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Original Article

Efficacy of total laparoscopic hysterectomy in the treatment of patients with uterine fibroids and its effect on coagulation-related indicators and inflammatory factors

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Abstract: Objective: To investigate the efficacy of total laparoscopic hysterectomy in the treatment of patients with uterine fibroids and its effect on coagulation-related indicators and inflammatory factors. Methods: 94 patients with uterine fibroids were divided into two groups according to the random number table, with 47 cases in each group. Patients in the control group were treated with routine laparotomy, while those in the observation group adopted laparoscopic hysterectomy. The surgery-related indicators, coagulation function indicators (prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen (Fbg)), serum inflammatory factors (interleukin-6 (IL-6), interleukin-8 (IL-8), C-reactive protein (CRP), tumor necrosis factor-α (TNF-α)), stress response indicators (norepinephrine (NE), epinephrine (E)) before and after operation, as well as changes in quality of life and complications, were compared. Results: The intraoperative blood loss, postoperative exhaust time and hospital stay in the observation group were less and shorter than those in the control group ($P<0.05$). Postoperatively, the prothrombin time and activated partial thromboplastin time in the observation group were higher than those in the control group, while fibrinogen was lower than that in the control group ($P<0.05$); the tumor necrosis factor-α, interleukin-8, interleukin-6 and C-reactive protein in both groups significantly increased after operation, but the increment of above indicators in the observation group after treatment was lower than that in the control group ($P<0.05$); norepinephrine and epinephrine in both groups after operation increased significantly, but the degree of increase in the observation group was significantly lower ($P<0.05$); the quality of life scores in the observation group after operation were all higher than those in the control group ($P<0.05$). There was no statistically significant difference in the incidence of complications between the observation the two groups ($P>0.05$). Conclusion: Total laparoscopic hysterectomy in patients with uterine fibroids has more obvious curative effect than open operation, which can significantly reduce the impact on the patient's blood coagulation function, inflammation response, stress response and the incidence of complications, while improving patient's quality of life.

Keywords: Uterine fibroids, open operation, laparoscopic hysterectomy, coagulation function, inflammatory factors, stress response

Introduction

At present, the pathogenesis of uterine fibroids is not clear, and it is believed that it may be associated with the complex interactions between sex hormones and local growth factors, as well as the cell mutations in the normal muscle layer [1]. Most patients have no obvious clinical symptoms, and uterine fibroids are often found in the pelvic ultrasound examination. The main treatment for uterine fibroids is conservative drug therapy, but if the patient fails to respond to drug therapy, hysterectomy should be considered. Now there are many clinical options for surgical procedures, and the topic of hysterectomy has always been the focus of clinical discussion and research, such as the selection of surgical methods, surgical indications, postoperative recovery and complications [2, 3]. Although the curative effect of traditional open total hysterectomy is positive, it can cause a large surgical trauma and a large

amount of intraoperative blood loss. Therefore, postoperative pain is obvious, which is not conducive to postoperative recovery [4]. With the proposal of the concept of minimally invasive operation in the 20th century, laparoscopic technique has been gradually applied in hysterectomy [5]. Although there are many clinical reports on total laparoscopic hysterectomy for uterine fibroids, there are few reports on the effects of total laparoscopic hysterectomy on coagulation-related indicators and inflammatory factors in patients with uterine fibroids. Based on this, the purpose of this study was to analyze the efficacy of total laparoscopic hysterectomy in the treatment of patients with uterine fibroids and its effect on coagulation-related indicators and inflammatory factors.

Materials and methods

General information

In this study, 94 patients who had undergone uterine fibroids operation in Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University) from July 2017 to April 2020 were selected and divided into the control group and observation group according to random number table, with 47 cases in each group. Patients in the control group were 35-49 years old, with an average of 42.3±5.8 years; the course of disease was 1-3 years, with an average of 2.1±0.5 years; classification of fibroids: 14 cases with submucosal fibroids, 18 cases with intramural fibroids and 15 cases with subserous fibroids; the average body mass index (BMI) was 24.78±1.75 kg/m^2; the number of uterine fibroids: 22 cases with single uterine fibroid and 25 cases with multiple uterine fibroids. Patients in the observation group were 36-52 years old, with an average of 44.6±5.9 years; the course of disease was 1-2 years, with an average of 1.6±0.7 years; classification of fibroids: 15 cases with submucosal fibroids, 18 cases with intramural fibroids and 14 cases with subserous fibroids; the average BMI was 24.56±1.71 kg/m^2; the number of uterine fibroids: 20 cases with single uterine fibroid and 27 cases with multiple uterine fibroids. Compared with the control group, the above-mentioned general information in the observation group was well balanced. This study was approved by the Ethics Committee of Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University).

Inclusion criteria and exclusion criteria

Inclusion criteria: Patients met the related diagnostic criteria of uterine fibroids in "Consensus of Chinese Experts on the Diagnosis and Treatment of Uterine Fibroids" [6]; patients had indications for total hysterectomy; patients had no previous history of uterine operation; patients had signed informed consent forms.

Exclusion criteria: Patients with coagulation dysfunction, history of surgical contraindication, uterine malformation, uterine malignant tumor, immune system dysfunction or cognitive disorder.

Methods

Control group: Patients in the control group underwent traditional open operation. The specific operation was as follows: The patient was asked to lie supine on the examination bed with the buttocks close to the bedside and put legs on the leg support to maximize the exposure of the perineum (lithotomy position of bladder). Conduct routine disinfection after general anesthesia. Make a surgical incision along the midline of the lower abdomen, extending from below the umbilicus to the upper edge of the symphysis pubis. Probe and expose the pelvic cavity and uterus. Apply hemostatic forceps to lift up the uterus. Cut off the uterine round ligament and pelvic funnel ligament; open up the posterior lobe of peritoneum; and cut off the uterosacral ligament. Open the posterior wall of the peritoneum and separate the anterior peritoneum of the uterine cavity to the outer opening of the uterus. Reflex the peritoneum and separate the bladder; ligate the blood vessels in each part of the uterus; pull upward and dissociate the uterus; and separate the anterior vaginal cavity from the uterus. Finally, remove the uterus and suture the broken ends of vagina layer by layer. A urinary tube was then placed and preventive antibiotic treatment was given.

Observation group: Laparoscopic operation was applied. The specific operation was as follows: The lithotomy position of bladder was exposed and anesthesia was conducted the same way as the control group. Make an incision at the upper edge of the umbilicus with a length of about 10 mm. Establish the pneumoperitoneum routinely. Insert the trocar and lap-

aroscope to probe the position of the lesion and perform the puncture under the microscope. Remove the uterine oviduct and round ligament sequentially by electrocoagulation; excise the uterus by unipolar electrocoagulation; suture the vaginal stump; flush the pelvic cavity and place the drainage tube.

Outcome measures

Primary outcome measures: (1) Curative effect indicators: The mean operating time, intraoperative blood loss, gastrointestinal function recovery time and hospital stay of patients in both groups were recorded.

(2) Blood coagulation function: 4 mL of venous blood was extracted before and after operation, and the serum was collected after centrifugation. The coagulation function indicators including PT, APTT and Fbg in both groups were detected by Sysm ex CA 7000 automatic coagulometer (purchased from SYSM EX company).

(3) Inflammatory factors: 4 mL of venous blood was drawn from the patient before operation and on the first day after operation, and the serum was collected after centrifugation. Serum CRP was determined by immunoturbidimetry with OTA-400 automatic biochemical analyzer provided by Shenyang Wantai Medical Equipment Co., LTD.; IL-6 and IL-8 were detected by radioimmunoassay with radioimmunoassay counter provided by Anhui Zhongke Zhongjia Scientific Instrument Co., Ltd.; TNF-α was detected by enzyme-linked immunosorbent assay with Beckman IAMMGE; the kit was provided by Shenzhen Kerunda Bioengineering Co., Ltd., and the operation was performed in strict accordance with the instructions.

Secondary outcome measures: (1) Stress response: 4 mL of venous blood was extracted before operation and on the first day after operation, and the serum was collected after centrifugation. The NE and E were detected by enzyme-linked immunosorbent assay with Beckman IAMMGE, and E was measured in resting state and supine position. The kit was provided by Shanghai Xinyu Biotechnology Co., Ltd., and the operation was performed in strict accordance with the instructions.

(2) Quality of life: The patients were followed up for 3 months, and the quality of life was assessed by the Quality of Life Questionnaire (QLQ C-30). The scale contained 5 items, including physical function, social function, role function, emotive function and cognitive function. The score for each item was set at 0 to 100 points, with a higher score indicating less functional impairment and higher quality of life.

(3) The perioperative complications of patients, including incision infection, pelvic adhesions and intestinal obstruction, were recorded. Complication rate = total number of cases with adverse reactions/total number of cases × 100%.

Statistical analysis

SPSS 18.0 software was used for statistical analysis. The measurement data (surgery-related indicators, coagulation function indicators, inflammatory factors, stress response indicators and quality of life scores) were expressed as mean ± standard deviation ($\bar{x}$ ± sd). Independent sample t-test was used for comparison between groups, and paired sample t-test was used for comparison within the group. The count data (complication rate) was expressed as percentage, and chi-square (χ^2) test was used for comparison. $P<0.05$ was considered statistically significant.

Results

Curative effect indicators

The intraoperative blood loss, gastrointestinal function recovery time and hospital stay in the observation group were less and shorter than those in the control group ($P<0.001$); there was no significant difference in mean operating time between the two groups ($P>0.05$). It can be seen that total laparoscopic hysterectomy was less invasive for patients with uterine fibroids and more conducive to the prognosis of patients. See **Table 1**.

Blood coagulation function

There was no significant difference in coagulation function between the two groups before operation ($P>0.05$); after operation, PT and APTT in the observation group were higher than those in the control group, and Fbg was lower than that in the control group ($P<0.001$); no patients in the two groups received blood

Table 1. Comparison of surgery-related indicators ($\bar{x}$ ± sd)

Items	Control group (n=47)	Observation group (n=47)	t	P
Mean operating time (min)	85.12±9.22	84.43±8.64	0.374	0.709
Intraoperative blood loss (mL)	210.51±29.73	156.72±15.73	10.964	0.000
Gastrointestinal function recovery time (h)	20.74±4.58	17.13±3.11	4.470	0.000
Hospital stay (d)	7.34±2.61	4.79±2.45	4.884	0.000

Table 2. Comparison of coagulation function ($\bar{x}$ ± sd)

	Control group (n=47)	Observation group (n=47)	t	P
PT (t/s)				
Before operation	11.28±1.59	11.69±1.86	0.869	0.387
After operation	12.12±1.61***	13.68±1.69***	4.582	0.000
APTT (t/s)				
Before operation	29.47±2.24	29.51±2.15	0.088	0.930
After operation	32.87±2.08***	36.79±4.75***	5.183	0.000
Fbg (g/L)				
Before operation	5.85±0.71	5.76±0.83	0.565	0.574
After operation	4.95±0.59***	3.97±0.40***	9.425	0.000

Note: Compared with the same group before operation, ***P<0.001. PT: prothrombin time; APTT: activated partial thromboplastin time; Fbg: fibrinogen.

transfusion therapy. It can be seen that total laparoscopic hysterectomy could help improve the coagulation function in patients with uterine fibroids. See **Table 2** and **Figure 1**.

Inflammatory factors

There was no significant difference in inflammatory factors between the two groups before operation (P>0.05); TNF-α, IL-8, IL-6 and CRP significantly increased in both groups after operation, but the increment of above indicators in the observation group after treatment was lower than that in the control group (P< 0.001). It can be seen that total laparoscopic hysterectomy was more conducive to reducing the inflammatory response in patients with uterine fibroids. See **Table 3** and **Figure 2**.

Stress response

There was no significant difference in stress response indicators between the two groups before operation (P>0.05); NE and E in both groups after operation increased significantly, but the degree of increase in the observation group was smaller (P<0.001). It can be seen that total laparoscopic hysterectomy was more conducive to reducing the stress response. See **Table 4** and **Figure 3**.

Quality of life

There was no significant difference in quality of life scores between the two groups before operation (P> 0.05); the quality of life scores of each item in the observation group after operation were all higher than those in the control group (P<0.001). It can be seen that total laparoscopic hysterectomy was more beneficial to improve the quality of life for patients with uterine fibroids. See **Table 5** and **Figure 4**.

Complications

There was no significant difference in the incidence of complications between the two groups (P>0.05). Thus, total laparoscopic hysterectomy does not increase the incidence of complications. See **Table 6**.

Discussion

In recent years, the incidence of uterine fibroids in China has been increasing, which seriously threatens the life and health of patients. The pathogenesis of uterine fibroids is relatively complicated, mainly related to the mutation of normal muscle cells, as well as the interaction of sex hormones and local growth factors. These factors have a direct stimulating effect on the growth and development of uterine fibroids [7, 8]. The intramural fibroids and submucosal fibroids are often affected by the size, location and number of fibroids, and thus have clinical manifestations such as prolonged or shortened menstruation, excessive or insufficient menstruation [9]. If patient's fibroids are too large, it can even be palpable from the lower abdomen, presenting increased secretions, lower abdomen bulge, urinary urgency, frequent urination, back pain and other severe

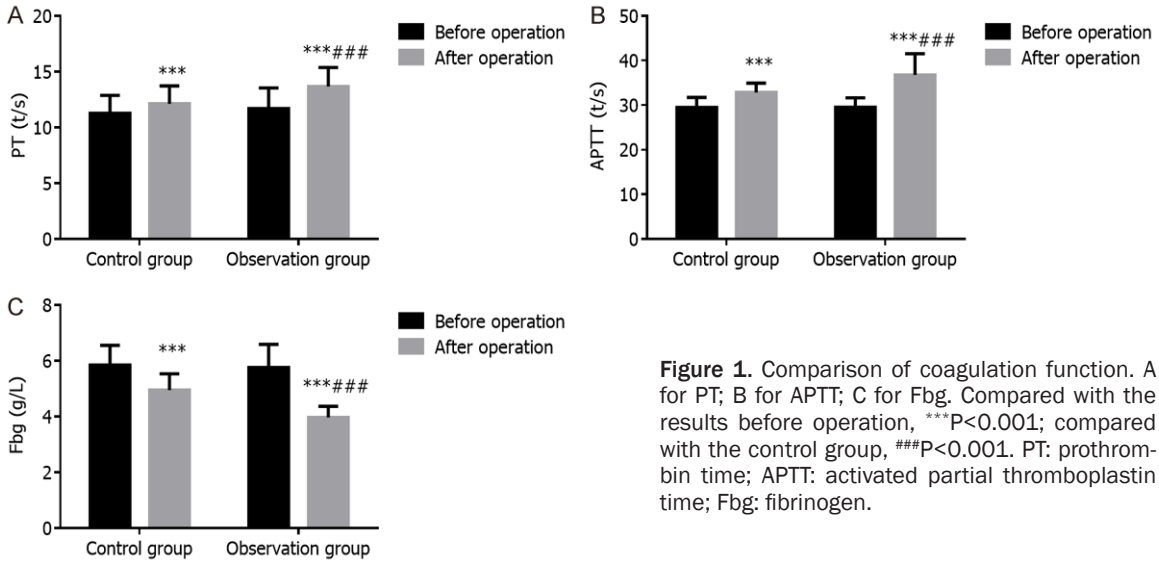

Figure 1. Comparison of coagulation function. A for PT; B for APTT; C for Fbg. Compared with the results before operation, ***P<0.001; compared with the control group, ###P<0.001. PT: prothrombin time; APTT: activated partial thromboplastin time; Fbg: fibrinogen.

Table 3. Comparison of inflammatory factors ($\bar{x}$ ± sd)

	Control group (n=47)	Observation group (n=47)	t	P
TNF-α (μg/mL)				
Before operation	1.52±0.61	1.55±0.62	0.237	0.814
After operation	6.35±1.02***	4.03±1.09***	13.383	0.000
IL-6 (μg/mL)				
Before operation	6.32±1.14	6.43±1.08	0.480	0.632
After operation	13.74±1.45***	9.36±1.32***	15.314	0.000
IL-8 (pg/mL)				
Before operation	4.85±0.71	4.76±0.83	0.565	0.573
After operation	9.83±1.59***	7.07±1.40***	8.932	0.000
CRP (mg/L)				
Before operation	5.78±3.59	5.69±3.86	0.117	0.907
After operation	11.45±2.61***	8.61±2.05***	5.867	0.000

Note: Compared with the same group before operation, ***P<0.001. IL-6: interleukin-6; IL-8: interleukin-8; CRP: C-reactive protein; TNF-α: tumor necrosis factor-α.

symptoms. If timely and effective treatment is not taken, the development of the disease will have a serious impact on the health and quality of life [10, 11].

In the past, total hysterectomy was usually used in the treatment of uterine fibroids, with definite surgical effect and relatively complete resection of fibroids. However, traditional hysterectomy causes a large incision in the patient's abdomen, resulting in a lot of intraoperative bleeding loss, obvious postoperative pain, and slow recovery of gastrointestinal and other body functions, which will prolong the hospital stay. It not only increases the patient's economic burden, but also increases their mental stress [12, 13]. In addition, operative trauma will produce certain stress response to the body, which stimulates the patient's hypothalamic-pituitary-adrenal axis and leads to abnormal physiological metabolism of metabolic response and neurosecretion. This stress response is associated with the duration of the operation, incision length, intraoperative blood loss and the prognosis [14]. Therefore, on the basis of not affecting the smooth progress of the operation and pathological treatment, minimizing the trauma of the operation to the body and reducing the stress response and inflammatory response have become a new therapeutic concept.

As a sensitive indicator of inflammatory response, CRP is also positively correlated with the inflammatory response in the body. When the body is infected by bacteria or tissue damage occurs, the concentration of CRP will increase significantly [15, 16]. TNF-α, with complex biological activity, acts on vascular endothelial cells. It plays a role in immune regulation, infection and inflammatory response [17, 18]. TNF-α can enhance the bactericidal effect

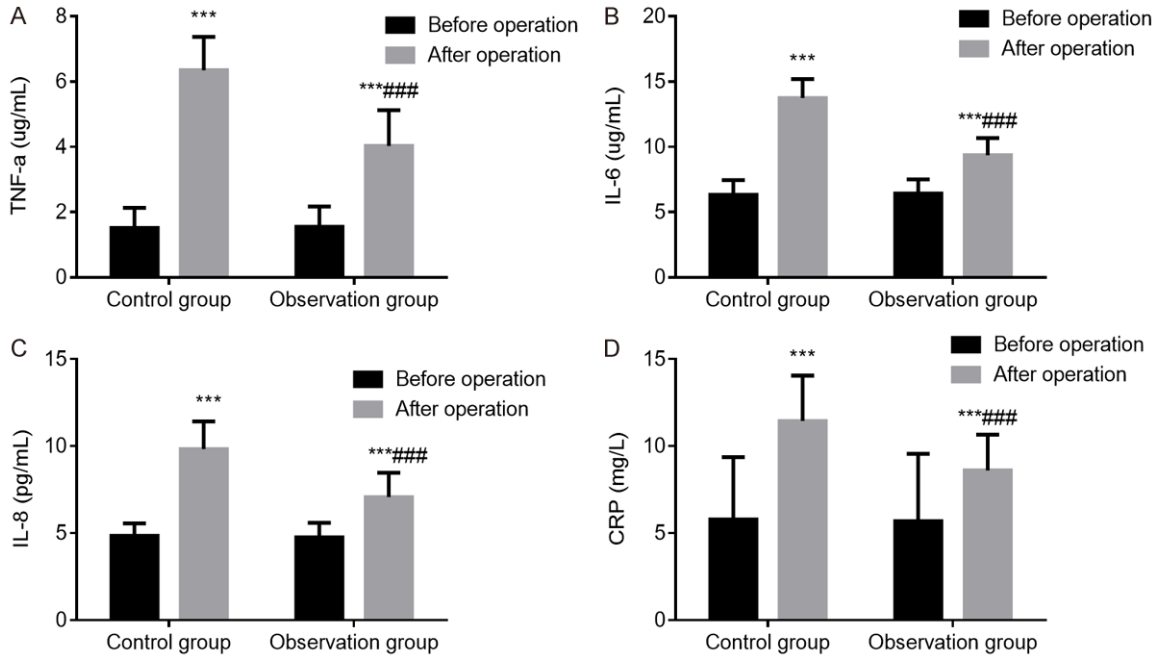

Figure 2. Comparison of inflammatory factors. A. TNF-α; B. IL-6; C. IL-8; D. CRP. Compared with the results before operation, ***P<0.001; compared with the control group, ###P<0.001. IL-6: interleukin-6; IL-8: interleukin-8; CRP: C-reactive protein; TNF-α: tumor necrosis factor-α.

Table 4. Comparison of stress response indicators ($\bar{x}$ ± sd)

	Control group (n=47)	Observation group (n=47)	t	P
NE (pmol/L)				
Before operation	752.24±75.37	760.63±76.58	0.535	0.594
After operation	2741.35±274.64***	1862.53±186.17***	18.159	0.000
E (pmol/L)				
operation	196.15±15.64	200.07±16.01	1.323	0.189
After operation	682.96±68.52***	592.82±59.38***	6.816	0.000

Note: Compared with the same group before operation, ***P<0.001. NE: norepinephrine; E: epinephrine.

by activating neutrophils; it can also promote inflammatory response by inhibiting or increasing the secretion of inflammatory factors, so it plays a core role in the process of cytokine inflammation. IL-6 and IL-8 are pleiotropic cytokines that can regulate the secretion of various cells. They are the key components of the inflammatory mediator network, and have the function of regulating immune response and hematopoietic function. During infection, trauma, stress response or other condition occurs in the body; it will activate the activity of inflammatory factors and promote the inflammatory response. At this time, IL-6 and IL-8 will be produced first and induce the secretion of CRP and TNF-α. Therefore, the above indicators can effectively reflect the stress response and trauma degree of the patients during operation [19]. This study indicated that the postoperative inflammation and stress response in the observation group were lower than those in the control group, which was basically consistent with the results reported by Wang et al. [20]. Thus, it can be seen that the total laparoscopic hysterectomy is less traumatic to the patients, so the inflammation and stress response produced are also less, which is more conducive to the smooth progress of the operation.

Due to various factors such as anesthesia, operative trauma, intraoperative infusion, etc., the immune system may become weak or unbalanced, leading to imbalanced differentiation of T lymphocyte subsets, endocrine system disorders and abnormal blood fibrinolytic system function. Abnormal coagulation function will cause hemorrhage during the opera-

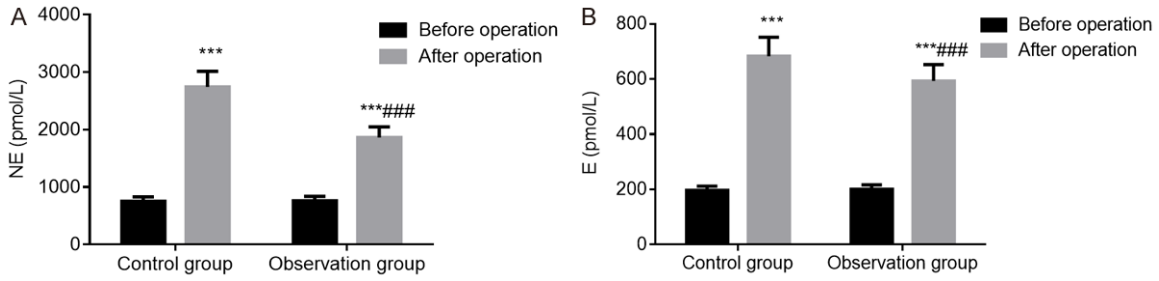

Figure 3. Comparison of stress response indicators. A. NE; B. E. NE for norepinephrine. Compared with the results before operation, ***P<0.001; compared with the control group, ###P<0.001. E: epinephrine.

Table 5. Comparison of quality of life scores ($\bar{x}$ ± sd, points)

	Control group (n=47)	Observation group (n=47)	t	P
Physical function				
Before operation	51.95±3.12	52.17±3.09	0.343	0.753
3 months after operation	71.45±6.46***	80.45±8.21***	5.906	0.000
Social function				
Before operation	71.75±6.47	71.46±6.38	0.219	0.827
3 months after operation	76.68±5.66***	82.14±7.84***	3.871	0.000
Role function				
Before operation	71.79±3.56	71.53±3.47	0.266	0.802
3 months after operation	76.17±4.67***	80.87±5.28***	4.571	0.000
Emotive function				
operation	62.45±3.63	62.34±3.76	0.144	0.886
3 months after operation	74.21±4.33***	81.54±4.21***	9.978	0.000
Cognitive function				
Before operation	72.32±3.53	71.64±3.66	0.917	0.316
3 months after operation	80.85±4.29***	86.15±6.13***	4.856	0.000

Note: Compared with the same group before operation, ***P<0.001.

tion, which will seriously threaten patient's safety and the operation. Therefore, reducing patient's body injury and intraoperative blood loss is of great significance for improving coagulation function [21]. This study showed that the intraoperative blood loss and coagulation function indicators in the observation group were less and better than those in the control group, which indicated that total laparoscopic hysterectomy was less traumatic, would lead to little intraoperative blood loss and could effectively reduce the impact on patient's coagulation function. Laparoscopy is a new minimally invasive operation in recent years. It has the advantages of simple operation, less trauma and quick recovery. Laparoscopy has been widely used in the treatment of uterine fibroids. This study showed that the recovery time of gastrointestinal function and hospital stay in the observation group were shorter than those in the control group. It is basically consistent with the results of Feng's study, and also consistent with the advantages of laparoscopy [22]. Compared with open operation, the surgical incision of laparoscopy is small and the lesion has less contact with outside, so it can avoid the poor prognosis caused by large abdominal incision like exogenous infection, and can also reduce the patient's operative pain. Moreover, the horizon of laparoscopy operation is clearer, and the operation has less trauma to the body, which is conducive to the early off-bed activity and promotes physical recovery [23, 24]. However, laparoscopic operation requires higher suture technique for the surgeons, so it is necessary to be proficient in the operation steps and skills. This study showed that the perioperative complications in

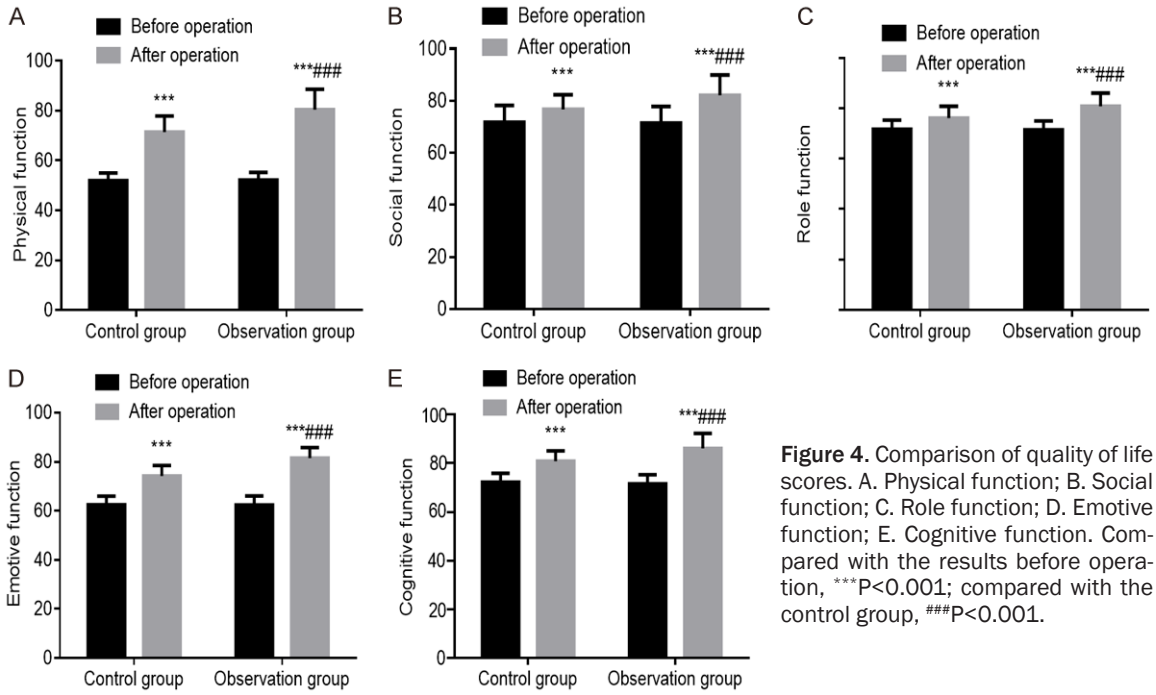

Figure 4. Comparison of quality of life scores. A. Physical function; B. Social function; C. Role function; D. Emotive function; E. Cognitive function. Compared with the results before operation, ***P<0.001; compared with the control group, ###P<0.001.

Table 6. Comparison of incidence of complications (n, %)

	Control group (n=47)	Observation group (n=47)	X^2	P
Incision infection	1 (2.23)	0 (0.00)	0.000	1.000
Pelvic adhesions	3 (6.38)	1 (2.23)	0.261	0.609
Intestinal obstruction	1 (2.23)	0 (0.00)	0.000	1.000
Total incidence	5 (10.64)	1 (2.23)	1.602	0.206

the observation group were similar to those in the control group, indicating that this type of operation did not increase complications. And after a three-month follow-up for the patients, it was found that the quality of life in the observation group was significantly higher than that in the control group. This showed that the application of total laparoscopic hysterectomy in the treatment of uterine fibroids was not only effective, but also had good long-term prognosis for patients. It could effectively improve patient's quality of life.

In summary, total laparoscopic hysterectomy for patients with uterine fibroids has a definite therapeutic effect. It can significantly reduce the impact on the patient's blood coagulation function, reduce inflammation and stress response, and improve quality of life. However, the number of samples collected in this study was small, and the long-term prognosis of patients had not been evaluated. The clinical study can be expanded and the observation time can be extended in the future for in-depth evaluation.

Disclosure of conflict of interest

None.

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