Int J Clin Exp Med 2020;13(4):2331-2338
www.ijcem.com /ISSN:1940-5901/IJCEM0102503

Original Article

Clinical efficacies of laparoscopic ovarian cyst resection and its effects on ovarian function

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Received September 19, 2019; Accepted November 25, 2019; Epub April 15, 2020; Published April 30, 2020

Abstract: Objective: To explore the clinical efficacies of laparoscopic ovarian cyst resection (LOCR) and its effects on ovarian function. Methods: Ninety patients requiring ovarian cyst resection were selected for prospective study, and were divided into control group (traditional laparotomy surgery, n=45) and observation group (laparoscopy surgery, n=45) according to the random number table. The surgical outcomes, the number of sinusoidal follicular, hormone levels, Doppler-examination related indexes and immune functions in the two groups were observed. Results: The observation group had significantly lower values than the control group in terms of operation duration, intraoperative blood loss, postoperative ventilation time and maximum body temperature (all P<0.05). The level of Estrogen (E2) of the two groups was decreased significantly after operation (P<0.001), and E2 level in the observation group was significantly higher than that in the control group (P<0.01). The levels of luteinizing hormone (LH), and follicle stimulating hormone (FSH) showed opposite trends to E2 changes in the two groups (both P<0.001). The number of sinusoidal follicles in the observation group was significantly larger than that in the control group (P<0.001). Postoperative CD3+ and CD4+ cell numbers, and CD4+/CD8+ of the observation group were significantly higher than those of the control group (all P<0.001). After treatment, peak systolic velocity (PSV) and resistance index (RI) were significantly reduced in both groups, but the observation group had significantly higher PSV and RI (all P<0.001) than the control group. Systolic/diastolic blood flow and pulsatility index showed opposite trends to PSV and RI changes in the two groups (all P<0.05). The incidences of menstrual changes, postoperative adhesion and pelvic pain in the observation group were significantly lower than those in the control group (all P<0.05), and sexual satisfaction in the observation group was significantly higher than that in the control group (P<0.001). Conclusion: compared with traditional laparotomy surgery, LOCR has a better efficacy with reduced surgical trauma, and decreased impacts on patients' immune function and ovarian basal blood flow.

Keywords: Laparoscopy, ovarian cyst resection, ovarian function, hormone level

Introduction

With the change of diet patterns, the increase of work pressure and the continuous aggravation of environmental pollution, the incidence of ovarian cysts in China shows an increasing trend year by year, and most of them are women of childbearing age between 30 and 40 years old [1-3]. Ovarian cyst is a clinically common benign tumor [4]. Its clinical symptoms include abdominal mass, lower abdominal pain and menstrual disorder, which can affect the ovulation and damage the quality of oocytes [5, 6]. Continuously increased size of masses will completely occupy the pelvic cavity, causing dyspnea, odynuria and constipation, with a great impact on the health and quality of life of patients [7]. However, the pathogenesis of ovarian cysts has not been fully explained. Researches have confirmed that such patients are often accompanied with pelvic infection, causing epithelial dysplasia, inflammatory exudation, inflammatory package and other lesions, eventually leading to the occurrence of ovarian cysts [8].

At present, Traditional Chinese Medicine treatment is mainly applicable for patients with cyst diameter ≤5 cm and who can be treated with conservative management, while for patients with cyst diameter >5 cm, surgical treatment is required [9]. Traditional laparotomy surgery is simple, and it can remove the ovarian cyst lesions to the greatest extent. But it is not very acceptable for patients of reproductive age due to large surgical trauma, excessive intraopera-

tive bleeding, long postoperative recovery time and obvious abdominal scar [10]. However, with the continuous development of minimally invasive technology and improvement of equipment, laparoscopic ovarian cyst resection (LOCR) has become a mainstream technology. This operation requires high technical skills of clinicians. And LOCR has higher acceptability with the advantages like less damage to ovarian tissue and pelvic cavity, lower postoperative pain degree, and shorter hospital stay [11]. Clinical data with increased clinical sample size also have pointed out that any type of pelvic surgery has the risk of damage to ovarian function, including insufficient ovarian stromal blood supply, abnormal hormone levels, abdominal inflammatory reaction and decreased ovarian reserve function after surgery, and even infertility [12-14]. At present, there is no conclusion about the effects of laparoscopy on immune function and ovarian stroma, and the effects of carbon dioxide pneumoperitoneum on hemodynamics and partial pressure of carbon dioxide in artery.

Materials and methods

General information

This study was approved by the Ethics Committee of Affiliated Hospital of Gansu Medical College (People's Hospital of Pingliang City). Ninety patients with ovarian cysts admitted to Affiliated Hospital of Gansu Medical College (People's Hospital of Pingliang City) from December 2016 to December 2018 and scheduled for surgical treatment were selected for prospective study. The patients were divided into control group (traditional laparotomy surgery, n=45) and observation group (LOCR, n=45) according to the random number table. All patients and their families were informed of the purpose and cautions of this study before surgery, and then signed the informed consent.

Inclusion criteria: Patients aged from 25 to 45 years old; patients who met the diagnostic criteria of ovarian cyst according to *Gynecology and Obstetrics (2004 Edition)* [15]; patients without relevant hormone therapy within six months before surgery; patients with negative tumor-related markers; patients who were in line with the surgical indicators of ovarian cyst.

Exclusion criteria: Patients with coagulation dysfunction, abnormal immune system and endocrine disease; patients with other tumors; patients with surgical contraindications; patients with malignant changes in uterine fibroids or endometrium; patients with mental disorder or confusion.

Methods

Two groups of patients underwent elective surgery after basic examination. The control group received laparotomy surgery to remove ovarian cysts. Details are as follows. The control group underwent effective lumbar epidural general anesthesia and local anesthesia with lidocaine hydrochloride (Nanjing Jinling Pharmaceutical Co., Ltd., China) in the surgical spot. After the patient achieved deep anesthesia with normal physiological indicators, the surgical incision was determined at the site 10-15 cm from the right midabdominal line and 5-6 cm from the upper lumbar iliac bone and was strictly sterilized. The superficial skin was cut open parallel to the midabdominal line and the fascia was separated by blunt dissection. Away from the blood vessels and nerves, the peritoneum was opened to 3-5 cm to find the lesion site, and the diseased tissues were completely excised. Then the ovary was sutured to stop bleeding. Normal saline containing penicillin and streptomycin was used to flush the affected part. After the blood stains were cleaned up in the surgical part, the abdominal suture was performed routinely. Then the surgical part was disinfected, and the drainage catheter was inserted.

In the observation group, an incision was made 3-5 cm above and below the umbilicus after the same anesthesia in the control group. A total of 12 mmHg CO_2 was injected using pneumoperitoneum machine (0620-030-020; STRYKER, USA) to maintain the pneumoperitoneum, and then the sterilized laparoscopic lens (26003AA/26003B; Storz, Germany) was inserted. With the help of digital video technology, the images captured by the laparoscopic lens were transmitted to the post-signal processing system through optical fiber and displayed on the special monitor in real time. The images of the patient's organs from different angles were displayed on the monitor screens. A 1-2 cm incision was made at the intersection point of the anterior superior iliac spine and the umbilical cord, and a unipolar electric hook was inserted to fix the cyst. The cyst was separated by blunt dissection and the tumor was excised by sharp resection. Electrocoagulation was performed on the surgical site, and the surgical part was strictly sterilized. After examination,

Table 1. Comparison of general information ($\bar{x}$ ± sd; n, %)

	Control group (n=45)	Observation group (n=45)	χ^2/t	P
Age (year)	32.0±8.3	29.6±6.8	1.448	0.151
Cyst diameter (cm)	8.26±1.25	8.52±1.28	0.947	0.347
Pathological type			1.141	0.565
Mature teratoma	12 (26.67)	15 (33.33)		
Serous cystadenoma	22 (48.89)	17 (37.78)		
Mucinous cystadenoma	11 (24.44)	13 (28.89)		
Course of disease (year)	3.60±0.35	3.46±0.58	1.363	0.176
Menstrual cycle (day)	25.70±3.20	26.17±4.09	0.600	0.552
Body mass index (kg/m^2)	25.20±2.45	24.23±4.04	1.363	0.176
Marriage (yes/no)	38/7	42/3	1.013	0.314
Childbearing history (yes/no)	29/16	35/10	1.947	0.163

the abdominal suture was performed routinely, and prophylactic antibiotics were injected.

Outcome measures

Main outcome measures: The operation duration, intraoperative blood loss, intestinal function recovery time and change of postoperative body temperature were recorded. Fasting venous blood was extracted at a fixed time point in the second or third day of the menstrual cycle before and two months after surgery; the menstrual cycle was regard as 30 days for the irregular one. With the help of a full-automatic chemiluminescence immune analyzer (UniCel DxI 800; Beckman Coulter, Inc., China), the antibodies of follicle-stimulating hormone (FSH; HOR-253; Shanghai Ximei Chemical Co., Ltd., China), luteinizing hormone (LH; Bioscience (Tianjin) Diagnostic Technology Co., Ltd., China), and estrogen (E2; Sichuan Maker Biotechnology Co., Ltd., China) were used to detect the levels of FSH, LH and E2. The number of patients with menstrual changes, postoperative adhesions and pelvic pain within 3 months after surgery was counted. According to the brief index of sexual function for women, the sexual satisfaction of patients was divided into four levels: very satisfied, satisfied, generally satisfied and unsatisfied. Sexual satisfaction = Number of case (very satisfied + satisfied)/total number of cases.

Secondary outcome measures: Blood routine was determined by hematology analyzer (UniCel DxH; BECKMAN COULTER, USA) and CD3+, CD4+ and CD8+ cell numbers were detected by flow cytometer (CytoFLEX S; BECKMAN COULTER, USA) before and 3 days after treatment. Doppler probe (DVM-4500, Blood Flow Detector Doppler; Hadeco Inc., Japan) was used for blood measurement to observe the ovarian stromal blood flow velocity. Resistant index (RI) = (Peak systolic velocity (PSV) - end diastolic velocity/PSV; pulsatility index (PI) = (PSV - end diastolic velocity)/mean velocity. The mean value of the two measurements for each patient was taken. Flying color doppler diagnostic ultrasound system (Neusoft Medical Systems Co., Ltd, China) with the frequency of 5.0-7.5 MHz vaginal probe was used to record the number of sinusoidal follicles. Adhesion was examined one week after surgery. Three months after surgery, menstrual changes, pelvic pain and sexual satisfaction were investigated through outpatient records and telephone follow-up.

Statistical analysis

Statistical analysis was conducted by SPSS21.0 software. Measurement data were expressed as mean ± standard deviation ($\bar{x}$ ± sd) and the data with normal distribution between two groups were compared by independent t test. Count data were expressed as percent (%) and were analyzed by chi-square test between two groups. A *P* value of below 0.05 is considered statistically significant.

Results

General information

No difference was seen in terms of age, course of disease, cyst diameter, menstrual cycle, body mass index, marriage, childbearing history and pathological type of cyst between the two groups (all P>0.05). See **Table 1**.

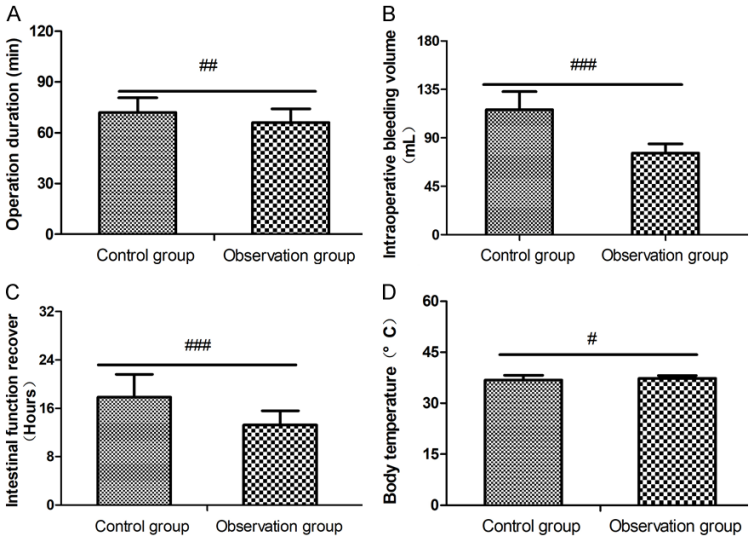

Figure 1. Comparison of surgical outcomes ($\bar{x}$ ± sd). A. Operation duration. Shorter operation duration means fewer adverse reaction. B. Intraoperative bleeding volume. More bleeding volume means worse prognosis. C. Intestinal function recovery time. Shorter recovery time suggests better prognosis. D. Body temperature. The higher temperature patients get, the higher risk of infection they are facing. #P<0.05, ##P<0.01, ###P<0.001.

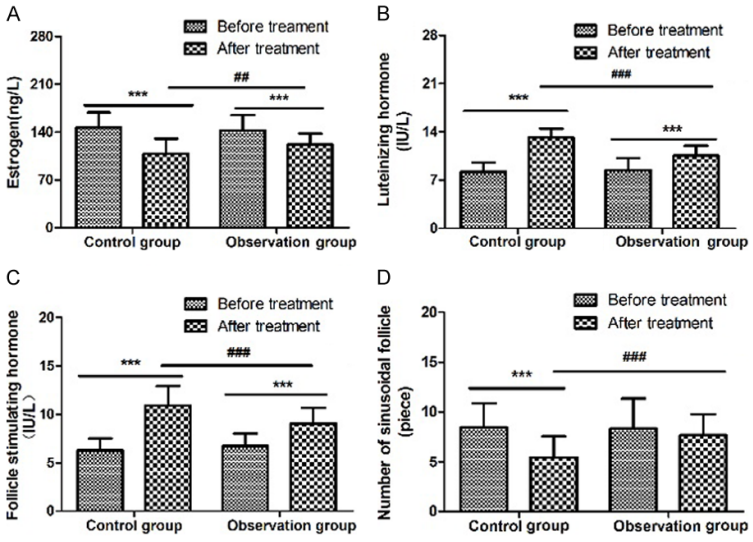

Figure 2. Comparisons of hormone levels and the number of sinusoidal follicles ($\bar{x}$ ± sd). A. Estrogen level. The lower level presents more serious damage to ovary. B. Luteinizing hormone. The higher level presents more serious damage to ovary. C. Follicle-stimulating hormone. The higher level presents more serious damage to ovary. D. The number of sinusoidal follicles. The higher number presents less damage to ovary. ***P<0.001, compared within the same group; ##P<0.01, ###P<0.001, compared between two groups.

Surgical outcomes

Compared with the control group, the observation group had significantly shorter operation duration and postoperative ventilation time, less intraoperative blood loss, and lower maximum body temperature (all P<0.05). See **Figure 1**.

Hormone levels and the number of sinusoidal follicular

Before treatment, there was no difference in the levels of E2, LH, and FSH, and the number of sinusoidal follicular between the two groups (all P>0.05). After treatment, the level of E2 in the two groups were decreased significantly (both P< 0.01) and the level of E2 in the observation group was higher than that in the control group (P<0.001). The levels of LH, and FSH showed opposite trends to E2 changes in the two groups (both P<0.001). The number of sinusoidal follicular in the observation group was larger than that in the control group (P<0.001). See **Figure 2**.

Immune functions

Before treatment, there was no difference in CD3+, CD4+ and CD8+ cell numbers and CD4+/CD8+ between the two groups (all P>0.05). After treatment, CD3+ and CD4+ cell numbers and CD4+/CD8+ in the two groups were decreased significantly and those in the observation group were higher than those in the control group (all P<0.001). See **Figure 3**.

Doppler-examination related indexes

Before treatment, no difference was seen in PSV, systolic/diastolic blood flow (S/D), RI and PI between the two groups (all P>0.05). After treatment, PSV and RI in the two groups were decreased significantly and those in the observation group were significantly higher than those in the control group (all P<0.001). S/D and PI showed

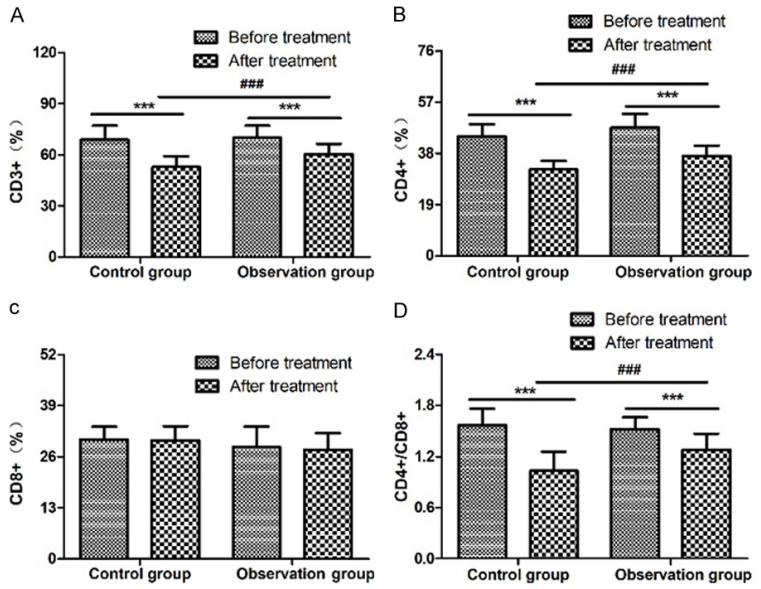

Figure 3. Comparison of immune functions ($\bar{x}$ ± sd). A. CD3+ (%). Higher percentage represents stronger immunity. B. CD4+ (%). Higher percentage represents stronger immunity. C. CD8+ (%). Lower percentage represents stronger immunity. D. CD4+/CD8+. Higher percentage represents stronger immunity. ***P<0.001, compared within the same group; ###P<0.001, compared between two groups. CD, cluster designation.

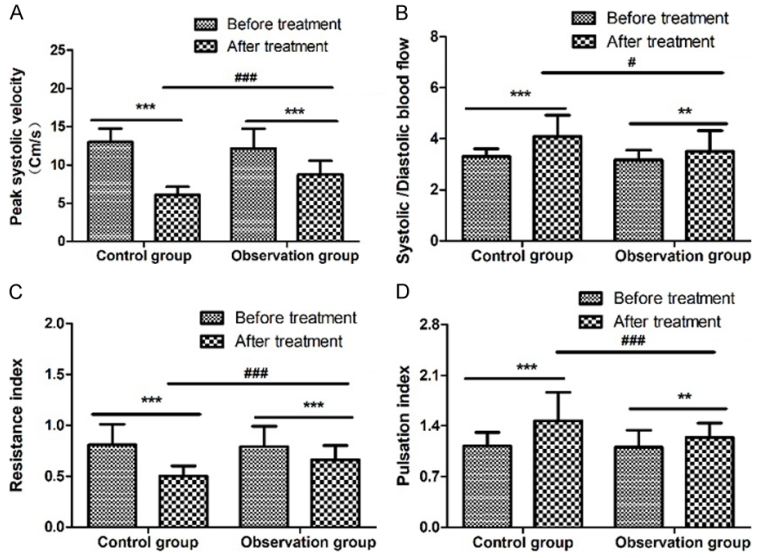

Figure 4. Comparison of Doppler-examination related index ($\bar{x}$ ± sd). A. Peak systolic velocity. The higher value presents faster blood speed. B. The ratio of systolic to end-diastolic blood flow velocity. The higher value presents better blood supply. C. Resistance index. The lower value presents weaker blood resistance. D. Pulsatility index. The higher value presents less blood supply. **P<0.01, ***P<0.001, compared within the same group; #P<0.05, ###P<0.001, compared between two groups.

opposite trends to PSV and RI changes in the two groups (all P<0.05). See **Figure 4**.

Short-term efficacy

After treatment, the incidences of menstrual changes, postoperative adhesion and pelvic pain in the observation group were significantly lower than those in the control group respectively (all P<0.05), and sexual satisfaction in the observation group was significantly higher than that in the control group (P<0.001). See **Table 2**.

Discussion

Traditionally, ovary is thought to be only associated with follicular formation, but it also plays an irreplaceable role in the metabolism of steroids and other hormones in the body [16]. Ovarian cyst is a common ovary disease, and its symptoms are not significant in the early stage so that it is not easy to attract attention [17, 18]. Several studies have reported that compared with traditional laparotomy surgery, LOCR can significantly reduce intraoperative blood loss, shorten postoperative recovery time and reduce postoperative complications, but it is not applicable for patients with possible ovarian malignancy [19-22]. Therefore, how to choose appropriate surgical treatment for patients is critical.

The ovarian tissue is brittle and vulnerable to unnecessary damage during surgery. Therefore, researchers are looking for appropriate surgical methods that can not only remove the cyst but also protect the normal ovarian tissue and avoid too much damage, so as to reduce the risk factors affecting ovarian stromal blood supply after surgery [23-25]. Laparoscopic electrocoagulation

Table 2. Comparison of short-term efficacy (n, %)

	Control group (n=45)	Observation group (n=45)	χ^2	P
Menstrual change	11 (24.44)	2 (4.44)	7.283	0.007
Postoperative adhesion	13 (28.89)	3 (6.67)	7.601	0.006
Satisfaction for sex life	18 (40.00)	35 (77.78)	13.260	0.000
Pelvic pain				
Before treatment	39 (86.67)	42 (93.33)	1.111	0.292
After treatment	15 (33.33)	6 (13.33)	5.031	0.025

is the most commonly used method, but it has too much damage to ovarian function. Thus, suture was performed to achieve hemostasis in this study. By this way, laparoscopic surgery has little impact on ovarian function in the removal of ovarian cysts and postoperative suture, thereby minimizing the impact on the number and quality of follicles [26]. Previous work has shown that laparoscopic surgery can also remove suspected small residual lesions during the surgery, effectively reducing the risk of postoperative recurrence and increasing the probability of pregnancy in similar patients [27]. Although laparoscopy is effective in the treatment of ovarian cysts, more clinical studies are needed.

The whole surgical process of laparoscopic surgery is conducted in a completely closed abdominal cavity. This surgical method can prevent the exposure of viscera to the external environment, reduce the damage of surgical instruments to organs and tissues and the adverse psychological effects caused by the damage. In addition, the internal situation of the pelvic cavity can be directly observed during the surgery, and small lesions can be more clearly found. These findings are consistent with the results of this study that compared with the control group, the observation group had significantly shorter operation duration and postoperative ventilation time, less intraoperative blood loss, and lower maximum body temperature [28]. Zaitoun et al. have confirmed that during treatment, LOCR still causes some substantial damage to the ovary, mainly due to the local inflammatory reaction caused by the surgery affecting the ovarian blood supply. Generally, reduced E2 and increased FSH are the most important manifestations of impaired ovarian function [29]. In this study, there were decreased E2 and increased FSH in the two groups after surgery, but the degree of change in the observation group was significantly lower than that in the control group. And the number of sinusoidal follicular in the observation group was larger than that in the control group. The studies of Gomatos. have confirmed that the stress response of the body caused by surgery can interfere with the stable state of the autoimmune system and increase the incidence of postoperative recurrence and infection [30]. It was found that the observation group were significantly higher than those in the control group in terms of CD3+ and CD4+ cell numbers and CD4+/CD8+. The above data have verified that LOCR can effectively reduce the damage of the cellular immune function of human body, so it is more conducive to prevent the occurrence of postoperative infection and maintain the steady state of the immune system to promote the recovery.

Studies have shown that the changes in ovarian stromal blood flow can reflect the therapeutic effect, and greater blood flow resistance in the ovarian stromal blood vessels will cause less ovarian blood supply [31]. It was found that after treatment, PSV and RI in the two groups were decreased significantly and those in the observation group were significantly higher than those in the control group, while S/D and PI showed opposite trends in the two group. The above results have proved that compared with laparotomy surgery, LOCR has significantly lower damage degree to ovarian function.

There are deficiencies in this study, such as small sample size, short statistical duration of various indicators, and none-evaluation of the effect of surgical methods on long-term clinical outcomes. In addition, a consensus on the way to carry out LOCR was not reached. The main contradiction is that LOCR can't provide effective evidence for cytological diagnosis, and there is a possibility of delayed diagnosis and spread of ovarian cancer.

In summary, compared with traditional laparoscopic surgery, LOCR has a better efficacy

with reduced surgical trauma, and decreased impacts on patients' immune function and ovarian basal blood flow.

Disclosure of conflict of interest

None.

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