0.027$), bilaterality ($r = -0.165$, $p = 0.020$), serum E2 level ($r = -0.178$, $p = 0.040$) (Table 3). Multivariate stepwise linear regression analysis revealed that age ($\beta = -0.324$, $p < 0.001$), rASRM scores ($\beta = -0.298$, $p < 0.001$) and serum CA125 level ($\beta = -0.176$, $p = 0.026$) independently and negatively predicted AMH levels (Table 3). The following equation: $Y = 11.658 - 0.203 X_1 - 0.019 X_2 - 0.002 X_3$ (where Y represents serum AMH level, X_1 represents age, X_2 represents rASRM scores, and X_3 represents serum CA125 level) were calculated. After rewriting the multiple regression equation as $X_2 = (11.658 - Y - 0.203 X_1 - 0.002 X_3)/0.019$, we were able to derive the rASRM scores based on each patient's serum AMH and CA125 level, and to clarify the stage of endometriosis.

Predictors for postoperative pregnancy

Among 134 patients with ovarian endometrioma, 108 had desires for pregnancy and were followed for 24 months. One patient with a low AMH level went through menopause one year after surgery. A total of nine patients were lost to follow up. The spontaneous pregnancy rate in women who received surgery was 45.37% (49/108) and ranged from 75.00% (3/4, stage II) to 31.88% (22/69, stage IV) (Fig. 3a).

We applied the X-tile software [19] to determine the optimal cut-off value of AMH for postoperative pregnancy, and the patients were classified into low AMH level (≤3.68 ng/ml, $n = 63$) and high AMH level groups (>3.68 ng/ml, $n = 45$) (Fig. 4). The results demonstrated that a value of 3.68 ng/ml had the most significant predictive value for postoperative pregnancy ($p < 0.001$, log-rank chi-square value = 24.33, the relative risk of low serum AMH level/ high serum AMH level: 1.00/2.96). The optimal cut-off values of CA125 were defined with medical reference range.

Kaplan-Meier survival analysis (Fig. 3b) found that women with a higher serum AMH level tended to have a higher probability of pregnancy throughout the follow-up period (log rank test, $P < 0.001$). Likewise, the Cox regression for pregnancy indicated that older age (per five-year increase, hazard ratio (HR),0.517; 95% CI, 0.299–0.896) and higher serum AMH level (versus lower, HR, 2.383; 95% CI, 1.093–5.197) were independent predictors (Fig. 5).

Discussion

In our study, we observed that preoperative serum AMH level were significantly lower in the endometrioma group than in the

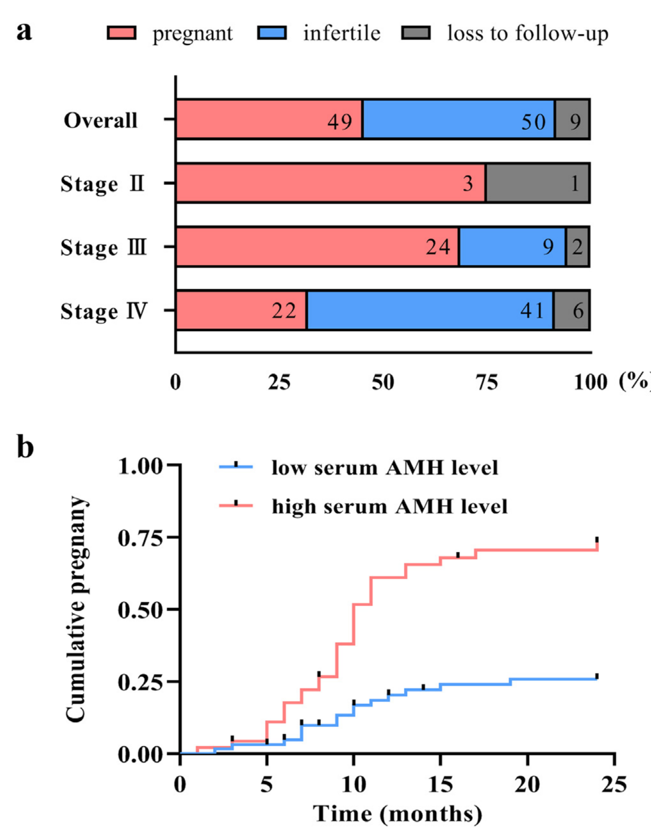

Fig. 3. Postoperative pregnancy follow-up.
a: The proportion of pregnant, infertile, and loss to follow-up in patients with endometrioma.
b: Kaplan-Meier analysis estimates of cumulative pregnancy over time for 24 months. Log rank test: P < 0.001.

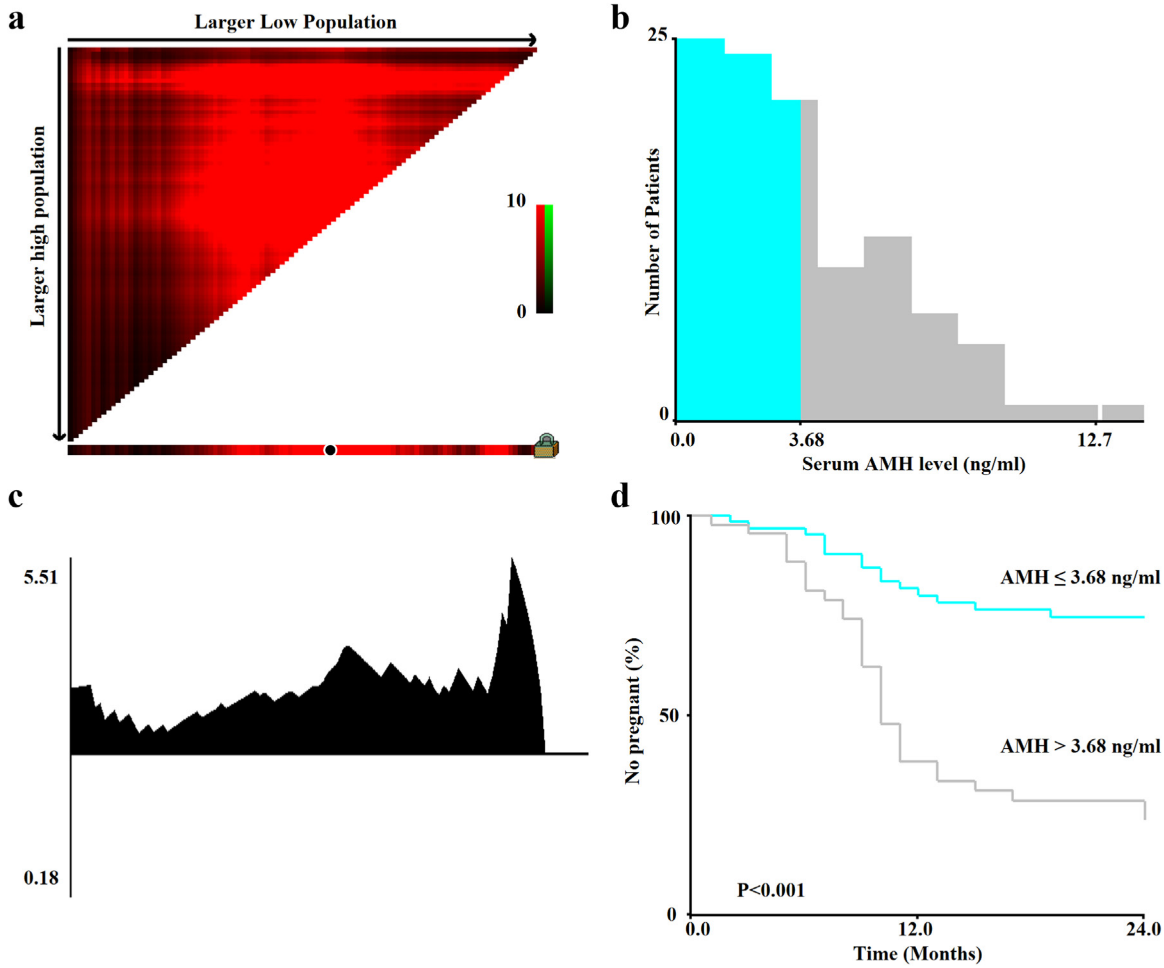

Fig. 4. X-tile plots of the serum AMH level on patients with endometrioma. The plot shows the χ^2 log-rank values that were created when the cohort was divided into two populations. The cut-off point, which is highlighted by a black/ white circle (a), is demonstrated on a histogram of the entire cohort (b), the relative risks for all cutoff points from low to high (left to right, x-axis), are calculated as event in high population / event risk in low population (c), a Kaplan-Meier overall survival curve (d). The preoperative serum AMH level was divided at the optimal cutoff point, as defined by the most significant point on the plot (> 3.68 and ≤ 3.68, p < 0.001).

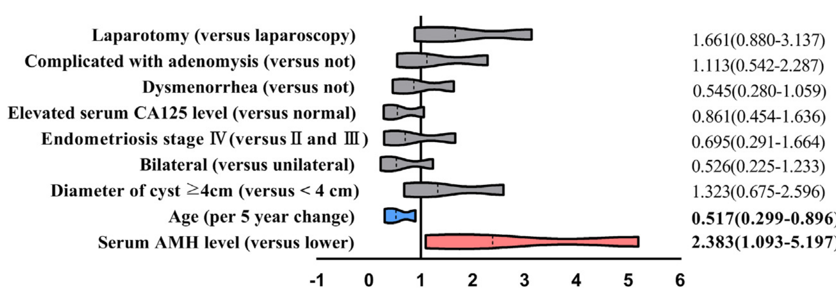

Fig. 5. Hazard ratios for pregnancy after multivariate cox regression analysis.

other two groups. Moreover, serum AMH level were negatively correlated with age, rASRM scores, serum CA125 level and predicting model that (rASRM scores)=[11.658-(serum AMH level)-0.203(age)-0.002(serum CA125 level)]/0.019 was constructed. Furthermore, multivariate Cox regression for postoperative pregnancy indicated that younger age and higher serum AMH level (cut-off value: >3.68 ng/ml) were independent predictors for postoperative pregnancy.

Unlike other benign ovarian cysts, endometriosis can impair fertility, and severe disease can reduce ovarian reserve [20]. Similar reductions and low levels of serum AMH in patients with endometriosis have been reported [21,22]. Moreover, exponentially increasing follicle loss after the age of 30 years might amplify the impact of endometrioma in diminishing ovarian reserve. Our results showed that endometrioma patients with cyst of diameter ≥4 cm, as well those with bilateral cysts and with infertility, appear to have reduced serum AMH levels. Consistent with our findings, Hwu et al [23] reviewed the relationship between the bilaterality of ovarian endometrioma and serum AMH level and found that serum AMH level in patients with bilateral ovarian endometriosis were significantly lower than those in unilateral patients, while other studies have demonstrated that preoperative AMH levels are negatively correlated with diameter of ovarian cysts [24]. Therefore, we hypothesized that the impact of endometrioma on ovarian reserve is higher with increased size of ovarian lesions, and multiple bilateral endometriomas could negatively affect the ovarian reserve. However, there are still limited data on how endometrioma size and bilaterality contribute to ovarian function. For endometriosis, most studies of AMH have investigated it as an assessment tool for ovarian reserve depletion after ovarian surgery [25–27], or to predict responses to assisted reproduction techniques [28–30]. Our results showed that preoperative serum AMH level was significantly lower in advanced endometriosis, and further correlation analysis suggested that it was negatively correlated with age, rASRM scores and serum CA125 level. Hence, we proposed that preoperative serum AMH level, combined with clinical parameters such as age and CA125, may help to predict the rASRM scores and severity of endometriosis. In patients with advanced endometrioma, great difficulty of surgery comes with significantly increased possibility of damage to the ovaries, therefore surgical treatment is hard to be the optimal choice. Furthermore, considering that there was one patient with a low AMH level that went through menopause one year after surgery in our study, we found that assessment before surgery is very important. For patients who desired to pregnancy, a recommendation that patients with lower serum AMH level and older age should undergo assisted reproductive technology (ART) rather than surgery may be suggested since our results indicated that older age and lower AMH level were both independently associated with postoperative infertility.

Interestingly, we also found that the serum level of FSH was significantly lower in women with endometrioma than in those of other groups. With the decrease in serum AMH level of patients with ovarian endometrioma, the number of antral follicle that can be recruited is reduced. Low FSH levels may be a self-protective mechanism, preventing excessive depletion of follicles. In addition, TG, TC, and LDL levels were reduced in patients with ovarian endometrioma, which was inconsistent with previous results from Crook et al. [31] who compared 29 patients with endometriosis with 29 healthy controls; these researchers found that TG levels in patients with endometriosis were significantly elevated, but there was no significant difference in TC, HDL, and LDL between groups. Also, there are researchers proposed that women with endometriosis also have an increased frequency of dyslipidemia. Patients with endometriosis may benefit from earlier screening for dyslipidemia as a preventive measure [32]. At present, the correlations among serum AMH, sex hormones, and lipid levels have not been clarified due to the lack of supporting data.

The strengths of this study included establishing a predictive model for rASRM scores and identifying the predictors for postoperative fertility. The exact role of the preoperative AMH level in clinical guidance has not been fully explained and therefore more research is needed on this topic. Some limitations should be noted despite significant findings. Firstly, limitation on small size of population should be noticed and a potential prediction model should be tested in larger population. Secondly, we did not have the measurements for assessing possible longitudinal changes of AMH through the follow-up. Thirdly, rASRM scores were generally high in the study population, and rASRM scores were strongly influenced by subjective factors. Another limitation was that the control group was a non-healthy population, other infertility factors that may reduce ovarian function cannot be ruled out. For other ovarian cyst group, it is hard to distinguish the effects of different benign tumors on ovarian reserve, owing to the small number of cases. In addition, although AMH levels are independent of the menstrual cycle, and not affected by the use of GnRH agonists or oral contraceptives, differences between individuals are large [33].

Social trends suggest that Chinese women desire pregnancy at increasing ages, so the importance of preserving ovarian function is emphasized up to a late age. The risk of lower ovarian reserve cannot be overlooked if women of reproductive age must undergo ovarian surgery before childbearing. Studies have shown that AMH can predict ovarian responses and to a certain extent predict reproductive outcomes [34,35]. Thus, clinically, the effect of AMH on the ovarian reserve of endometriosis needs to be determined. Timely detection of AMH levels to assess the severity of ovarian endometriosis and possibility of postoperative pregnancy success is necessary for patients with a suspected decline in ovarian reserve, so that better medical interventions and treatment guidance can be provided. Hereby we have provided new insight and a potential method for predicting the severity of endometriosis based on serum AMH level and identified that low AMH level and older age were independent risk factors for postoperative infertility. In these circumstances, clinical recommendations for older women diagnosed with advanced endometriosis with lower serum AMH levels may include undergoing ART rather than undergoing surgery.

Acknowledgements

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