Original Article
Effects of total laparoscopic hysterectomy on the clinical outcomes of patients with uterine fibroids

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Abstract: Objective: To clarify the effects of total laparoscopic hysterectomy (TLH) on sex hormone levels, quality of life (QOL) and complications such as lower-extremity deep vein thrombosis (DVT) in patients with uterine fibroids (UFs). Methods: In this retrospective study, 136 patients with UFs treated in Hainan General Hospital from March 2018 to December 2020 were collected as research participants, of which 65 patients received total abdominal hysterectomy (TAH) were included in the control group and 71 patients who received TLH were assigned to the research group. The two groups were compared regarding the following items: response rate, surgical indexes, rehabilitation indicators, changes in sex hormone levels and QOL, and the occurrence of lower-extremity DVT. Results: The research group showed a significantly higher response rate, and better indicators of surgical treatment and rehabilitation than the control group (P<0.05). The sex hormones in the research group were more stable than that in the control group. The QOL was also significantly better and the incidence of total complications was statistically lower in the research group compared with the control group (both P<0.05). Conclusions: TLH is a feasible and safe alternative than traditional TAH for UFs, as it can effectively improve patients' sex hormone levels and QOL, and reduce the incidence of complications, which is worthy of clinical promotion.

Keywords: Total laparoscopic hysterectomy, uterine fibroids, sex hormones, quality of life, complications

Introduction

Uterine fibroids (UFs) are uterine benign neoplasms that can affect the fertility of women of childbearing age, with an incidence that varies greatly and, there is an estimated incidence of 40-80% in women of childbearing age who are diagnosed with UFs [1]. UF patients may be asymptomatic or accompanied by severe and chronic symptoms, the most common of which are massive menstrual bleeding, fatigue, pelvic pain, constipation or infertility [2, 3]. People with UFs not only experience pain, but may even develop infertility, leading to a significant reduction in quality of life (QOL) [4]. It is shown that age, race, endogenous and exogenous sex hormones, obesity, uterine infection and lifestyle are all risk factors of UFs [5]. The current treatment of UFs is mainly drug therapy and surgery, but the efficacy is not satisfactory [6, 7]. Therefore, it is very important to seek effec-

tive treatments for UFs. This study mainly explores and analyzes two surgical treatment methods for UFs, aiming to provide new strategies and clinical reference for the management of UFs patients.

Surgery is the preferred treatment for UFs patients [8, 9]. For women with fertility needs, the fibroids can be removed through laparotomy, laparoscopic or hysteroscopic surgery according to the size, location and type of the fibroids. However, surgical removal may lead to serious complications, and different surgical methods have different effects on fertility, so the ideal surgical method should be selected according to the specific situation [10]. Currently, both hysterectomy and myomectomy can improve patients' long-term health-related QOL [11]. Studies have shown that ovarian function can be affected despite normal blood supply in patients undergoing total abdominal

hysterectomy (TAH) [12]. In addition, UFs, especially the massive ones, are associated with acute venous thromboembolism (VTE) and other complications due to the following reasons [13]: first, the mass compression from large fibroids can lead to pelvic and lower limb venous stasis; second, abnormal menstruation and excessive bleeding in patients with UFs cause polycythemia and reactive thrombocytopenia, leading to a higher risk of VTE [14, 15]. However, the effects of total laparoscopic hysterectomy (TLH) and TAH on sex hormone levels and complications such as DVT formation in patients with UFs remain unknown.

The innovation of this study lies in the multidimensional analysis of the efficacy, sex hormone levels, QOL and complications of TLH and TAH in patients with UFs, providing valuable references for the selection of appropriate surgical methods for patients with UFs.

Clinical data and methods

Clinical data collection

This retrospective study enrolled 136 patients with UFs treated in the Hainan General Hospital from March 2018 to December 2020 and 65 patients who received TAH were included into the control group and the other 71 patients who received TLH were assigned into the research group according to the treatment method. Patients were included according to the following inclusion criteria: Diagnosis of UFs by imaging according to UFs related diagnostic guidelines [16]; No fertility needs; In line with surgical resection indications; Presence of clinical symptoms such as excessive menstrual volume, prolonged menstruation, and frequent urination; Tolerance to anesthesia; Complete clinical data; High degree of cooperation in hospital follow-up; and Normal cognitive function. Patients and their families were informed of the study and signed an informed consent. Patients were excluded according to the following exclusion criteria: Pelvic surgery history; Malignant tumor(s); Communication barriers; Liver and kidney dysfunction; Pregnancy; Dropouts; History of mental illness or psychotropic drug usage; Use of medication within the recent six months that might affect the results of this study. This study was approved by the Medical Ethics Committee of Hainan General Hospital.

Sample collecting and testing

For all the enrolled patients, 5 mL of fasting venous blood was collected before operation, as well as 48 hours and 3 months after operation for immediate testing. The prothrombin time (PT), activated partial thromboplastin time (APTT) and thrombin time (TT) were measured by STA Compact Max automatic hemagglutinometer (Beijing Stago Diagnosis Trading Co., Ltd., 58732). The luteinizing hormone (LH), follicle-stimulating hormone (FSH) and estradiol (E2) were determined by enzyme-linked immunosorbent assay (ELISA) in strict accordance with the instructions of the kits (Wuhan Fine Biotech Co., Ltd., EH0397, EH0393, FN-EU0390).

Outcome measures

Primary outcome measures: (1) The clinical efficacy of the two groups was observed. Overall response rate = (cured + markedly effective + effective) cases/total cases *100%. Cured: the patient was able to get out of bed 24-48 h after surgery, and the wound healed with no pain; Markedly effective: the patient could get out of bed 24-48 h after operation, but there was slight wound pain; Effective: the patient has mild wound pain within 48 h after the operation, with no obvious pain during bed rest, but obvious pain during activities; Ineffective: the patient's pain status did not relieve or worsened 48 h after surgery.

(2) The changes of sex hormone levels, including LH, FSH and E_2, were compared between the control group and the research group before and after treatment.

(3) The 36-Item Short-Form Health Survey (SF-36) was used to evaluate the QOL of patients in the two groups before and after treatment. Out of 100 points, the higher the score, the better the QOL.

(4) Surgical indexes, including operation time and intraoperative blood loss, were observed in both groups.

(5) The total incidence of complications, including DVT, was compared between the two groups.

Table 1. Baseline data

Variables	Control group (n = 65)	Research group (n = 71)	t/x^2 value	P value
Age (Y)	39.6±6.3	41.2±6.5	1.455	0.148
BMI (kg/m^2)	20.76±1.88	21.15±2.03	1.159	0.248
History of smoking				
Yes	18 (27.69)	23 (32.39)	0.356	0.551
No	47 (72.31)	48 (67.61)		
History of alcoholism				
Yes	31 (47.69)	38 (53.52)	0.461	0.497
No	34 (52.31)	33 (46.48)		
Family history				
Yes	11 (16.92)	17 (23.94)	1.023	0.312
No	54 (83.08)	54 (76.06)		
Residence				
Urban	36 (55.38)	32 (45.07)	1.444	0.230
Rural	29 (44.62)	39 (54.93)		
Location of UFs				
Subserosal	19 (29.23)	25 (35.21)	0.947	0.623
Intermuscular	25 (38.46)	22 (30.99)		
Subserosal and intramuscular	21 (32.31)	24 (33.80)		
Age of menarche				
<13 years old	33 (50.77)	29 (40.85)	1.347	0.246
≥13 years old	32 (49.23)	42 (59.15)		
Maximum diameter of UFs (cm)				
<5	48 (73.85)	56 (78.87)		
≥5	17 (26.15)	15 (21.13)	0.477	0.490
Number of UFs				
Single	40 (61.54)	42 (59.15)	0.081	0.777
Multiple	25 (38.46)	29 (40.85)		

Secondary outcome measures: Rehabilitation indicators of the two groups were observed, including the time to anal exhaust and ambulation and the length of hospital stay.

Statistical analysis

The software used for data processing was SPSS20.0 (Cabit Information Technology, Shanghai, China) and that for image rendering was Prism 8 (Softhead Technology, Shenzhen, China). Counting data were expressed as percentages (%) and compared using the Chi-square (represented by χ^2). Measurement data were expressed as (Means ± SD); Normally distributed data were compared between groups using the independent samples t-test, and intra-group comparison before and after treatment was performed using paired t-tests, and expressed as t. Difference with *P* value <0.05 was considered statistical.

Results

Baseline data

The comparison of baseline data revealed no significant difference between the control group and the research group in terms of age, body mass index (BMI), smoking/alcoholism/family history, place of residence, age of menarche, as well as location of, or maximum diameter and number of UFs (P>0.05), indicating comparability. See **Table 1**.

Comparison of clinical efficacy

We evaluated the clinical effects of the two treatments by comparing the overall treatment efficacy. The data showed that the overall response rate of the research group was significantly higher than that of the control group (P<0.05). See **Table 2**.

Table 2. Comparison of clinical efficacy between the two groups

Groups	Cured	Markedly effective	Effective	Ineffective	Total effective rate
Control group (n = 65)	19 (29.23)	22 (33.85)	12 (18.46)	12 (18.46)	53 (81.54)
Research group (n = 71)	26 (36.62)	24 (33.80)	17 (23.94)	4 (5.63)	67 (94.37)
t value					5.379
P value					0.020

Table 3. Comparison of surgery related indicators

Groups	Operation time (min)	Intraoperative blood loss (mL)
Control group (n = 65)	105.8±14.7	121.5±15.7
Research group (n = 71)	98.2±13.5	96.4±15.3
t value	3.131	9.438
P value	0.002	<0.001

Comparison of surgery related indicators

We evaluated the surgical performance of the two treatments by comparing surgical indicators between the two groups. The data identified statistically shorter operation time and less intraoperative blood loss in the research group compared with the control group (both P<0.05). See **Table 3**.

Comparison of coagulation function

As mentioned above, UFs are related to VTE in patients, and in the hypercoagulation state, PT and APTT are shortened and TT is prolonged. Therefore, we evaluated the influence of the two treatment methods on coagulation function of patients by detecting coagulation function indicators in the two groups. The data showed that there were no significant differences in PT, APTT and TT between the control group and the research group at 24 h before surgery (P>0.05). At 48 h after surgery, plasma PT and APTT were shortened, while TT was prolonged in both groups, but without statistical difference between the two groups (P>0.05). However, there was significant difference between the preoperative and postoperative PT, APTT and TT levels in the research group (P<0.05); and in the control group, TT elevated significantly after surgery compared with the preoperative level (P<0.05). See **Figure 1**.

Changes in sex hormone levels

We assessed the effect of the two treatments on patients' sex hormone levels by measuring the changes in sex hormone levels in the two groups. LH, FSH and E_2 showed no significant differences between the two groups before operation (P>0.05). At 3 months after operation, LH and FSH levels elevated in both groups (P<0.001), with less significant increases in the research group compared with the control group (P<0.001). The level of E_2 reduced in both groups at 3 months after operation, and the level was higher in the research group compared with the control group (P<0.001). See **Figure 2**.

Comparison of rehabilitation indicators

We evaluated the rehabilitation indicators of patients in the two groups to analyze the impact of the two surgeries on patients' recovery. Statistically, the time to anal exhaust and ambulation in the research group were significantly shorter than that in the control group (P<0.05). See **Table 4**.

Comparison of QOL

The SF-36 score was used to evaluate the QOL in both groups to analyze the impact of the two treatments on patients' QOL. The results showed that the QOL, which was similar in both groups before surgery (P>0.05), elevated significantly in both groups at 3 months after surgery (P<0.001), with more evident improvement in the research group compared with the control group (P<0.001). See **Figure 3**.

Incidence of complications

The incidence of complications in the two groups was analyzed to evaluate the impact of the two treatment methods on the safety of patients. The results showed the total incidence of complications in the control group was significantly higher than that in the research group (P<0.05). See **Table 5**.
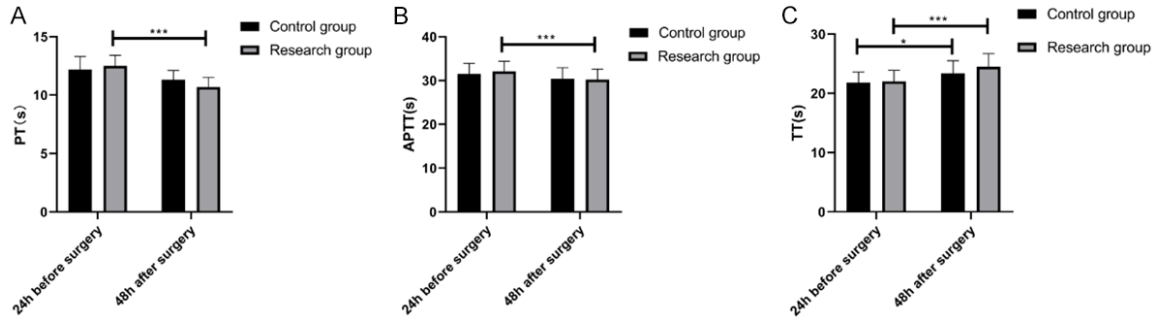
Figure 1. Comparison of coagulation function indicators. A. Comparison of PT level between the two groups before and after operation; B. Comparison of APTT level between the two groups before and after operation; C. Comparison of TT level between the two groups before and after operation. Paired t-test was used; *indicates P<0.05 and ***indicates P<0.001 compared between the two groups.
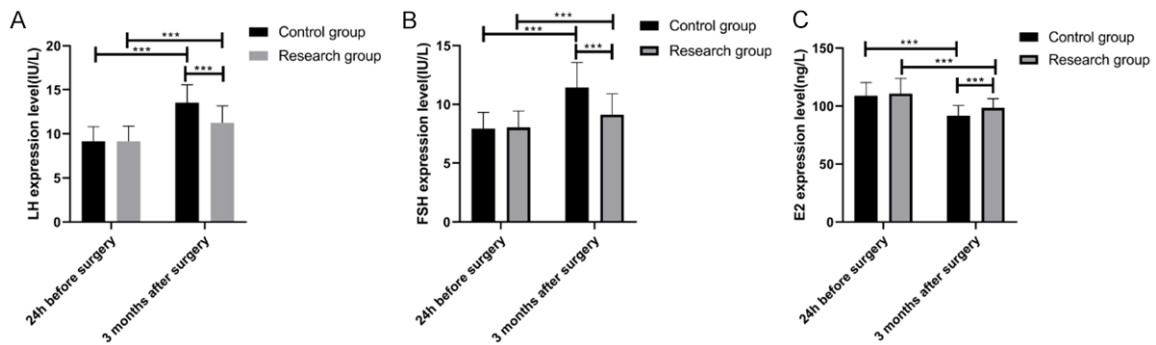

Figure 2. Changes of sex hormone levels. A. Comparison of LH level between the two groups before and after surgery; B. Comparison of FSH level between the two groups before and after surgery; C. Comparison of E_2 level between the two groups before and after operation. Paired t-test was used; ***indicates P<0.001 compared between the two groups.

Table 4. Comparison of rehabilitation indicators

Groups	Time to anal exhaust (h)	Time to ambulation (d)
Control group (n = 65)	29.23±6.12	2.62±0.61
Research group (n = 71)	24.61±5.85	2.07±0.65
t value	4.500	5.076
P value	<0.001	<0.001

Discussion

The pathogenesis of UFs remains unclear, but family history and unhealthy lifestyle are considered as the major risk factors for the disease [17]. Symptoms associated with UFs can negatively affect the daily life and QOL of patients. The presentations of UFs vary from patient to patient, with many cases developing multiple symptoms; nonetheless, approximately one third of patients experience severe menstrual bleeding, which may lead to life-threaten-

ing anemia [18, 19]. UFs are also associated with 10% of infertility cases [20]. Currently, hysterectomy is the most common surgical treatment for UFs, accounting for about 75% of UFs surgeries [21]. Laparoscopic surgery is a new type of minimally invasive surgical method and an inevitable trend in the development of surgical methods in the future [3]. In virtue of less trauma, short hospital stay and quick recovery, it significantly reduces the disease and economic burden of patients, and is therefore widely used in clinical practice [22]. The purpose of this study was to compare the effects of TAH and TLH on sex hormone levels, QOL and incidence of complications in UF patients.

This study first compared the clinical efficacy of the two surgical modalities and found that TLH had a significantly higher total clinical response
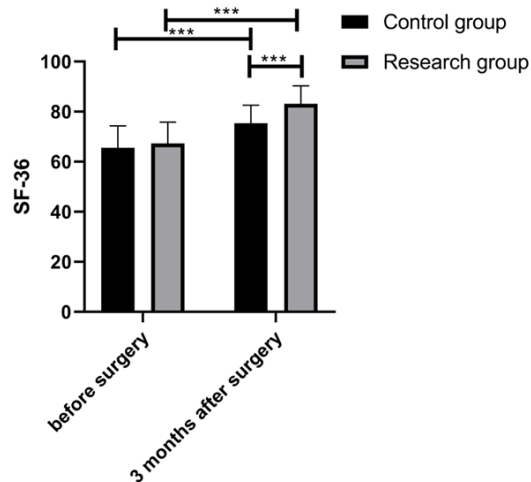
Figure 3. Comparison of SF-36 scores between the two groups before and after surgery. Paired t-test was used; ***indicates P<0.001 compared between the two groups.

rate than TAH. The research results of Dojki et al. [23] showed that TLH had minimal postoperative complications and was a safe, acceptable and feasible alternative to the traditional hysterectomy. Then, by comparing the surgery related indicators, we found that the operation time and the intraoperative blood loss in the research group were significantly less than those in the control group. This indicates that TLH can effectively reduce the damage to patients' blood vessels, and is more conducive to patients' rehabilitation. The results of Maccio et al. [24] showed that TLH was a safe and feasible surgical procedure for patients with a uterus ≥1.5 kg, with intraoperative blood loss of about 100 mL and no major postoperative complications. However, the resulting surgical trauma is prone to cause a series of changes in postoperative platelet-related parameters, as well as coagulation and fibrinolysis functions, which leads to coagulation disorders and increased risk of venous thrombotic disease, endangering the life of patients [25]. PT, APTT and TT are important indexes to evaluate coagulation function [26]. During hemostasis and thrombosis, PT and APTT are shortened and TT is prolonged when the human body is in a hypercoagulation state [27]. In this study, it was found that the bodies of patients in both groups were in a hypercoagulation state 48 h after surgery. The coagulation indexes of the research group were significantly improved after surgery compared with those before sur-

gery, but there was no significant difference between the research group and the control group. For patients with UFs, there will be a large number of procoagulant substances in the blood to stimulate the body to release massive tissue factors, which will activate the coagulation system, leading the body to be in a state of hypercoagulation [28]. The results of this study revealed that the coagulation function of the research group was more stable than that of the control group, indicating that TLH has less effect on the coagulation function of patients.

The ovaries are an essential endocrine organ of the human body, which can secrete hormones and eggs; while E_2, FSH and LH can reflect both ovarian function and the influence of surgical trauma on surrounding tissues [29, 30]. The uterus of the patients is not preserved after hysterectomy, so the ovarian function of most patients will be weakened after surgery, and the decline of ovarian function may be earlier than that of those with normal uterine anatomy [31]. In this study, the LH, FSH and E_2 levels of patients in the two groups were detected, and it was found that TLH for UFs patients had little effect on ovarian endocrine, which is beneficial to the postoperative recovery and the improvement of QOL of patients. Then, we evaluated patients' postoperative recovery, and the results identified that TLH effectively accelerated the postoperative rehabilitation of patients compared to TAH. We also confirmed that patients' QOL in the research group was significantly higher than that in the control group. This may be because laparoscopic surgery is less traumatic, which results in significantly reduced discomfort in patients and accelerated postoperative recovery, contributing to their improved QOL. At the end of the study, we measured the incidence of complications. It was found that DVT and incision infection were the main complications in the two groups, and TLH led to a lower incidence of postoperative complications with high safety. VTE is rare after hysterectomy for benign indications. A study by Duyar et al. [32] showed that patients undergoing TAH had a higher risk of postoperative VTE than those undergoing minimally invasive hysterectomy, which is similar to our research. TLH can be performed under direct vision and can fully separate the adhesions between the abdominal cavity and

Table 5. Incidence of complications

Groups	Incision infection	Subcutaneous emphysema	Abdominal infection	DVT	Total
Control group (n = 65)	4 (6.15)	2 (3.08)	1 (1.54)	9 (13.85)	16 (24.62)
Research group (n = 71)	1 (1.41)	1 (1.41)	0 (0.00)	3 (4.23)	5 (7.04)
t value					8.026
P value					0.005

pelvic cavity, which is relatively safe. However, it should be noted that this operation is more technically demanding than open surgery, requiring the operator to have richer clinical experience and a full understanding of the anatomy of the uterus.

Overall, this study found that TLH is an ideal surgical treatment for UFs, but the recurrence of UFs will increase with the increase of postoperative years regardless of open or laparoscopic resection [33]. The limitations of this study are as follows: 1) The sample size is small, so the sample size should be expanded to improve the accuracy of the research results; 2) Risk factors affecting the clinical outcome of patients with UFs have not been analyzed, and relevant analysis will help to further improve the efficacy. It is hoped that these limitations can be supplemented in future studies to improve this investigation.

To sum up, compared with traditional TAH, TLH is an alternative method with higher feasibility and safety for the treatment of UFs, as it can effectively improve patients' sex hormone levels and QOL, and reduce the incidence of complications, which is worthy of clinical promotion.

Disclosure of conflict of interest

None.

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