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Original Article

Clinical study of the impact on ovarian reserve by different hemostasis methods in laparoscopic cystectomy for ovarian endometrioma

Chun-Hua Zhang, Ling Wu*, Pei-Quan Li

Huai'an Maternal and Child Health Care Center, Huai'an City, PR China

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ABSTRACT

Objective: To evaluate the impact of different hemostasis methods on ovarian reserve in laparoscopic cystectomy in treatment of ovarian endometrioma for the long-term.

Materials and Methods: A total of 207 patients with ovarian endometrioma, aged from 18 years to 45 years, were randomized into three groups: Group A (69 patients) treated by bipolar electrocoagulation hemostasis in laparoscopic cystectomy for ovarian endometrioma; Group B (69 patients) with ultrasound scalpel hemostasis; and Group C (69 patients) with suture technique hemostasis. The follicle-stimulating hormone (FSH), anti-Mullerian hormone (AMH), antral follicle count (AFC), and peak systolic velocity (PSV) were observed and compared at the 3rd day of the 1st, 3rd, 6th, and 12th menstrual cycle after surgery.

Results: (1) A total of 13 out of 207 patients failed; four in Group A, five in Group B, and four in Group C. There was no statistically significant difference between groups ($p > 0.05$). The failure rate was the highest during the 3rd month in the follow up (10 cases). (2) FSH: at the 1st month, 3rd month, 6th month, and 12th month follow up, FSH was higher in Group A and Group B than in Group C ($p < 0.05$). (3) AMH: AMH was significantly lower in Group A and Group B than in Group C ($p < 0.05$) during the same period. (4) AFC: no difference of AFC was observed at the 1st month and 3rd month ($p > 0.05$), whereas at the 6th month and 12th month, AFC in Group C was obviously higher than that in Group A and Group B ($p < 0.05$). (5) PSV: at the 1st month, 3rd month, 6th month, and 12th month follow up, PSV was significantly lower in Group A and in Group B than in Group C ($p < 0.05$).

Conclusion: Ultrasonic scalpel or bipolar electrocoagulation hemostasis applied to laparoscopic cystectomy is associated with a significant reduction of ovarian reserve. Electrocoagulation of hemostasis should be used with caution.

Introduction

Endometriosis, often presenting with infertility, is a common disease of women with rising incidence [1]. Ovarian endometrioma is the most commonly encountered diagnosis, accounting for 17–44% pelvic endometriosis, and the incidence of bilateral ovarian endometrioma is up to 29% [2]. The reduction of ovarian reserve due to follicle loss and even premature ovarian failure in laparoscopic cystectomy of ovarian endometrioma has attracted a large amount of domestic and foreign attention [3]. Although follicle-stimulating hormone (FSH) is one of the monitoring indexes of ovarian reserve, it has certain limitations. In a majority of unilateral ovarian endometriomas, compensated by healthy ovaries, no obvious difference is seen in FSH. At present, antral follicle count (AFC) and peak systolic velocity (PSV) are the commonly used indexes to evaluate ovarian reserve, as well as anti-Mullerian hormone (AMH), without effect on the menstrual cycle to a great extent [4]. Researchers hope that FSH, AMH, AFC, and PSV levels can be observed during different periods in the follow up, so that the impact on ovarian reserve by different hemostasis methods in laparoscopic cystectomy of ovarian endometrioma can be assessed accurately.

* Corresponding author. Huai'an Maternal and Child Health Care Center, Huai'an City, PR China.
E-mail address: 18705130528@163.com (L. Wu).

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Materials and methods

Patients

A total of 207 patients, aged from 18 years to 45 years with a mean age of 31.8 ± 8.2 years, primarily diagnosed with ovarian endometrioma in our hospital, were studied between March 2013 and September 2013. The patients were randomized into three groups, with 69 cases in each group. The inclusion criteria were as follows: (1) aged from 18 years to 45 years; (2) primarily diagnosed with unilateral or bilateral ovarian endometrioma by ultrasonography and clinical examination; (3) regular menstrual cycles with 25–35 days in the first 6 months of operation; and (4) informed consent. The exclusion criteria were as follows: (1) previous intake of contraceptive pills or hormone medicines; (2) history of ovarian surgery; (3) confirmed diagnosis of endocrine system disease or polycystic ovary syndrome; (4) excision of hysterectomy and adnexa; (5) ovarian malignant cancer; and (6) conditions incompatible with the ideas of the investigators.

Methods

A total of 207 patients with ovarian endometriomas, treated by laparoscopic cystectomy, were averagely randomized into three groups: Group A (69 patients) with bipolar electrocoagulation hemostasis; Group B (69 patients) with ultrasound scalpel hemostasis; and Group C (69 patients) with suture technique hemostasis. The FSH, AMH, AFC, and PSV were observed and compared at the 3rd day of the 1st, 3rd, 6th, and 12th menstrual cycle after surgery.

Surgical techniques

The procedures were performed as follows. All patients underwent the surgery under general anesthesia with endotracheal intubation and were placed in the Trendelenburg position. Then, the pneumoperitoneum was established in laparoscopic operation. A sharp cortical incision on the ovarian cyst surface and less vessels regions was made using scissors. The cyst wall was incised and the entire cyst was stripped away from the normal ovarian tissue completely by blunt dissection of opposite traction using two grasping forceps, followed by washing with saline after puncture, until there was clear cystic fluid. All patients were divided into three groups by a random number table, according to different hemostasis methods: bipolar electrocoagulation hemostasis (Group A), ultrasound scalpel hemostasis (Group B), and suture technique hemostasis (Group C). Bipolar electrocoagulation (WOLF, Germany, rated power of 25 W) hemostasis was performed in the bleeding site, accompanied by washing, in case more ovarian tissue was damaged excessively by electric coagulation. Ultrasound scalpel (Johnson & Johnson, USA) hemostasis was operated in the clear bleeding site. Natural curling was observed at ovarian hemorrhage in both groups above, without suture or other managements. Absorbable sutures (3-0; Johnson & Johnson) were used to suture the cortex and the medulla for hemostasis in Group C, avoiding ovarian cortex curl.

Outcome measures

FSH and AMH of fasting venous blood, obtained on the 3rd day of menstrual cycle prior to surgery, were determined through an ELISA kit. AFC and PSV of bilateral ovariectomy were measured after no difference of ovarian cyst diameter was observed by transvaginal color ultrasound. The number of follicles with a 2–10-mm inner diameter in bilateral ovarian cysts were calculated through ultrasonography. PSV was tested until at least five consecutive and stable waveforms were obtained when the flow spectrum appeared stable in the ovarian stromal artery. The final value of the blood flow parameters was the mean of two values.

Follow up

The FSH, AMH, AFC, and PSV were measured and compared on the 3rd day of the 1st, 3rd, 6th, and 12th menstrual cycle after surgery, whereas AFC and PSV were statistically analyzed for unilateral ovarian endometrioma. Routine obstetric examination was performed in the termination patient in case of pregnancy.

Statistical analysis

Statistical analysis was performed using SPSS version 16.0. The continuous variables were described using the mean ± standard deviation (SD) ($\bar{x}\pm s$) and the incidences were presented as number and percentage. The χ^2 and the Student t test were used for analysis of categorical variables in cases where the variables showed a normal distribution. The mean comparison was expressed as Q test. All results were considered statistically significant at $p < 0.05$.

Results

Comparison of basic clinical data

No statistically significant difference was observed in age, cyst diameter, gravidity, and parity of patients in the three groups ($p > 0.05$) (Table 1).

Comparison of compliance

A total of 13 out of 207 patients failed, including four cases in Group A (5.8%), five cases in Group B (7.2%), and four cases in Group C (5.8%). There was no statistically significant difference between groups ($p > 0.05$) ($\chi^2 = 0.3810$, $p > 0.05$). The failure rate was the highest during the 3rd month in the follow up (10 cases). The reasons included no follow up, no association, and others (Table 2).

Assessment of detection indexes

Comparison of detection indexes: (1) there was no statistically significant difference in preoperative FSH and AMH levels between groups (p > 0.05). At the 1st month, 3rd month, 6th month, and 12th month follow up, FSH levels in Group A and Group B were higher than those in Group C; AMH levels in Group A and Group B were lower than those in Group C. All results were considered statistically significant ($p < 0.05$; Tables 3 and 4). (2) No statistically significant difference of preoperative AFC and PSV was observed between groups ($p > 0.05$). At the 1st month, 3rd month, 6th month, and 12th month follow up, AFC and PSV in Group C were obviously higher than those in Group A and Group B, with statistical significance ($p < 0.05$), with the exception of no difference of AFC in the 1st month after operation ($p > 0.05$; Tables 5 and 6).

Table 1
Baseline characteristics of patients.

Groups	No.	Age (y)	Cyst diameter (cm)	Gravidity (time)	Parity (time)
Group A	69	30.9 ± 8.2	5.2 ± 2.6	1.24 ± 0.24	0.54 ± 0.40
Group B	69	31.4 ± 8.5	4.9 ± 2.9	1.21 ± 0.29	0.52 ± 0.37
Group C	69	33.1 ± 7.2	5.3 ± 2.7	1.30 ± 0.17	0.49 ± 0.41

Table 2
Comparison of failures.

Reasons of failures	Group A ($n = 69$)					Group B ($n = 69$)					Group C ($n = 69$)				
	1 mo after surgery	3 mo after surgery	6 mo after surgery	12 mo after surgery	Total	1 mo after surgery	3 mo after surgery	6 mo after surgery	12 mo after surgery	Total	1 mo after surgery	3 mo after surgery	6 mo after surgery	12 after surgery	Total
No follow up	2	1	0	0	2	1	2	0	0	2	1	0	0	0	1
No association	1	0	0	0	1	0	0	1	0	0	0	0	1	0	1
Others[a]	0	0	0	0	0	1	0	0	0	1	1	0	1	0	2
Total	3	1	0	0	4	3	2	0	0	5	2	0	2	0	4

[a] Others included immigration, diseases, etc.

Safety evaluation

The patients with ovarian endometrioma in the three groups did not have serious adverse reactions during treatment. All of the patients were cured, accompanied by no obvious differences in menstrual cycle and amount of menses during perioperation. Recurrence of ovarian endometrioma was not observed in the follow up during 12 months.

Discussion

Endometriomas are a common cause of gynecologic morbidity and the most common ovarian cysts encountered at surgery. Ovaries play an important role in sex hormone metabolism, and endocrine and ovarian reserve is associated with the fertility and quality of life. Therefore, the surgical principle of avoiding excessive damage to normal ovarian tissue to maintain the ovarian reserve for reproductive women has gained wide acceptance [4]. Methods of hemostasis with low risk of ovarian reserve impairment are applied to clinical practice on the basis of future fertility, which contributes to recurrence of ovarian reserve and avoids damage to fertility, even future life. In the study, the effects of different hemostasis methods, including bipolar electrocoagulation, ultrasound scalpel, and suture technique on ovarian reserve in laparoscopic cystectomy for ovarian endometrioma were prescribed, in order to investigate the causes of ovarian reserve impairment and protect ovarian reserve maximally.

Characteristics and technique of endometriotic cystectomy

The pathogenesis of an endometriotic cyst is still controversial. One hypothesis is that endometrioma was formed by progressive invagination of the ovarian cortex after accumulation of menstrual debris originating from the shedding of superficial endometriotic active implants. Therefore, it is inevitable that stripping the cyst wall will damage part of the ovarian tissue, owing to dense extensive adhesion between the pseudocyst formed by invagination and normal ovarian tissue. The distinctions between them are the color of normal ovarian tissue and the capsule wall, and the smoothness of the capsule wall in laparoscopy. Normal ovarian tissue is shown as pink–white compared with gray or gray–yellow of the capsule wall. The cleavage plane between the cyst wall and the adjacent ovarian cortex is identified and separated after the fibrous adhesions are incised using scissors without thermal damage. Then, the cyst wall is completely stripped off from the normal ovarian tissue by opposite traction, reserving the normal ovarian tissue as much as possible [5]. Care is required, especially for hemorrhage, in the dissection of the surface of the hilum ovarii. Patients may depend too much on various electric coagulation hemostasis devices, sometimes even repeated electric coagulation, as a result of hemostasis difficulty after the stripping operation. Bipolar coagulation is the most common hemostatic method due to the characteristics of convenience and efficiency, compared with ultrasound scalpel hemostasis with less scab, exact effect, and clear vision. However, there is growing attention as to whether the hemostasis of bipolar coagulation and ultrasound scalpel will affect the ovarian reserve through thermal damage. Some patients with reduction of ovarian reserve, even premature ovarian failure after surgery, have been reported in some studies [1].

Effect of endometriotic cystectomy on ovarian reserve

With the development of a laparoscopic technique, laparoscopic cystectomy remains the first-line choice for endometriotic cysts. However, a large number of clinical practices suggest that both traditional open and laparoscopic cystectomy may have effects on ovarian reserve to different extents, including decreased estradiol with increasing FSH and luteinizing hormone, and menstrual changes. The mechanism of endometrioma-associated damage on ovarian reserve may include: the normal ovarian tissue is damaged by stress of the ovarian cyst before surgery; laparoscopic cystectomy contributes partly to normal ovarian tissue loss and reduction of normal ovarian tissue after surgery; and intraoperative hemostasis, especially electric coagulation hemostasis, may damage the ovarian cortex and destroy the blood supply, thereby reducing the ovarian reserve [5]. The study demonstrated that FSH

Table 3
Perioperative follicle-stimulating hormone (FSH) level of patients ($\bar{x}\pm s$).

Group	No.	FSH (U/L)				
		Preoperative	Postoperative			
			1 mo	3 mo	6 mo	12 mo
A	69	5.38 ± 1.72	11.9 ± 4.0*	10.0 ± 4.0*	9.7 ± 4.2*	9.6 ± 4.0*
B	69	5.79 ± 1.58	11.7 ± 4.0*	11.0 ± 3.4*	9.3 ± 4.1*	9.2 ± 3.9*
C	69	6.02 ± 1.69	9.2 ± 3.3	6.8 ± 2.8	7.0 ± 3.1	6.5 ± 2.8

Follow up for 1 month: Group A, 66 cases; Group B, 66 cases; Group C, 67 cases.
Follow up for 3 months: Group A, 65 cases; Group B, 64 cases; Group C, 67 cases.
Follow up for 6 months: Group A, 65 cases; Group B, 64 cases; Group C, 65 cases.
Follow up for 12 months: Group A, 65 cases; Group B, 64 cases; Group C, 65 cases.
* $p < 0.05$ compared with Group C.

Table 4
Perioperative anti-Mullerian hormone (AMH) level of patients ($\bar{x}\pm s$).

Group	No.	AMH (μg/L)				
		Preoperative	Postoperative (mo)			
			1	3	6	12
A	69	4.3 ± 1.8	1.9 ± 0.7*	1.8 ± 1.0*	1.9 ± 0.8*	2.0 ± 0.9*
B	69	4.1 ± 1.9	1.5 ± 0.9*	1.8 ± 0.9*	1.9 ± 1.0*	2.0 ± 1.0*
C	69	4.2 ± 1.8	2.9 ± 1.8	3.0 ± 1.8	3.0 ± 1.5	3.1 ± 1.6

Follow up for 1 month: Group A, 66 cases; Group B, 66 cases; Group C, 67 cases.
Follow up for 3 months: Group A, 65 cases; Group B, 64 cases; Group C, 67 cases.
Follow up for 6 months: Group A, 65 cases; Group B, 64 cases; Group C, 65 cases.
Follow up for 12 months: Group A, 65 cases; Group B, 64 cases; Group C, 65 cases.
* $p < 0.05$ compared with Group C.

Table 5
Perioperative antral follicle count (AFC) level of patients ($\bar{x}\pm s$).

Group	No.	AFC				
		Preoperative	Postoperative			
			1 mo	3 mo	6 mo	12 mo
A	69	4.0 ± 1.6	3.2 ± 1.6	3.6 ± 1.3*	3.9 ± 1.4*	4.2 ± 1.5*
B	69	4.0 ± 1.7	3.0 ± 1.7	3.6 ± 1.4*	3.9 ± 1.3*	4.0 ± 1.2*
C	69	4.1 ± 1.5	3.1 ± 1.4	4.7 ± 1.3	6.0 ± 1.9	6.3 ± 2.0

Follow up for 1 month: Group A, 66 cases; Group B, 66 cases; Group C, 67 cases.
Follow up for 3 months: Group A, 65 cases; Group B, 64 cases; Group C, 67 cases.
Follow up for 6 months: Group A, 65 cases; Group B, 64 cases; Group C, 65 cases.
Follow up for 12 months: Group A, 65 cases; Group B, 64 cases; Group C, 65 cases.
* $p < 0.05$ compared with Group C.

Table 6
Perioperative peak systolic velocity (PSV) level of patients ($\bar{x}\pm s$).

Group	No	PSV (cm/s)				
		Preoperative	Postoperative (mo)			
			1	3	6	12
A	69	13.9 ± 4.5	8.0 ± 3.7*	8.2 ± 3.9*	8.3 ± 4.0*	8.2 ± 3.7*
B	69	13.4 ± 4.2	8.1 ± 3.8*	7.9 ± 3.5*	8.0 ± 3.7*	8.2 ± 4.0*
C	69	13.7 ± 4.6	11.1 ± 3.4	12.1 ± 3.8	11.7 ± 2.9	12.2 ± 3.5

Follow up for 1 month: Group A, 66 cases; Group B, 66 cases; Group C, 67 cases.
Follow up for 3 months: Group A, 65 cases; Group B, 64 cases; Group C, 67 cases.
Follow up for 6 months: Group A, 65 cases; Group B, 64 cases; Group C, 65 cases.
Follow up for 12 months: Group A, 65 cases; Group B, 64 cases; Group C, 65 cases.
* $p < 0.05$ compared with Group C.

levels with bipolar electrocoagulation and ultrasound scalpel were obviously higher than those with the suture technique compared with lower AMH. In addition, AFC and PSV of the suture technique declined less than those of bipolar electrocoagulation and ultrasound scalpel, which was associated with absorbable sutures. The number of ovarian follicles increased and the blood supply was gradually improved when the suture was absorbed. By contrast, AFC and PSV with bipolar electrocoagulation and ultrasound scalpel decreased significantly, presenting irreversible damage to the ovary. The reasons for reduction of ovarian reserve may include cyst damage, ovarian tissues loss, and hemostasis such as electrocoagulation etc. Maneschi et al [6] reported that the number of follicles was reduced for patients with ovarian endometrioma, indicating that the cyst could damage ovarian tissue. In addition, 93% ovarian endometrioma was related to ovarian stromal extrusion caused by menstrual ectopic endometrium production. Then, the tinctorial cellulose analogues replaced the ovarian stroma and changed the structure. Brosens et al [7] indicated that endometrial tissues were observed in ovarian stroma and follicles. Hachisuga and Kawarabayashi [8] concluded that ovarian endometrioma was adhesive between the broad ligament of the uterus and ovarian stroma. Cysts were caused by stromal fibrosis with no clear interface, therefore, damage to the ovarian stroma was inevitable in cystectomy using stripping. Muzii et al [9] found that normal ovarian tissues were observed in the cyst wall of 54% endometrioma cystectomy, but rarely found in nonovarian endometrioma cystectomy. In addition, according to Hachisuga and Kawarabayashi [8], the normal ovarian tissues were presented in most sections of ovarian endometrioma.

Comparative analysis of different hemostasis methods in endometrioma cystectomy

A total of 207 patients were studied in a randomized and parallel controlled trial. The random number table was made through statistical software and placed in sealed envelopes coded by sequence. Only the statisticians knew the number in the envelope. An assistant researcher was informed to take the appropriate surgical approach according to the packet in the envelope after the patients signed informed consent and were screened into groups. The sample size was determined by the noninferiority test. The results of FSH, AMH, AFC, and PSV demonstrated that the bipolar electrocoagulation and ultrasound scalpel hemostasis were notably worse than the suture hemostasis technique in terms of ovarian reserve damage, which was consistent with reports abroad [10]. Additionally, recovery of ovarian reserve in the suture hemostasis technique was obviously higher than those in the others, which illustrated that the residual ovarian tissues and vessels were damaged slightly by the hemostasis of suture. Thereby, the antral follicles and ovarian tissue could secret gonadal hormone to maintain the normal physiological needs. The reduction of ovarian reserve may be associated with ovarian endometrioma. The normal ovarian tissues loss or damage caused by cysts adhesion and unidentified dissection surface in endometrioma cystectomy also contribute to reduce ovarian reserve. In addition, thermal damage and conduction of bipolar coagulation led to destruction of the ovarian blood supply and normal ovarian tissues. Although no significant difference of tissues was observed, the structure had actually been destroyed. Fedele et al [11] showed that the patients with unilateral ovarian endometrioma were treated by laparoscopic cystectomy and divided into two groups: one with bipolar electrocoagulation, the other with suture hemostasis. There was no statistically significant difference of postoperative FSH between them ($p = 0.06$), but the group with suture hemostasis was better than that with bipolar electrocoagulation in the aspect of ovarian reserve. It was essential to protect the ovarian blood supply system, which played an important role in maintaining ovarian function. In this study, the results also showed that ovarian perfusion presented a noticeable drop in cases with bipolar electrocoagulation and ultrasonic scalpel hemostasis compared with cases with suture hemostasis, which suggested that damage of ovarian blood supply was irreversible. Hemorrhage and oozing of blood were observed in the dissection surface between the cyst wall and adjacent ovarian cortex, especially in hilum ovarii. Repeated cauterization of electrocoagulation and ultrasonic scalpel hemostasis to condense tissues could damage vessels, and subsequently cause a tissue reaction such as postoperative adhesions and local scars, affecting ovarian blood circulation, and even ovarian blood supply. Any one or more of follicular growth, development, maturation, ovulation, and luteinization in the ovarian cortex was impeded without enough ovarian blood supply. Especially for follicular growth and development, the lower response and reduction of ovarian reserve would be observed, even with premature ovarian failure. Horikawa et al [12] concluded that the number of mature follicles and pregnancy rate in *in vitro* fertilization remarkably decreased for the patients treated by endometrioma cystectomy compared with those without operation. Suture hemostasis was superior to electrocoagulation hemostasis in terms of maintaining ovarian reserve and blood supply. However, the disadvantages of suture hemostasis were a difficult operation and a long hemostatic time. Thus, suture hemostasis could not be used for rapid hemostasis [13]. A comprehensive perioperative nursing intervention on psychology, lifestyle, surgery, and diet was performed for patients to further promote the rehabilitation of ovarian reserve. In the meantime, patients should pay more attention to preventing wound infection and improving wound healing after surgery.

In conclusion, bipolar electrocoagulation and ultrasonic scalpel hemostasis applied to laparoscopic cystectomy led to reduction of ovarian reserve. Therefore, electrocoagulation hemostasis should be used with caution due to irreversible damage of ovarian reserve.

Especially for fertile patients, suture hemostasis of laparoscopic cystectomy is a better option based on ovarian reserve, blood supply, and iatrogenic injury. To strengthen the follow up of survival and early detection of sex hormone after operation contributes to the timely discovery of premature ovarian failure. In the clinic, holistic assessment including age of patients, medical history, symptoms, cyst characteristics, and distribution of cavitas pelvis endometriosis on ovarian reserve should be performed. In addition, patients should be treated with more normal ovarian tissues and less thermal damage of hemostasis, minimizing the impact on ovarian reserve.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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