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ORIGINAL ARTICLE

Retrospective Study

Efficacy and safety of minimally invasive laparoscopic surgery under general anesthesia for ovarian cancer

Xian Qin, Chen Chen, Yang Liu, Xian-Hong Hua, Jia-Yi Li, Meng-Jie Liang, Fang Wu

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Xian Qin, Chen Chen, Yang Liu, Xian-Hong Hua, Department of Anesthesiology, The First People's Hospital of Jiangxia District, Wuhan 430200, Hubei Province, China

Jia-Yi Li, Meng-Jie Liang, Fang Wu, Department of Obstetrics and Gynecology, The First People's Hospital of Jiangxia District, Wuhan 430200, Hubei Province, China

Corresponding author: Fang Wu, MBChB, Department of Obstetrics and Gynecology, The First People's Hospital of Jiangxia District, No. 1 Zhifang Cultural Avenue, Jiangxia District, Wuhan 430200, Hubei Province, China. wufang771025@163.com

Abstract

BACKGROUND

Ovarian cancer is one of the most common malignant tumors in female reproductive system in the world, and the choice of its treatment is very important for the survival rate and prognosis of patients. Traditional open surgery is the main treatment for ovarian cancer, but it has the disadvantages of big trauma and slow recovery. With the continuous development of minimally invasive technology, minimally invasive laparoscopic surgery under general anesthesia has been gradually applied to the treatment of ovarian cancer because of its advantages of less trauma and quick recovery. However, the efficacy and safety of minimally invasive laparoscopic surgery under general anesthesia in the treatment of ovarian cancer are still controversial.

AIM

To explore the efficacy and safety of general anesthesia minimally invasive surgery in the treatment of ovarian cancer.

METHODS

The clinical data of 90 patients with early ovarian cancer in our hospital were analyzed retrospectively. According to the different surgical treatment methods, patients were divided into study group and control group (45 cases in each group). The study group received minimally invasive laparoscopic surgery under general anesthesia for ovarian cancer, while the control group received traditional open surgery for ovarian cancer. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), clinical efficacy and safety of the two groups were compared.

RESULTS

The intraoperative blood loss, length of hospital stay, postoperative gas evacuation time, and postoperative EORTC QLQ-C30 score of the study group were significantly better than those of the control group ($P < 0.05$). The incidence of postoperative complications in the study group was significantly lower than in the control group ($P < 0.05$). The two groups had no significant differences in the preoperative adrenocorticotropic hormone (ACTH), androstenedione (AD), cortisol (Cor), cluster of differentiation 3 positive (CD3+), and cluster of differentiation 4 positive (CD4+) indexes ($P > 0.05$). In contrast, postoperatively, the study group's ACTH, AD, and Cor indexes were lower, and the CD3+ and CD4+ indexes were higher than those in the control group ($P < 0.05$).

CONCLUSION

Minimally invasive laparoscopic surgery under general anesthesia in patients with early ovarian cancer can significantly improve the efficacy and safety, improve the short-term prognosis and quality of life of patients, and is worth popularizing.

Key Words: Early-stage ovarian cancer; Efficacy; Minimally invasive; Laparoscopy; Safety; Surgery

Core Tip: This study found that compared with traditional open surgery, minimally invasive laparoscopic surgery under general anesthesia has better curative effect, faster recovery speed, lower risk of complications and less impact on immune function in the treatment of patients with early ovarian cancer. Therefore, minimally invasive laparoscopic surgery under general anesthesia can be the first choice for patients with early ovarian cancer.

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INTRODUCTION

Ovarian cancer is one of the malignant tumors of the female reproductive system. It is mainly characterized by lower abdominal masses and abdominal effusion as clinical manifestations. According to reports, the mortality rate of ovarian cancer ranks first among gynecological malignancies. Most cases originate from the ovarian epithelium and during the course of the disease, local infiltration and distant metastasis are common[1]. Ovarian cancer accounts for 2.5% of female malignancies, and the 5-year survival rate for early-stage ovarian cancer is as high as 93%. However, early-stage ovarian cancer usually presents no characteristic symptoms, making diagnosis relatively difficult. Approximately 70% of ovarian cancer patients are diagnosed in the late stage, resulting in a poor prognosis with a 5-year survival rate of less than 30%[2-4]. Therefore, early and accurate diagnosis as well as standardized treatment can better improve the prognosis of ovarian cancer patients[5]. Currently, surgery remains the main treatment for early-stage ovarian cancer. However, traditional surgical procedures, primarily open surgeries, have many drawbacks including large trauma and slow patient recovery. With the continuous development of laparoscopic techniques, their application in the treatment of early-stage ovarian cancer has become more widespread[6,7].

Compared to the issues of large incision and slow recovery associated with open surgery, laparoscopic techniques have the following advantages: smaller trauma[8], simultaneous diagnosis and treatment, faster recovery[9], shorter hospitalization time[10], better abdominal cosmetic effect, and easy preservation of imaging data. In the diagnosis and treatment of ovarian cancer, laparoscopic techniques can complement open surgeries. In clinical practice, laparoscopic exploration is performed for suspected pelvic masses, and if intraoperative frozen pathology confirms ovarian cancer, the procedure can be converted to open surgery for comprehensive staging, thus avoiding the need for a second surgery[11,12]. For patients with advanced ovarian cancer, laparoscopic exploration can be performed. If evaluated as suitable for primary tumor debulking, the procedure can be directly converted to open surgery for tumor debulking[13,14].

Therefore, this study focuses on early-stage ovarian cancer patients and evaluates the application value of open surgery and minimally invasive laparoscopic surgery under general anesthesia in this population, aiming to provide clinical reference for the optimal selection of surgical approaches in the treatment of early-stage ovarian cancer.

MATERIALS AND METHODS

General information

A retrospective analysis was conducted on the clinical data of 90 early-stage ovarian cancer patients admitted to our department from January 2022 to January 2023. According to different surgical treatment methods, the patients were

divided into a study group and a control group, with 45 cases in each group. The study group underwent laparoscopic ovarian cancer surgery, while the control group underwent open abdominal ovarian cancer surgery. Pathological examination was performed on all tumors, including all histological types of ovarian cancer. After comprehensive staging, epithelial ovarian cancer was defined as stage I or II disease according to the International Federation of Gynecology and Obstetrics (FIGO) classification, excluding patients with stage III or IV disease.

Inclusion criteria

Inclusion criteria: (1) Confirmed diagnosis of ovarian cancer through imaging and cytology examination; (2) Diagnosed with early-stage ovarian cancer according to the FIGO criteria; (3) Suitable for surgical intervention; and (4) No tumor metastasis.

Exclusion criteria: (1) Presence of other tumors; (2) Organ failure; (3) Inability to tolerate surgery; or (4) Allergy to anesthesia drugs.

Data collection

Retrospective review of electronic medical records of all included patients was conducted to collect demographic and clinical characteristics, preoperative assessment, surgical description (duration, amount of bleeding, tumor rupture, and intraoperative complications), postoperative complications and their occurrence time, tolerance to oral intake and activity, and length of hospital stay.

Study methods

Study group: Study group (Laparoscopy group) performed laparoscopic lymph node dissection for treatment. The patient received general anesthesia and was placed in the lithotomy position with bladder lithotomy. After disinfection, aseptic drapes were placed and a uterine elevator was inserted through the vagina. A puncture needle was inserted about 3 cm above the umbilicus, and pneumoperitoneum was established with an insufflation pressure of 12-14 mmHg. After the procedure was completed, a laparoscope was inserted, and the patient's position was adjusted to a high hip and low head position under the monitoring of the laparoscope. Cannulation was performed under laparoscopic guidance at the lower abdomen on both sides, with 2 or 3 5-mm Trocar ports. The abdominal and pelvic cavities were thoroughly explored, and approximately 200 mL of 0.9% saline solution was used for irrigation of the abdominal and pelvic cavities. The irrigation fluid was then collected and sent for examination. Based on intraoperative exploration, ovarian tumors and adnexa were removed, and rapid frozen sections were performed to examine the tumor lesions. Bilateral adnexectomy, hysterectomy, pelvic lymph node dissection, and abdominal aorta lymph node dissection were performed according to the pathological results. The excised tissues were placed in specimen bags.

Control group: In the control group (open surgery group), under general anesthesia, the patient was placed in a supine position. After routine disinfection and draping, the midline of the abdomen was used as the surgical incision. The abdomen was opened layer by layer to expose the lesion site, and the same tumor cell reduction technique as the laparoscopy group was performed. Postoperatively, all patients received chemotherapy when conditions allowed.

Observation indicators

Perioperative indicators: Operation time, intraoperative bleeding volume, number of lymph nodes cleaned, postoperative anal exhaust time, time to get out of bed, and length of hospital stay.

Occurrence of complications: Incision infection, pulmonary infection, urinary retention, venous thrombosis, and intestinal obstruction, *etc.*

Quality of life: The quality of life of patients was evaluated before surgery, 1 month after surgery, and 3 months after surgery using the Chinese version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire. It includes 30 items with a total score of 126 points. A higher score indicates a better quality of life[15].

Stress response: 5 mL of fasting morning venous blood was taken before surgery and 1 d after surgery, centrifuged at 3000 rpm for 10 min to separate serum, and enzyme-linked immunosorbent assay was used to detect adrenocorticotropic hormone (ACTH), androstenedione (AD), and cortisol (Cor).

Immune function: 5 mL of fasting morning venous blood was collected before surgery and 1 day after surgery, and the supernatant was taken after centrifugation for flow cytometry to detect cluster of differentiation cluster of differentiation 3 positive (CD3+) and CD4+ levels.

Statistical analysis

Statistical analysis was performed using SPSS 22.0 statistical software. Continuous variables were expressed as mean ± SD and compared using *t*-test or *F*-test. Categorical variables were expressed as percentages [*n* (%)] and compared using χ^2 test. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

Comparison of baseline characteristics between the two patient groups

Study group (using laparoscopic ovarian cancer surgery) patients aged 35 to 66 years, with an average age of 55.0 ± 17.1 years; Body mass index (BMI) score of 24.1 ± 3.9 kg/m^2; tumor average diameter 6.84 ± 2.15 cm; FIGO clinical stage: stage I in 21 cases, accounting for 46.67%, stage II in 24 cases, accounting for 53.33%; pathological classification: mucinous carcinoma in 20 cases, accounting for 44.44%, serous adenocarcinoma in 16 cases, accounting for 35.56%, endometrioid carcinoma in 6 cases, accounting for 13.33%, clear cell carcinoma in 3 cases, accounting for 6.67%; control group (using open abdominal ovarian cancer surgery) patients aged 34 to 65 years, with an average age of 55.8 ± 18.8 years; BMI score of 24.7 ± 4.2 kg/m^2; tumor average diameter 6.92 ± 2.21 cm; FIGO clinical stage: stage I in 23 cases, accounting for 51.11%, stage II in 22 cases, accounting for 48.89%; pathological classification: mucinous carcinoma in 21 cases, accounting for 46.67%, serous adenocarcinoma in 15 cases, accounting for 33.33%, endometrioid carcinoma in 5 cases, accounting for 11.11%, clear cell carcinoma in 4 cases, accounting for 8.89%. The general clinical data of the research group and the control group were compared, and there was no statistically significant difference ($P > 0.05$), indicating comparability, as shown in Table 1.

Comparison of perioperative conditions between two groups of patients

The research group had significantly less intraoperative bleeding compared to the control group. The postoperative anal exhaust time, time to get out of bed, and length of hospital stay were significantly shorter in the research group compared to the control group. The differences between the two groups were statistically significant ($P < 0.05$). There was no statistically significant difference in surgical time and number of lymph node dissections compared to the control group ($P > 0.05$), as shown in Table 2.

Comparison of incidence of complications between the two groups

The incidence of complications in the study group was significantly lower than that in the control group, with a statistically significant difference ($\chi^2 = 7.688$, $P < 0.05$), as shown in Table 3.

Comparison of quality of life between the two groups of patients

There was no statistically significant difference in preoperative quality of life scores between the study group and control group ($P > 0.05$); however, the postoperative 1-month and 3-month quality of life scores in the study group were significantly higher than those in the control group ($P < 0.05$), as shown in Table 4.

Comparison of stress response between the two groups

There was no difference in the preoperative levels of ACTH, AD, and Cor between the two groups ($P > 0.05$). However, after the surgery, all these indicators in the study group were significantly lower than those in the control group ($P < 0.05$), as shown in Table 5.

Comparison of immune function between the two groups

There was no difference in preoperative CD3+ and CD4+ levels between the two groups ($P > 0.05$). However, after the surgery, these indicators in the study group were higher than those in the control group ($P < 0.05$), as shown in Table 6.

DISCUSSION

Ovarian cancer is a common clinical condition. Early ovarian cancer refers to stage I and II Ovarian cancer. Due to its deep anatomical location, early ovarian cancer may have no typical clinical manifestations. It is often diagnosed when patients present with menstrual disorders, lower abdominal pain or discomfort, or palpable masses. Most patients are already in the advanced stage when diagnosed, and the treatment results are poor. Moreover, this disease has a high incidence and mortality rate. Surgery is one of the main treatment methods for early ovarian cancer. Open surgery is the traditional treatment method for early ovarian cancer, aiming to remove tumor tissue as much as possible to achieve a macroscopically tumor-free effect. However, this surgical approach has limitations such as large incisions and slow postoperative recovery[16]. In recent years, minimally invasive laparoscopic surgery under general anesthesia has been applied in the treatment of various diseases due to its minimally invasive advantages. Under laparoscopic visualization, it can fully utilize its advantages of minimally invasiveness and magnified vision, making the surgical procedure smoother[17]. With the further development of minimally invasive laparoscopic surgery under general anesthesia, adopting minimally invasive laparoscopic surgery under general anesthesia to treat early ovarian cancer will become a new standard procedure.

This study shows that the research group has lower blood loss and higher number of lymph node clearances compared to the control group. The postoperative exhaust time and length of stay in the hospital are both shorter, indicating that minimally invasive laparoscopic surgery under general anesthesia can significantly reduce intraoperative blood loss, improve the number of lymph node clearances, accelerate postoperative exhaust time, and shorten hospital stay. The analysis suggests that laparoscopy can enlarge the surgical field of view, better distinguish anatomical levels, and provide a more comprehensive clearance of pelvic lymph nodes and para-aortic lymph nodes[18]. In addition, laparoscopic instruments are more delicate and can cut tissues closely, reducing damage to surrounding organs and minimizing

Table 1 Basal characteristics of patients included in the study, according to surgical approach, *n* (%)

Index	Study group (*n* = 45)	Control group (*n* = 45)	*t*/χ^2 value	*P* value
Age (yr)	55.0 ± 17.1	55.8 ± 18.8	0.211	> 0.05
BMI (kg/m^2)	24.1 ± 3.9	24.7 ± 4.2	0.702	> 0.05
Tumor diameter (cm)	6.84 ± 2.15	6.92 ± 2.21	0.174	> 0.05
FIGO			0.178	> 0.05
I	21 (46.67)	23 (51.11)		
II	24 (53.33)	22 (48.89)		
Type of pathology			0.645	> 0.05
Mucinous cancer	20 (44.44)	21 (46.67)		
Serous carcinoma	16 (35.56)	15 (33.33)		
Endometrioid cancer	6 (13.33)	5 (11.11)		
Clear cell carcinoma	3 (6.67)	4 (8.89)		

BMI: Body mass index; FIGO: International Federation of Gynecology and Obstetrics.

Table 2 Perioperative comparison between study and control groups (mean ± SD)

Index	Study group (*n* = 45)	Control group (*n* = 45)	*t* value	*P* value
Duration of surgery (min)	257.41 ± 28.16	255.23 ± 28.37	0.366	> 0.05
Intraoperative bleeding quantity (min)	323.76 ± 40.25	387.44 ± 43.23	7.232	< 0.05
Lymph node clearance number of sweeps (pcs)	25.78 ± 3.35	26.04 ± 3.17	0.378	> 0.05
Postoperative anus exhaust time (d)	1.96 ± 0.42	2.61 ± 0.54	6.374	< 0.05
Get out of bed after surgery time (d)	2.85 ± 0.53	3.92 ± 0.64	8.638	< 0.05
Postoperative hospitalization time (d)	13.29 ± 2.11	16.66 ± 2.24	7.346	< 0.05

Table 3 Comparison of complications between study and control groups, *n* (%)

Index	Study group (*n* = 45)	Control group (*n* = 45)	χ^2 value	*P* value
Incision infection	1 (2.22)	2 (4.44)		
Lung infections	1 (2.22)	3 (6.67)		
Urinary retention	1 (2.22)	2 (4.44)		
Venous thrombosis	0 (0.00)	1 (2.22)		
Ileus	0 (0.00)	1 (2.22)		
Total	5 (6.67)	9 (20.00)	7.688	< 0.05

intraoperative blood loss. On the other hand, open surgery has limited visual range and more restrictions on surgical instruments, resulting in fewer lymph node clearances and more blood loss during the procedure. Therefore, open surgery requires a longer recovery time and extended length of hospital stay compared to minimally invasive laparoscopic surgery under general anesthesia[19].

Surgical safety has always been an important concern in clinical practice. Studies have shown that the incidence and recurrence rates of complications were significantly lower in the study group compared to the control group, indicating that minimally invasive laparoscopic surgery under general anesthesia can significantly reduce postoperative complications and have a high level of safety. The reasons for this analysis are that minimally invasive laparoscopic surgery under general anesthesia causes less tissue damage, reduces the risk of postoperative infections and other complications, and promotes milder reflex spasms of the anal sphincter due to smaller incisions and less postoperative pain. As a result, the risks of postoperative urinary retention and urinary incontinence are lower[20,21]. At the same time, performing surgical treatment under laparoscopy allows physicians to clearly explore the diseased tissue and its surrounding tissues. With the magnification function of laparoscopy, physicians can more thoroughly remove tumor tissues, thereby reducing

Table 4 Quality of life scores comparison between study and control groups (mean ± SD, points)

Index	Study group (*n* = 45)	Control group (*n* = 45)	*t* value	*P* value
Preoperatively	65.62 ± 9.58	66.12 ± 10.26	0.239	> 0.05
One month after surgery	66.25 ± 8.95	60.42 ± 8.53	3.163	< 0.05
Three months after surgery	78.95 ± 12.39	66.84 ± 11.34	4.837	< 0.05
F value	23.467	5.447		
P value	< 0.05	< 0.05		

Table 5 Comparison of the two sets of stress responses (mean ± SD)

Index	Group	Study group (*n* = 45)	Control group (*n* = 45)	*t* value	*P* value
ATCH (pmol/L)	Before surgery	11.22 ± 5.35	11. 64 ± 5.51	0.367	> 0.05
	After surgery	14.21 ± 12.03	20. 35 ± 12.37	2.387	< 0.05
AD (pmol/L)	Before surgery	30.35 ± 7.49	31. 22 ± 7.48	0.551	> 0.05
	After surgery	39.69 ± 8.71	46. 86 ± 7.36	4.218	< 0.05
Cor (nmol/L)	Before surgery	230.51 ± 8.92	231. 64 ± 8.76	0.606	> 0.05
	After surgery	299.13 ± 9.42	312. 02 ± 9.64	6.4150	< 0.05

ATCH: Adrenocorticotropic hormone; AD: Androstenedione; Cor: Cortisol.

Table 6 Comparison of the two groups of immune function (mean ± SD)

Index	Group	Study group (*n* = 45)	Control group (*n* = 45)	*t* value	*P* value
CD3+	Before surgery	53.54 ± 5.07	55.56 ± 5.12	1.881	> 0.05
	After surgery	50.85 ± 5.16	43.12 ± 5.82	6.667	< 0.05
CD4+	Before surgery	35.32 ± 4.95	33.91 ± 5.53	1.274	> 0.05
	After surgery	32.64 ± 3.06	27.61 ± 3.24	7.571	< 0.05

CD3+: Cluster of differentiation 3 positive; CD4+: Cluster of differentiation 4 positive.

the postoperative recurrence rate and improving the prognosis of ovarian cancer patients[22].

Stress response mainly refers to the changes in various neuroendocrine systems in the body after trauma caused by surgery or anesthesia, which is closely related to the trauma of surgery[3]. ACTH is secreted by the pituitary gland and has the function of promoting the secretion of corticosteroids by the adrenal cortex. When the body is stimulated by trauma such as surgery, it can cause pituitary-adrenal axis excitation, which in turn triggers a series of neuroendocrine responses, belonging to the body's adaptive stress response[23]. Some studies have pointed out that the higher the level of Cor, the more severe the trauma in patients. Sustained high levels of serum Cor can lead to patient death. Therefore, dynamic monitoring of serum Cor levels can serve as a sensitive indicator to evaluate the body's stress response, which helps in assessing the patient's stress status[24]. AD belongs to adrenal medullary hormones, which are rapidly metabolized in the body. Testing AD can help assess medullary function, maintain sympathetic nervous system activity, and promote normal heart rhythm. It is reported that the postoperative research group had lower levels of ACTH, AD, and Cor compared to the reference group, indicating that minimally invasive laparoscopic surgery under general anesthesia treatment for early-stage ovarian cancer patients had a smaller impact on the body's stress response. This may be related to the minimally invasive nature of minimally invasive laparoscopic surgery under general anesthesia, smaller surgical incisions, less damage to the abdominal-pelvic tissues, timely and reasonable hemostasis, and less trauma to the body, which can help reduce the body's stress response and promote postoperative recovery.

CD3+ is an antigen found on the surface of T lymphocytes, mainly mature T cells, and it represents the immune function of the body. CD4+ cells play an important role in the immune system, mainly expressed by helper T cells, and they are receptors for TCR recognition of antigens. Abnormal levels of T lymphocytes can lead to a decrease in physiological functions in the body[25,26]. The study concluded that the CD3+ and CD4+ markers in the postoperative research group were higher compared to the reference group, indicating that minimally invasive laparoscopic surgery under general anesthesia for early ovarian cancer has minimal impact on the immune function of patients. This may be

due to the advantages of minimally invasive laparoscopic surgery under general anesthesia, such as minimally invasive and high safety, which can avoid damage to normal organ tissues of patients during surgery, thereby reducing damage to the body and minimizing the impact on immune function. At the same time, early ovarian cancer itself has a reduced immune function due to the influence of malignant tumors. Compared to open surgery, minimally invasive laparoscopic surgery under general anesthesia can accurately and effectively remove tumors, contributing to the recovery of immune function. This further confirms the effectiveness and feasibility of minimally invasive laparoscopic surgery under general anesthesia for early ovarian cancer.

Limitations

As a retrospective study, this study also has limitations, such as the relatively small number of patients in the study, which may affect the universality of the results. Because the study is a retrospective collection of patients' clinical data, the potential confounding factors cannot be completely ruled out, which may have an impact on the rigor of the results. In the future, a large sample prospective study will be further carried out to further verify the accuracy of the results.

CONCLUSION

In summary, minimally invasive laparoscopic surgery under general anesthesia for early-stage ovarian cancer patients can further improve treatment efficacy, promote quick postoperative recovery, and have minimal impact on the body's stress response and immune function. The risk of postoperative complications is low.

ARTICLE HIGHLIGHTS

Research background

The background of this study mainly focuses on patients with early ovarian cancer, and evaluates the application value of open surgery and minimally invasive laparoscopic surgery under general anesthesia in this population, aiming at providing clinical reference for the choice of the best surgical method for early ovarian cancer.

Research motivation

The research motivation of this study is to evaluate the application value of open surgery and endoscopic surgery for patients with early ovarian cancer, aiming at providing clinical reference for the best choice of surgical methods in the treatment of early ovarian cancer.

Research objectives

The objectives of this study is to evaluate the application value of open surgery and minimally invasive laparoscopic surgery under general anesthesia in patients with early ovarian cancer, so as to improve the therapeutic effect, promote postoperative recovery, and reduce the risk of postoperative complications, and provide reference for clinical treatment.

Research methods

According to the different surgical methods of patients, this study was randomly divided into study group (laparoscopic group) and control group (open surgery group). The study group received minimally invasive laparoscopic surgery under general anesthesia, while the control group received traditional open surgery. All patients received chemotherapy after operation.

Research results

This study evaluates the application value of open surgery and minimally invasive laparoscopic surgery under general anesthesia in the treatment of early ovarian cancer. The results show that minimally invasive laparoscopic surgery under general anesthesia can further improve the therapeutic effect of early ovarian cancer patients, promote rapid postoperative recovery, reduce the stress response and immune function of patients, and the incidence of postoperative complications is low.

Research conclusions

Minimally invasive minimally invasive laparoscopic surgery under general anesthesia is safe and effective in the treatment of early ovarian cancer, which can significantly reduce the stress response and immune function of patients, promote patients' rapid recovery after surgery and reduce the risk of postoperative complications.

Research perspectives

This study focuses on patients with early ovarian cancer and evaluates the application value of open surgery and minimally invasive minimally invasive laparoscopic surgery under general anesthesia in this population, aiming at providing clinical reference for the choice of surgical methods for early ovarian cancer. The results show that minimally invasive laparoscopic surgery under general anesthesia can further improve the therapeutic effect, promote patients' rapid recovery after operation, and have minimal impact on patients' stress response and immune function.

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FOOTNOTES

Co-first authors: Xian Qin and Chen Chen.

Author contributions: Qin Xand Chen C designed the research; Liu Y, Hua XH, Li JY and Liang MJ contributed new reagents/analytic tools; Qin X and Chen C analyzed the data; Wu F, Qin X and Chen C wrote the paper; all authors were involved in the critical review of the results and have contributed to, read, and approved the final manuscript; Qin X and Chen C contributed equally to this work as co-first authors equally to this work. The reasons for designating Qin X and Chen C as co-first authors are threefold. First, Data analysis: All two authors analyzed or explained the data of the article; second, Design and implementation of the experiment: All two authors participated in the design and implementation of the experiment; third, Data interpretation: All two authors have made important contributions to data interpretation.

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Country/Territory of origin: China

ORCID number: Fang Wu 0009-0008-6384-6245.

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