Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

The time-interval of ovarian reserve recovery after laparoscopic unilateral ovarian nonendometriotic cystectomy: a prospective cohort study

huaping Li (zdlhp@126.com)
Gynecologic Oncology Associates
bing Yan
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
yanli Wang
the frist people hospital of zhengzhou
yahong Liu
Shanghai University of Medicine and Health Sciences affiliated zhoupu hospital
zhou Liu
Shanghai University of Medicine and Health Sciences affiliated zhoupu hospital

---

Research

Keywords: unilateral ovarian nonendometriotic cyst, ovarian reservere

Posted Date: December 15th, 2019

DOI: https://doi.org/10.21203/rs.2.18649/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Abstract

Background: Ovarian benign cyst, frequently seen in women of reproductive age, is one of the most important causes of damaging effect of ovarian reserve. Laparoscopic ovarian cystectomy is established as the gold standard surgical approach to the ovarian benign cyst. Studies have shown that potential fertility can be directly impaired by laparoscopic ovarian cystectomy and diminished ovarian reserve. There is little data about the time-interval of ovarian reserve recovery after the laparoscopic unilateral ovarian cystectomy. The objective of this study was to investigate the time-interval of ovarian reserve recovery after laparoscopic unilateral ovarian nonendometriotic cystectomy.

Method: In the first part of the study, a total number of 67 patients with unilateral ovarian nonendometriotic cyst who underwent laparoscopic unilateral ovarian cystectomy were recruited as a postoperative observation group (POG). A total number of 69 same-aged healthy women without ovarian cyst who did not undergo surgery were recruited as a referent group (RFG).The serum anti-Müllerian hormone (AMH) levels were measured using a commercially available enzyme-linked immunosorbent assay kit; the Follicle-stimulating hormone (FSH)and E2 levels, measured using a chemiluminescent reagent kit. The ovarian arterial resistance index (OARI) and AFC were measured by transvaginal ultrasonography on the 3rd-5th day of the same menstrual cycle. In the second part of the study, a prospective postoperative 6-month follow-up of cases was performed.

Results: When compared with RFG, the AFC of POG's cyst side showed no difference in the 1st, 3rd, 6th postoperative month ($F = 0.03, 0.02, 0.55$; $P = 0.873, 0.878, 0.460$). The OARI of POG's cyst side presented no difference in the 1st, 3rd, 6th postoperative month ($F = 0.73, 3.57, 1.75$; $P=0.395, 0.061, 0.188$). In the first month, the postoperative AMH levels declined significantly, 1.88 ng/ml (IQR: 1.61-2.16 ng/ml) in POG and 2.57 ng/ml (IQR: 2.32-2.83 ng/ml) in RFG ($F = 13.43$; $P = 0.000$). At the time interval, the rate of decline was significantly lower postoperatively than preoperatively in POG (32.75 %),and was also the case in the comparison of POG with RFG (26.67 %).

Conclusions: After the laparoscopic unilateral ovarian cystectomy, the optimal time-interval can be the 6th month for ovarian reserve recovery. Semiannually, AMH levels were to be detected to find those whose window time to conceive was likely to be shorter than others of the same age.

Introduction

Ovarian benign cyst, frequently seen in women of reproductive age, is one of the most important causes of damaging effect of ovarian reserve[1, 2]. Laparoscopic ovarian cystectomy is established as the gold standard surgical approach to the ovarian benign cyst[3]. However, some previous studies have shown that potential fertility can be directly impaired by laparoscopic ovarian cystectomy[4-6], and diminished ovarian reserve (DOR) and even premature ovarian failure[7-9], respectively. Many previous researches have confirmed the ovarian reserve damage after the laparoscopic stripping of endometrioma[10-15].Those who had undergone laparoscopic cystectomy for endometrioma showed lower AMH levels

than the healthy women without ovarian cysts (4.2 ± 2.3 vs. 2.8 ± 2.2 ng/ml; P = 0.02), and also AFC lower levels (14.7 ± 4.1 vs. 9.7 ± 4.8 ng/ml; P < 0.01)[11].The decline rate of AMH levels was significantly greater in the bipolar coagulation group than in the suture group during laparoendoscopic single-site cystectomy for ovarian endometriomas (42.2 % vs 24.6 %, P = 0.001)[13]. Benign gynecologic diseases are often implicated infertility problems, and therefore, fertility-preserving interventions are required for the benign gynecologic diseases[12].

Ovarian reserve is defined as a woman's reproductive potential in terms of the number and quality of her remaining oocytes[2]. In 2015, The American College of Obstetricians and Gynecologists recommended that ovarian reserve testing should be performed on those who had ovarian surgery[16]. Ovarian reserve testing should allow individualization of treatment protocols to achieve optimal response while minimizing safety risks[16, 17] .

The abnormally elevated follicle-stimulating hormone (FSH) is almost synonymous with late DOR (high positive predictive value), but the majority of women who are tested (including those with DOR) will have a normal test result (low negative predictive value)[18]. The high values of estradiol (E2) have been associated with both poor ovarian response and failure to achieve pregnancy[19]; measurement of both FSH and E_2 on cycle day 3 may therefore help decrease the incidence of false negative testing[20]. AMH levels rise in young women in adolescence and peak at about 25 years of age, then gradually decline until reaching undetectable levels a few years prior to menopause[21]. Therefore, it reflects the size of the primordial oocyte pool[22]. AMH level testing is a useful screening test in women at high risk of diminished ovarian reserve [17], especially in assessing ovarian reserve for young women with cancer[23]. But, the study did not observe a significant decrease in serum AMH levels 3 months after endometriomas cystectomy[24], on the other hand ,the recovery of AMH serum level has been observed 3–6 months after endometriomas cystectomy[25].

Antral follicle count (AFC) is the sum of follicles in both ovaries as observed on ultrasound in the early follicular phase (day 2-4) of the menstrual cycle. A previous study showed that the OARI of patients with hypoestrogenic amenorrhoea were decreased when compared with the eumenorrhoeic subjects [26].

However, there is little data about the time-interval of ovarian reserve recovery after the laparoscopic unilateral ovarian cystectomy. If little is known about the changing curve of ovarian reserve after the surgery, a question still remains how we can accomplish the individualization of treatment protocols. Therefore, we conducted a six-month prospective cohort study to monitor the ovarian reserve in the patients with benign nonendometriotic ovarian cyst who had undergone laparoscopic unilateral ovarian cystectomy. The monitoring took the form of detecting the serum levels of AMH, and FSH and E2, those data acquired using enzyme-linked immunosorbent assay kit and chemiluminescent reagent kit. The data of AFC and OARI were detected using transvaginal ultrasonography.

Materials And Methods

For the current study, which was registered by the Chinese clinical trial Registry (the name of clinical trial registry was *The effect of ovarian reserve after laparoscopic ovarian unilateral nonendometriotic cystectomy*, URL was *www.chictr.org.cn/,* the registration number was *ChiCTR1800016705*,date of trial registration was 19 June,2018),and approved by the Committee of Medical Ethics, Shanghai Punan Hospital(NO.2014031). All the women were required to provide written informed consent forms before participation. Serum samples were collected from these women prospectively enrolled from 2014 through 2016 to be used to ascertain the time-interval of ovarian reserve recovery after the laparoscopic unilateral ovarian cystectomy. Based on the inclusion and exclusion criteria (Table 1), a total number of 67 patients with the unilateral ovarian benign nonendometriotic cyst, who had undergone a laparoscopic cystectomy, were invited to participate in the postoperative observation group (POG), and 69 same-aged women formed the referent group (RFG). Because of their pregnancies within six months after the surgery, 11 participants were excluded in POG, and because of their pregnancies and personal reasons, 9 withdrew from RFG (Figure 1).

Study treatment

The laparoscopic unilateral ovarian cystectomy was performed by the same surgical team. The weak position of the cyst surface was opened with an ultrasound knife upon the visual exploration of pelvic cavity and ovarian cysts, the cyst detached completely from the ovarian cortex while saving the healthy ovarian cortex as much as possible. During the operation, hemostatic method was ensured with bipolar electrocoagulation forceps at the power of 25 watts and for the duration of no more than 5 seconds. A loose knot was made of 2/0 absorbable sutures for controlling bleeding and reshaping ovarian morpholog. The specimens were examined under intraoperative rapid freezing pathology in order to exclude malignancy, which was followed by the pathological routine examination.

After the surgery, the women were monitored and observed in the hospital wards for 48 hours to watch for surgical or anesthesia-associated complications. For all the women, the operative and post-operative course was successful without any specific complication.

Measurements

In POG, the fasting blood of each was collected on the morning of her menstrual cycle's second day to be examined one month prior to the laparoscopic unilateral ovarian cystectomy; the same collecting procedure was performed in RFG, the serum separated from the whole blood and transferred into a sterile polypropylene tube to be stored at -80°C. After the operation, the samples were examined in the 1st, 3rd and 6th month.

In RFG, the serum was collected at the same time point. The serum AMH levels were measured using a commercially available enzyme-linked immunosorbent assay kit (Beckman, Germany); the FSH and E2 levels, measured using a chemiluminescent reagent kit (Siemens, Germany). According to Rosendahl M and J.G. Bentzen1's experimental methods[27, 28], OARI and AFC were measured by transvaginal ultrasonography (Philips, Germany) on the 3rd-5th day of the same menstrual cycle.

Statistics

SPSS10.0 software package (SPSS Inc., Chicago, IL, USA) was applied to the statistical analysis. In the cases of quantitative variables, after the normality of the data was checked, mean ± SD and median (range) were used to describe normal and non-normal distribution, respectively. Comparisons were made between the two groups based on one-way ANOVA. Statistically, $p < 0.\ 05$ was considered as significant.

Results

Between POG and RFG, no significant differences were found in age, BMI, OARI (the cyst-side ovary), AFC (the cyst-side ovary), median baseline levels of antimüllerian hormone, estradiol (E2), FSH and CA125; such data were detected one month prior to the laparoscopic unilateral ovarian cystectomy (P > 0.05; Table 2).

In the POG, the cyst size was 4.67± 3.12cm; pathological types were teratoma (13 cases, 23.2%), ovarian serous cystadenoma(10 cases,17.9%), ovarian mucious cystadenoma(9 cases,16.1%),ovarian simple cyst(11 cases,19.6%), others(13 cases, 23.2%);the indication for surgery was abdominal pain(13 cases，26.7%),risk of torsion (10 cases,17.9%)，infertility (9cases,16.1%), potentially malignant (11cases19.6%),others (13 cases, 23.2%)，the duration of surgery was 56.5 ± 22.3 min; the blood loss was 50.4± 21.6 ml; the hospital stay was 3.6 ± 1.4(days) (Table 3).

The AFC of the cyst side showed no significant difference in POG when compared with that in RFG postoperatively in the 1^{st}, 3^{rd} and 6^{th} month (F=0.03, 0.02, 0.55; *P*=0.873, 0.878, 0.460). No statistical significances were observed between the three detecting time intervals (F=0.22; *P*=0.808) and between detecting time interval and grouping (F=0.32; *P*=0.881). In the OARI of the cyst side, no statistical significances were observed between POG and RFG in the 1^{st}, 3^{rd}, 6^{th} month postoperatively (F=0.73, 3.57, 1.75; P=0.395, 0.061, 0.188); between three detecting time intervals (F=1.69; *P*=0.185); and between detecting time interval and grouping (F=1.086; *P*=0.355; Table 4).

It was intriguing that AMH levels of POG declined significantly in the 1^{st} postoperative month (1.88 ng/ml [IQR, 1.61-2.16ng/ml]), when compared with those of RFG (2.57 ng/ml [IQR, 2.32-2.83ng/ml]; F=13.43; *P*=0.000; Figure 2). At the time interval, the rate of decline was significantly lower (Figure 3) postoperatively than preoperatively in POG (32.75 %), and was also the case in the comparison of POG with RFG (26.67 %). In the 3^{rd} and 6^{th} month, however, the postoperative AMH levels were found to be similar between POG and RFG (F=1.42, 0.75; *P*=0.784, 0.102) (Table 5).

These evidences showed the postoperative AMH levels restored gradually to the preoperative in the 6^{th} month, showing a statistical significance between three detecting time intervals (F=14.21; P= 0.000). As indicated by Table 4, the interaction between the detecting time and grouping was statistically significant (F=111.89; P=0.000). The postoperative E2 and FSH levels were similar in the 1^{st}, 3^{rd}, and 6^{th} month between POG and RFG (P > 0.05). There was no statistical significance between the three detecting time

intervals (P > 0.05), between the detecting time point and treatment factors (P > 0.05), and between the treatment factors (P > 0.05).

Discussion

In the current study, we undertook a prospective cohort study to test our hypothesis that the optimal time-interval of ovarian reserve recovery can be in the 6th month after the laparoscopic unilateral ovarian nonendometriotic cystectomy. We found that the ovarian reserve decreased after the surgery, and that in comparison with E_2, FSH levels and OARI and AFC, the serum AMH levels could be a convenient and reliable marker for testing ovarian reserve in the short-term. Intriguingly, AMH levels in POG showed a significant decline in the 1st post-operative surgery (1.88ng/ml [IQR, 1.61-2.16ng/ml]), when compared with that in RFG (2.57 ng/ml [IQR,2.32-2.83 ng/ml]) (F=13.43; *P*=0.000), the declining rate was significantly lower than that preoperatively in POG (32.75 %) and than that in RFG (26.67 %); the AMH levels showed a reduction in POG than in RFG in the 3rd post-operative month (2.26 ng/ml vs. 2.49 ng/ml; F=1.42; *P*=0.784); and the AMH levels developed a graduate restoration to those preoperatively in POG and RFE, respectively (2.41ng/ml vs. 2.60 ng/ml; F=0.75;P=0.102) in the 6th post-operative month.

The best surrogate marker for oocyte quality is age[16]. Actually, age is a rough indicator; therefore we need more useful and accurate indicators for discussing prognosis and recommending a treatment plan in short-term clinical practice, especially for those younger women with decreased or diminished ovarian reserve. It is reasonable to inform the woman that her window of pregnancy possibility may be shorter than anticipated, before formulating an individualized treatment protocol. Over the years, various tests and markers of ovarian reserve have been reported such as the basal FSH in 1988, the antral follicle count (AFC) in 1997 and AMH in 2002[29-31]. The basal FSH plus E_2 levels, AMH levels, AFC as appropriate ovarian reserve screening tests should be used in clinic practice[16, 18].

With the increase of reproductive age, the basal FSH level is various because of the inherent variability of each reproductive cycle, FSH multiple cut-off points >10 IU/L (10-20 IU/L) associated with diminished ovarian reserve, but its sensitivity is generally poor (11-86%)[19, 20]. In terms of predicting failure to evaluate ovarian reserve at a short time, therefore, a single FSH value has limited reliability[30]. The basal E_2 has low predictive accuracy for poor ovarian response and failure to conceive; therefore, this test should not be used in isolation to assess ovarian reserve[19]. In the current study, the E_2, FSH levels were similar between POG and RFG in the 1st, 3rd and 6th postoperative month, respectively (P>0.05); thus E2 and FSH levels was not an effective and sensitive indicator of ovarian reserve changes in the short term.

AFC correlates with the quantity of remaining follicles, and good intercycle and interobserver reliability has been demonstrated[32, 33]. However, since AFC has inherent variability related to technology and inter-observer variability[18], it is difficult to assess the exact number of antral follicles of the cystic ovary before cystectomy[34]. In the current study, AFC presented similarity between POG and RFG in the 1st, 3rd

and 6th month postoperatively (P>0.05). Our findings suggest that AFC cannot evaluate ovarian reserve in the short term, especially after laparoscopic ovarian nonendometriotic cystectomy.

AMH has been reported to relatively independent of gonadotropins circulating at physiologic levels, allowing for testing anytime throughout the menstrual cycle[35-38]. The level of AMH declines by 5.6% per year[39], which reflects the size of the primordial oocyte pool[40]. An undetectable AMH level suggests diminished ovarian reserve and may allow a treatment to be tailored to each individual[17, 41]. The recent studies have shown that serum AMH level has been accepted as the most reliable and easily measurable marker for post-operative assessment of ovarian reserve, for it can show a postoperative decline[5, 42-51].

In recent years, many doctors have paid growing attention to the ovarian reserve, their concerns ranging from the decline of ovarian reserve in cancer patients undergoing chemotherapy or radiotherapy to the impact of various gynecological operations on ovarian reserve.

Recent studies have suggested that AMH could be used to predict ovarian follicle loss and follow the evolution of ovarian reserve during chemotherapy. Pretreatment serum AMH concentrations could predict long-term ovarian function after chemotherapy for the patients with early breast cancer; this marker was the only significant predictor of menses compared with age, Inhibin B and FSH, a 55% decrease of AMH levels after one chemotherapy cycle[52]. In 2017, a study analyzed a large prospective multicentric cohort of 249 breast cancer patients [53], in which with the mean basal AMH levels of 4.19 ng/ml (median 2.95 ng/ml), AMH levels were of 0.78 ± 1.40 ng/ml four months after chemotherapy cycle completion. The breast cancer patients were reported to have AMH levels above 0.7 ng/ml before chemotherapy, and those aged under 40 were overweight or obese (BMI > 25) were more likely to regain ovarian function[54]. Radiation therapy was also recognized as highly ovario-toxic even at low doses, associated to 149 extremely low or undetectable AMH dosages in the post-treatment patients[55]. In 2018, a prospective pilot study showed decreased ovarian reserve of thyroid carcinoma patients after radioiodine therapy, the median AMH levels being 3.25 (0.32-17.42), 1 (0.01-3.93), 1.13 (0.08-6.12), and 1.37 (0.09-6.1) ng/ml before and in the 3rd, 6th, and 12th month after therapy[56]. A prospective study showed that AMH levels of 42 pediatric females with cancer who had underwent fertility preservation procedures dropped by approximately 40-50%, and their AMH levels after anti-cancer and ovarian folliculus preservation therapy increased until approximatly10 years later and then decreased[57].

Furthermore, the damage of gynecological surgeries on ovarian function can be evaluated by comparing pre- and post-operative AMH levels. A pilot randomized controlled trial in 2013 suggested that AMH levels were not significantly different at the baseline in the 4-6 postoperative weeks, in the 3rd postoperative month among women with salpingectomy during laparoscopic hysterectomy versus no salpingectomy[58]. The previous studies showed that serum AMH level is a statistically significant decline after ovarian nonendometriotic cystectomy[42, 43, 45, 47]. It was reported that ovarian reserve evaluated with AMH was reduced in patients with ovarian endometriomas when compared with those with other benign ovarian cysts, and with those with healthy ovaries[59].The current study indicated that

the ovarian reserve decreased after the surgery, and that in comparison with E2, FSH levels and OARI and AFC, the serum AMH levels could be a convenient and reliable marker for testing ovarian reserve in the short-term. AMH levels showed a significant decline in POG when compared with those in RFG (1.88 ng/ml vs. 2.57 ng/ml; P=0.000) in the 1st post-operative month, the declining rate significantly lower than the preoperative in POG (32.75 %) as well as than that in RFG (26.67 %).Our finding was similar with those previously reported. AMH can be used to evaluate ovarian reserve after chemotherapy and gynecological operation. However, some researchers have pointed out that AMH is not a hormone but a paracrine factor. The mechanism of AMH secretion into the peripheral circulation is unknown; however, there has been sufficient evidence to suggest that the reduced serum AMH in women with endometriomas can indicate a real and definitive damage to the ovarian reserve rather than only a transient and potentially reversible interference with ovarian physiology[60].

The mechanism of the decline of ovarian reserve following ovarian cystectomy remains largely unknown. It is partially because of the removal of some healthy ovarian tissue in laparoscopic ovarian nonendometriotic cystectomy, which exist a certain number of oocytes; it is possibly related to the use of electrocoagulation for hemostasis in the operation, which can cause damages to the healthy ovarian tissue[5, 6, 61]. A previous study showed that the number of acquired eggs was significantly decreased in IVF after surgery[62]. Therefore, the hemostatic method in the current study was ensured with bipolar electrocoagulation forceps at the power of 25 watts and for the duration of no more than 5 seconds, then with a loose knot made of 2/0 absorbable sutures for controlling bleeding . Thus it is imperative that the ovarian tissue be protected as much as possible during the operation.

In 2018, a small randomized clinical trial suggested that the AFC of the operated ovary was significantly increased in the patients with endometriomas who had undergone CO2 fiber laser vaporization when compared with those with endometriomas after laparoscopic cystectomy, AMH levels found to be significantly reduced at the time interval of 3 months in those after laparoscopic cystectomy when compared with those who had undergone CO2 fiber laser vaporization[63]. The CO2 fiber laser vaporization treatment may mislead the treatment of potential malignant patients due to the lack of pathological results. However, the previous studies provided an alternative treatment to endometriomas and nonendometriomas with minimal damage to the adjacent healthy ovarian tissue. The current study also provided a clinical strategy to find the women with decreased or diminished ovarian reserve by detecting AMH every six months after laparoscopic unilateral ovarian nonendometriotic cystectomy.

However, the current study has several weaknesses. The major limitation was the recruitment of patients with unilateral ovarian nonendometriotic cyst and the healthy women without ovarian cyst, excluding bilateral nonendometriotic cysts and endometrial cyst. The impact on ovarian reserve could be limited by ovarian unilateral cysts, and the mechanism of the postoperative endocrine and paracrine changes in the healthy ovaries is still unknown. Consequently, AFC and OARI were detected at the pre- and postoperative intervals, the AFC of POG's cyst side showing no difference in the 1st, 3rd, 6th postoperative month and the OARI of POG's cyst side presenting no difference in the 1st, 3rd, 6th postoperative month. Therefore,

the optimal time-interval can be the 6th month for ovarian reserve recovery after the laparoscopic ovarian unilateral cystectomy.

Another limitation was the relatively short follow-up. The postoperative measuring of ovarian reserve was performed every six months for two years, which can depict a change curve of ovarian reserve. We will continue our efforts to disentangle the intricate relations between ovarian cysts, ovarian reserve and the impact of surgery. Future studies should aim to reveal the optimal interval of ovarian reserve recovery of the patients with unilateral ovarian nonendometriotic cyst and bilateral nonendometriotic cysts and endometrial cyst after surgery. Moreover, it is necessary that we have a better understanding of the mechanism of causing the decreased ovarian reserve to develop a clinical strategy and ameliorate the surgical techniques in use.

Since there is a dearth of literature on the changing curve of ovarian reserve, we cannot determine an optimal time-interval of ovarian reserve recovery after laparoscopic unilateral ovarian nonendometriotic cystectomy. The current study suggested that the optimal interval of ovarian reserve recovery could be in the 6^{th} month following the laparoscopic ovarian nonendometriotic cystectomy. Based on our findings, it can serve as a clinical strategy to detect AMH levels at the time-interval of the 6th month after the surgery, which is to be semiannually performed. If the test results suggest decreased or diminished ovarian reserve, it is reasonable for the gynecologist and reproductive endocrinology physician to inform the woman that her window of opportunity to conceive may be shorter than that of those women at the same age, encouraging her to conceive sooner rather than later.

Declarations

Acknowledgements

The authors express their appreciation to all of the patients for their participation in this study.

Competing interests

The author declares no potential conflict of interests.

Authors' contributions

Li HuaPing designed and performed the research, analyzed the data, and drafted the manuscript; Liu Zhou guided the research, and Yan Bing, Wang YanLi, Shu ZhiMing, Liu YaHong collected and analyzed the data. All of the authors read and approved the final manuscript.

Funding

This project was supported by the Seed Fund Program of Shanghai University of Medicine & Health Sciences(No.HMSF-17-21-027);The Medical Leaders Training Program of Health Bureau of Shanghai Pudong in China (No.PWRq2016-15) ;Health Bureau of Shanghai in China (No.201740291).

Ethics approval and consent to participate

Ethics approval (NO.2014031) was received from the Committee of Medical Ethics, Shanghai Punan Hospital and written informed consent was obtained from all participants.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

Abbreviations

AFC: Antral follicle count; AMH: Anti-Müllerian hormone.; FSH: Follicle-stimulating hormone; OARI: Ovarian arterial resistance index; POG: Postoperative observation group. RFG: Referent group;

References

[1] Mohamed AA, Al-Hussaini TK, Fathalla MM, El Shamy TT, Abdelaal, II, Amer SA. The impact of excision of benign nonendometriotic ovarian cysts on ovarian reserve: a systematic review. American journal of obstetrics and gynecology. 2016;215:169-76.

[2] Zhang XR, Ding LL, Tang R, Sheng Y, Qin YY, Chen ZJ. [Effects of cystectomy for ovary benign cyst on ovarian reserve and pregnancy outcome of in vitro fertilization-embryo transfer cycle]. Zhonghua fu chan ke za zhi. 2016;51:180-5.

[3] Alborzi S, Foroughinia L, Kumar PV, Asadi N, Alborzi S. A comparison of histopathologic findings of ovarian tissue inadvertently excised with endometrioma and other kinds of benign ovarian cyst in patients undergoing laparoscopy versus laparotomy. Fertility and sterility. 2009;92:2004-7.

[4] Raffi F, Metwally M, Amer S. The impact of excision of ovarian endometrioma on ovarian reserve: a systematic review and meta-analysis. The Journal of clinical endocrinology and metabolism. 2012;97:3146-54.

[5] Kang JH, Kim YS, Lee SH, Kim WY. Comparison of hemostatic sealants on ovarian reserve during laparoscopic ovarian cystectomy. European journal of obstetrics, gynecology, and reproductive biology. 2015;194:64-7.

[6] Pergialiotis V, Prodromidou A, Frountzas M, Bitos K, Perrea D, Doumouchtsis SK. The effect of bipolar electrocoagulation during ovarian cystectomy on ovarian reserve: a systematic review. American journal of obstetrics and gynecology. 2015;213:620-8.

[7] Somigliana E, Ragni G, Benedetti F, Borroni R, Vegetti W, Crosignani PG. Does laparoscopic excision of endometriotic ovarian cysts significantly affect ovarian reserve? Insights from IVF cycles. Human reproduction (Oxford, England). 2003;18:2450-3.

[8] Geber S, Ferreira DP, Spyer Prates LF, Sales L, Sampaio M. Effects of previous ovarian surgery for endometriosis on the outcome of assisted reproduction treatment. Reproductive biomedicine online. 2002;5:162-6.

[9] Ho HY, Lee RK, Hwu YM, Lin MH, Su JT, Tsai YC. Poor response of ovaries with endometrioma previously treated with cystectomy to controlled ovarian hyperstimulation. Journal of assisted reproduction and genetics. 2002;19:507-11.

[10] Urman B, Alper E, Yakin K, Oktem O, Aksoy S, Alatas C, et al. Removal of unilateral endometriomas is associated with immediate and sustained reduction in ovarian reserve. Reproductive biomedicine online. 2013;27:212-6.

[11] Uncu G, Kasapoglu I, Ozerkan K, Seyhan A, Oral Yilmaztepe A, Ata B. Prospective assessment of the impact of endometriomas and their removal on ovarian reserve and determinants of the rate of decline in ovarian reserve. Human reproduction (Oxford, England). 2013;28:2140-5.

[12] Iwase A, Nakamura T, Nakahara T, Goto M, Kikkawa F. Assessment of ovarian reserve using anti-Mullerian hormone levels in benign gynecologic conditions and surgical interventions: a systematic narrative review. Reproductive biology and endocrinology : RB&E. 2014;12:125.

[13] Song T, Kim WY, Lee KW, Kim KH. Effect on ovarian reserve of hemostasis by bipolar coagulation versus suture during laparoendoscopic single-site cystectomy for ovarian endometriomas. Journal of minimally invasive gynecology. 2015;22:415-20.

[14] Asgari Z, Rouholamin S, Hosseini R, Sepidarkish M, Hafizi L, Javaheri A. Comparing ovarian reserve after laparoscopic excision of endometriotic cysts and hemostasis achieved either by bipolar coagulation or suturing: a randomized clinical trial. Archives of gynecology and obstetrics. 2016;293:1015-22.

[15] Biacchiardi CP, Piane LD, Camanni M, Deltetto F, Delpiano EM, Marchino GL, et al. Laparoscopic stripping of endometriomas negatively affects ovarian follicular reserve even if performed by experienced surgeons. Reproductive biomedicine online. 2011;23:740-6.

[16] Committee opinion no. 618: Ovarian reserve testing. Obstetrics and gynecology. 2015;125:268-73.

[17] Testing and interpreting measures of ovarian reserve: a committee opinion. Fertility and sterility. 2012;98:1407-15.

[18] Tal R, Seifer DB. Ovarian reserve testing: a user's guide. American journal of obstetrics and gynecology. 2017;217:129-40.

[19] Broekmans FJ, Kwee J, Hendriks DJ, Mol BW, Lambalk CB. A systematic review of tests predicting ovarian reserve and IVF outcome. Human reproduction update. 2006;12:685-718.

[20] Esposito MA, Coutifaris C, Barnhart KT. A moderately elevated day 3 FSH concentration has limited predictive value, especially in younger women. Human reproduction (Oxford, England). 2002;17:118-23.

[21] La Marca A, Sighinolfi G, Radi D, Argento C, Baraldi E, Artenisio AC, et al. Anti-Mullerian hormone (AMH) as a predictive marker in assisted reproductive technology (ART). Human reproduction update. 2010;16:113-30.

[22] Nelson SM. Biomarkers of ovarian response: current and future applications. Fertility and sterility. 2013;99:963-9.

[23] Peigne M, Decanter C. Serum AMH level as a marker of acute and long-term effects of chemotherapy on the ovarian follicular content: a systematic review. Reproductive biology and endocrinology : RB&E. 2014;12:26.

[24] Ercan CM, Sakinci M, Duru NK, Alanbay I, Karasahin KE, Baser I. Antimullerian hormone levels after laparoscopic endometrioma stripping surgery. Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology. 2010;26:468-72.

[25] Goodman LR, Goldberg JM, Flyckt RL, Gupta M, Harwalker J, Falcone T. Effect of surgery on ovarian reserve in women with endometriomas, endometriosis and controls. American journal of obstetrics and gynecology. 2016;215:589.e1-.e6.

[26] Pellizzari P, Esposito C, Siliotti F, Marchiori S, Gangemi M. Colour Doppler analysis of ovarian and uterine arteries in women with hypoestrogenic amenorrhoea. Human reproduction (Oxford, England). 2002;17:3208-12.

[27] Rosendahl M, Ernst E, Rasmussen PE, Andersen CY. True ovarian volume is underestimated by two-dimensional transvaginal ultrasound measurement. Fertility and sterility. 2010;93:995-8.

[28] Bentzen JG, Forman JL, Larsen EC, Pinborg A, Johannsen TH, Schmidt L, et al. Maternal menopause as a predictor of anti-Mullerian hormone level and antral follicle count in daughters during reproductive age. Human reproduction (Oxford, England). 2013;28:247-55.

[29] Scott RT, Jr., Hofmann GE, Oehninger S, Muasher SJ. Intercycle variability of day 3 follicle-stimulating hormone levels and its effect on stimulation quality in in vitro fertilization. Fertility and sterility. 1990;54:297-302.

[30] Kwee J, Schats R, McDonnell J, Lambalk CB, Schoemaker J. Intercycle variability of ovarian reserve tests: results of a prospective randomized study. Human reproduction (Oxford, England). 2004;19:590-5.

[31] Jayaprakasan K, Campbell B, Hopkisson J, Clewes J, Johnson I, Raine-Fenning N. Establishing the intercycle variability of three-dimensional ultrasonographic predictors of ovarian reserve. Fertility and sterility. 2008;90:2126-32.

[32] Hendriks DJ, Mol BW, Bancsi LF, Te Velde ER, Broekmans FJ. Antral follicle count in the prediction of poor ovarian response and pregnancy after in vitro fertilization: a meta-analysis and comparison with basal follicle-stimulating hormone level. Fertility and sterility. 2005;83:291-301.

[33] Jayaprakasan K, Campbell B, Hopkisson J, Johnson I, Raine-Fenning N. A prospective, comparative analysis of anti-Mullerian hormone, inhibin-B, and three-dimensional ultrasound determinants of ovarian reserve in the prediction of poor response to controlled ovarian stimulation. Fertility and sterility. 2010;93:855-64.

[34] Iwase A, Hirokawa W, Goto M, Takikawa S, Nagatomo Y, Nakahara T, et al. Serum anti-Mullerian hormone level is a useful marker for evaluating the impact of laparoscopic cystectomy on ovarian reserve. Fertility and sterility. 2010;94:2846-9.

[35] Fanchin R, Taieb J, Lozano DH, Ducot B, Frydman R, Bouyer J. High reproducibility of serum anti-Mullerian hormone measurements suggests a multi-staged follicular secretion and strengthens its role in the assessment of ovarian follicular status. Human reproduction (Oxford, England). 2005;20:923-7.

[36] Hehenkamp WJ, Looman CW, Themmen AP, de Jong FH, Te Velde ER, Broekmans FJ. Anti-Mullerian hormone levels in the spontaneous menstrual cycle do not show substantial fluctuation. The Journal of clinical endocrinology and metabolism. 2006;91:4057-63.

[37] La Marca A, Stabile G, Artenisio AC, Volpe A. Serum anti-Mullerian hormone throughout the human menstrual cycle. Human reproduction (Oxford, England). 2006;21:3103-7.

[38] Tsepelidis S, Devreker F, Demeestere I, Flahaut A, Gervy C, Englert Y. Stable serum levels of anti-Mullerian hormone during the menstrual cycle: a prospective study in normo-ovulatory women. Human reproduction (Oxford, England). 2007;22:1837-40.

[39] Bentzen JG, Forman JL, Johannsen TH, Pinborg A, Larsen EC, Andersen AN. Ovarian antral follicle subclasses and anti-mullerian hormone during normal reproductive aging. The Journal of clinical endocrinology and metabolism. 2013;98:1602-11.

[40] van Disseldorp J, Lambalk CB, Kwee J, Looman CW, Eijkemans MJ, Fauser BC, et al. Comparison of inter- and intra-cycle variability of anti-Mullerian hormone and antral follicle counts. Human reproduction (Oxford, England). 2010;25:221-7.

[41] Nelson SM, Yates RW, Fleming R. Serum anti-Mullerian hormone and FSH: prediction of live birth and extremes of response in stimulated cycles–implications for individualization of therapy. Human reproduction (Oxford, England). 2007;22:2414-21.

[42] Ergun B, Ozsurmeli M, Dundar O, Comba C, Kuru O, Bodur S. Changes in Markers of Ovarian Reserve After Laparoscopic Ovarian Cystectomy. Journal of minimally invasive gynecology. 2015;22:997-1003.

[43] Kwon SK, Kim SH, Yun SC, Kim DY, Chae HD, Kim CH, et al. Decline of serum antimullerian hormone levels after laparoscopic ovarian cystectomy in endometrioma and other benign cysts: a prospective cohort study. Fertility and sterility. 2014;101:435-41.

[44] Yoon BS, Kim YS, Seong SJ, Song T, Kim ML, Kim MK, et al. Impact on ovarian reserve after laparoscopic ovarian cystectomy with reduced port number: a randomized controlled trial. European journal of obstetrics, gynecology, and reproductive biology. 2014;176:34-8.

[45] Huang BS, Wang PH, Tsai HW, Hsu TF, Yen MS, Chen YJ. Single-port compared with conventional laparoscopic cystectomy for ovarian dermoid cysts. Taiwanese journal of obstetrics & gynecology. 2014;53:523-9.

[46] Kim SH, Kwon SK, Kim DY, Chae HD, Kim CH, Kang BM. The impact of laparoscopic ovarian cystectomy on serum anti-Müllerian hormone levels in women with endometrioma and other benign ovarian cysts: a prospective cohort study. Fertility and sterility. 2013;100:S363.

[47] Amooee S, Gharib M, Ravanfar P. Comparison of anti-mullerian hormone level in non-endometriotic benign ovarian cyst before and after laparoscopic cystectomy. Iranian journal of reproductive medicine. 2015;13:149-54.

[48] Chen Y, Pei H, Chang Y, Chen M, Wang H, Xie H, et al. The impact of endometrioma and laparoscopic cystectomy on ovarian reserve and the exploration of related factors assessed by serum anti-Mullerian hormone: a prospective cohort study. Journal of ovarian research. 2014;7:108.

[49] Ding Y, Yuan Y, Ding J, Chen Y, Zhang X, Hua K. Comprehensive Assessment of the Impact of Laparoscopic Ovarian Cystectomy on Ovarian Reserve. Journal of minimally invasive gynecology. 2015;22:1252-9.

[50] Jang WK, Lim SY, Park JC, Lee KR, Lee A, Rhee JH. Surgical impact on serum anti-Mullerian hormone in women with benign ovarian cyst: A prospective study. Obstetrics & gynecology science. 2014;57:121-7.

[51] Alper E, Oktem O, Palaoglu E, Peker K, Yakin K, Urman B. The impact of laparoscopic ovarian cystectomy on ovarian reserve as assessed by antral follicle count and serum AMH levels. Fertility and sterility. 2009;92:S59.

[52] Anderson RA, Rosendahl M, Kelsey TW, Cameron DA. Pretreatment anti-Mullerian hormone predicts for loss of ovarian function after chemotherapy for early breast cancer. European journal of cancer (Oxford, England : 1990). 2013;49:3404-11.

[53] Dezellus A, Barriere P, Campone M, Lemanski C, Vanlemmens L, Mignot L, et al. Prospective evaluation of serum anti-Mullerian hormone dynamics in 250 women of reproductive age treated with

chemotherapy for breast cancer. European journal of cancer (Oxford, England : 1990). 2017;79:72-80.

[54] Su HC, Haunschild C, Chung K, Komrokian S, Boles S, Sammel MD, et al. Prechemotherapy antimullerian hormone, age, and body size predict timing of return of ovarian function in young breast cancer patients. Cancer. 2014;120:3691-8.

[55] Gracia CR, Sammel MD, Freeman E, Prewitt M, Carlson C, Ray A, et al. Impact of cancer therapies on ovarian reserve. Fertility and sterility. 2012;97:134-40.e1.

[56] Evranos B, Faki S, Polat SB, Bestepe N, Ersoy R, Cakir B. Effects of Radioactive Iodine Therapy on Ovarian Reserve: A Prospective Pilot Study. Thyroid : official journal of the American Thyroid Association. 2018.

[57] Abir R, Ben-Aharon I, Garor R, Yaniv I, Ash S, Stemmer SM, et al. Cryopreservation of in vitro matured oocytes in addition to ovarian tissue freezing for fertility preservation in paediatric female cancer patients before and after cancer therapy. Human reproduction (Oxford, England). 2016;31:750-62.

[58] Findley AD, Siedhoff MT, Hobbs KA, Steege JF, Carey ET, McCall CA, et al. Short-term effects of salpingectomy during laparoscopic hysterectomy on ovarian reserve: a pilot randomized controlled trial. Fertility and sterility. 2013;100:1704-8.

[59] Muzii L, Di Tucci C, Di Feliciantonio M, Galati G, Di Donato V, Musella A, et al. Antimullerian hormone is reduced in the presence of ovarian endometriomas: a systematic review and meta-analysis. Fertility and sterility. 2018;110:932-40.e1.

[60] Somigliana E. Ovarian reserve, endometriomas, and surgery: research must go on. Fertility and sterility. 2018;110:856-7.

[61] Muzii L, Bianchi A, Croce C, Manci N, Panici PB. Laparoscopic excision of ovarian cysts: is the stripping technique a tissue-sparing procedure? Fertility and sterility. 2002;77:609-14.

[62] Celik HG, Dogan E, Okyay E, Ulukus C, Saatli B, Uysal S, et al. Effect of laparoscopic excision of endometriomas on ovarian reserve: serial changes in the serum antimullerian hormone levels. Fertility and sterility. 2012;97:1472-8.

[63] Candiani M, Ottolina J, Posadzka E, Ferrari S, Castellano LM, Tandoi I, et al. Assessment of ovarian reserve after cystectomy versus 'one-step' laser vaporization in the treatment of ovarian endometrioma: a small randomized clinical trial. Human reproduction (Oxford, England). 2018;33:2205-11.

Tables

Due to technical limitations, tables 1, 2, 3, 4, and 5 are only available as downloads in the supplemental files section.

Figures

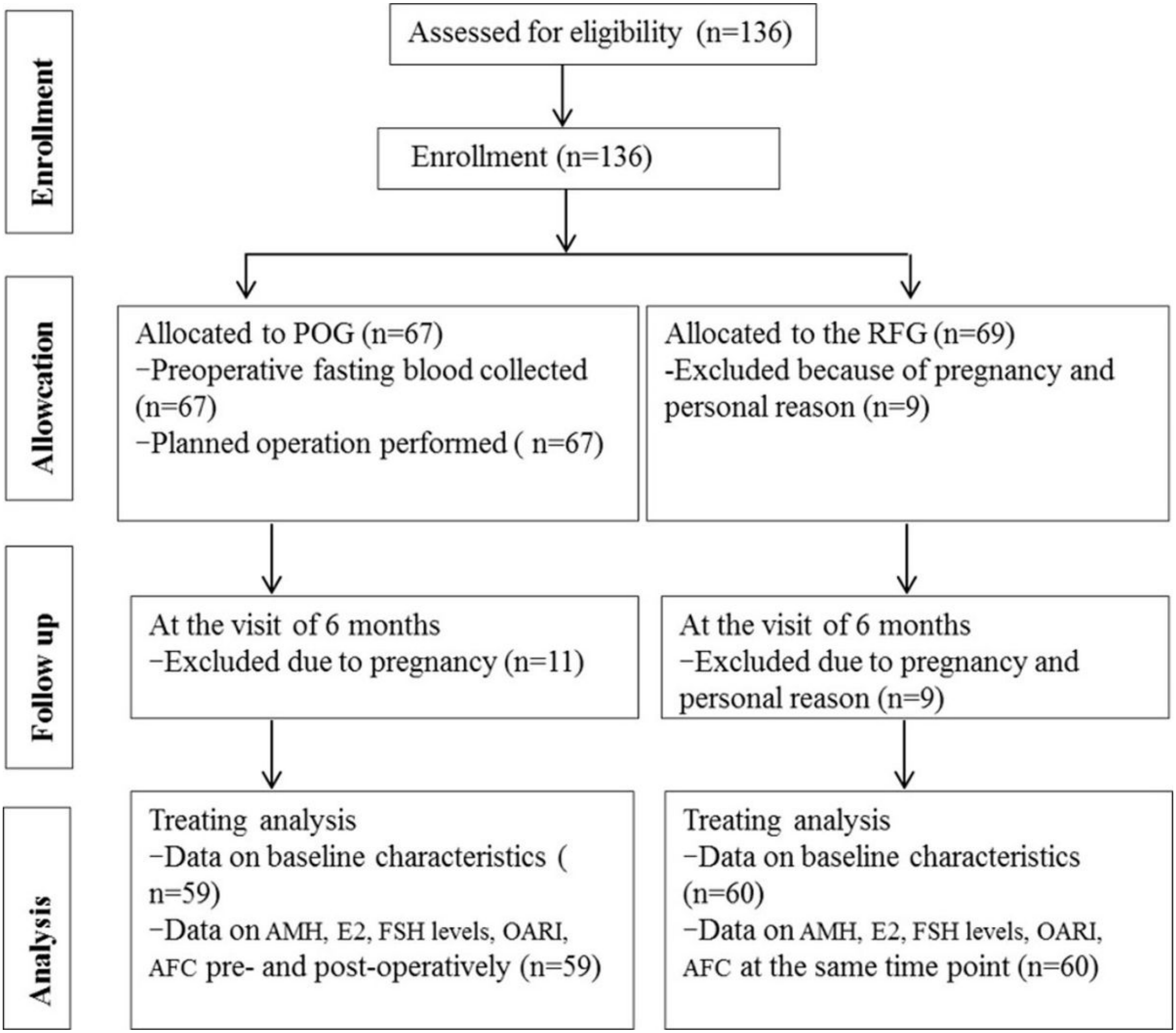

Figure 1

Enrollment, randomization and follow-up of the study subjects

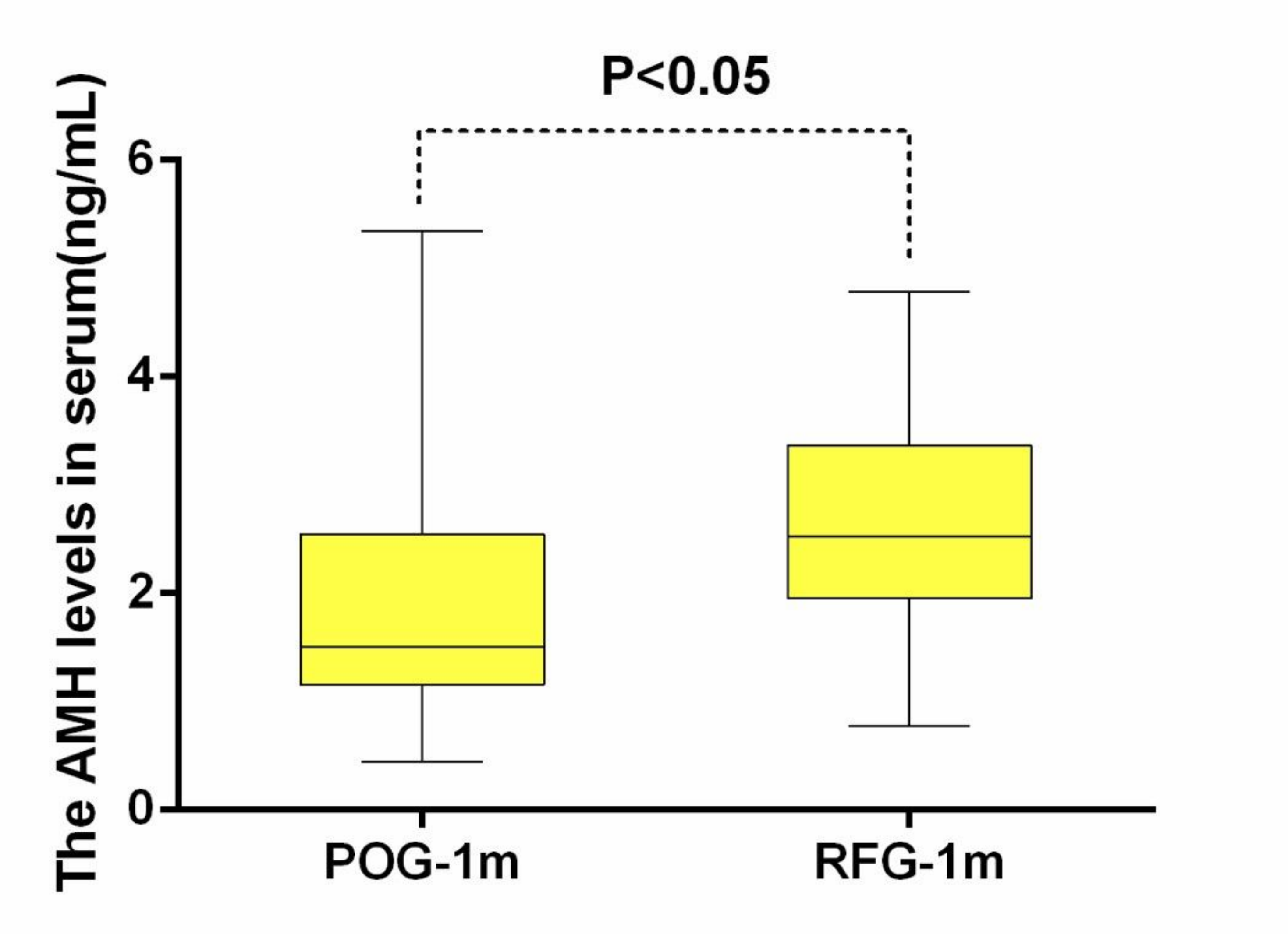

Figure 2

The serum AMH levels of POG and RFG in the 1st postoperative month. The serum AMH levels of POG in the 1st postoperative month were 1.88 ng/ml (IQR, 1.61-2.16 ng/ml),the serum AMH levels of RFG in the 1st postoperative month were 2.57 ng/ml [IQR,2.32-2.83 ng/ml). Results are expressed as mean ± SD, *P < 0.05.

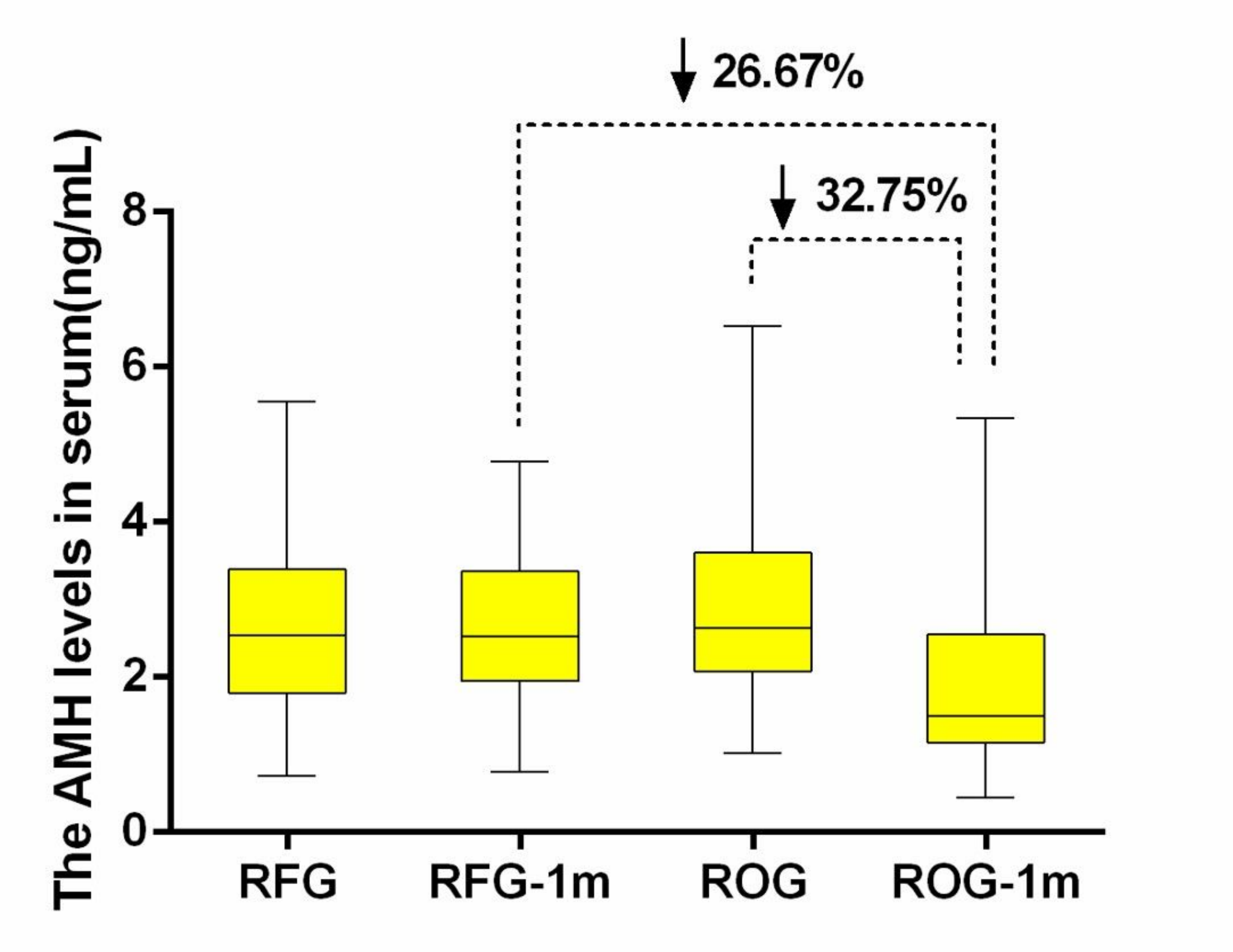

Figure 3

The decline rate of serum AMH levels of POG and RFG The rate of decline was 32.75%, the comparison of AMH levels of POG in1st postoperatively with preoperatively of POG (1.88 ng/ml vs 2.81 ng/ml); the rate of decline was 26.67%, the comparison of AMH levels of POG in1st postoperatively with RFG (1.88 ng/ml vs 2.57 ng/ml),Results are expressed as %.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- table4.jpg
- table5.jpg
- table2.jpg
- table3.jpg

- table1.jpg