

ORIGINAL ARTICLE

Laparoscopic radical resection for large-volume renal carcinoma: via retroperitoneal or transperitoneal approach?

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Summary

Purpose: The aim of this study was to investigate the clinical efficacy and safety of laparoscopic radical resection through retroperitoneal and transperitoneal approaches in treating large-volume renal carcinoma.

Methods: A total of 116 patients with large-volume (>7 cm) renal carcinoma underwent laparoscopic radical resection for renal carcinoma. Among them, 58 were treated through retroperitoneal approach (Retroperitoneal group), and 58 were treated through transperitoneal approach (Abdominal group). The levels of interleukin-6 (IL-6), IL-12 and IL-1 β in the patients were compared before and after operation. Furthermore, the levels of tumor markers were explored, and the tumor recurrence and survival of the patients were followed up and recorded.

Results: Compared with those in Abdominal group, the patients in Retroperitoneal group had remarkably shorter operation time, time of renal artery occlusion, time of intestinal exhaust and length of hospital stay after operation as well as notably smaller intraoperative blood loss. The levels of

IL-6, IL-12 and IL-1 β were elevated after operation in both groups in comparison with those before operation. Besides, the concentrations of serum CA50, CA125 and CEA declined obviously after treatment in the two groups in contrast with those before treatment, while no statistically significant differences in the concentrations of serum CA50, CA125 and CEA were observed between the two groups after treatment. The follow-up results indicated that the average survival and progression-free survival were 18.3 months and 16.0 months, respectively, in Retroperitoneal group, and 19.1 months and 16.8 months, respectively, in Abdominal group.

Conclusions: The retroperitoneal laparoscopic radical resection for large-volume renal carcinoma possesses exact therapeutic effects, and it has shorter operation time, less blood loss, fewer impacts on inflammatory responses in patients and higher safety than transperitoneal laparoscopic radical resection.

Key words: large-volume renal carcinoma, laparoscope, retroperitoneal approach, efficacy.

Introduction

Renal carcinoma, one of the common tumors of the urinary system, accounts for 2-3% of malignant tumors in adults and 80-90% of renal malignancies [1]. It is insensitive to treatments such as radiotherapy, chemotherapy and targeted therapy, so operation and long-term follow-up are the preferred therapeutic methods for the disease, and minimally invasive technique has superiority to other methods [2]. The feasibility, safety and

therapeutic effect of laparoscopic radical resection for renal carcinoma have been verified by a large amount of literature, and laparoscopic operation has advantages such as smaller trauma and blood loss, milder wound pain and faster post-operative recovery compared with open operation [3-5]. There are two conventional approaches of laparoscopic radical resection, namely transperitoneal approach and retroperitoneal approach. In

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retroperitoneal laparoscopy, the renal tumor can be completely resected on the basis of minimal invasion, the renal function impairment can be relieved, and the interference in abdominal viscera and postoperative complications are reduced [6]. Large numbers of studies have demonstrated that transperitoneal and retroperitoneal laparoscopic radical resection for common renal carcinoma (diameter < 7 cm) has equivalent efficacy and safety [6-8]. However, the operative risk for large-volume renal carcinoma (diameter >7 cm) is increased prominently due to a large volume of tumor body and abundant blood supply, and no unified conclusion has been reached in the treatment with transperitoneal approach or retroperitoneal approach.

In the present study, the clinical data of 116 patients with large-volume renal carcinoma who were admitted to and treated in the Department of Urinary Surgery of our hospital from January 2014 to September 2016 were retrospectively reviewed. The clinical efficacy and safety were analyzed and compared between transperitoneal and retroperitoneal laparoscopic radical resection for large-volume renal carcinoma, so as to provide more reasonable references for the selection of clinical treatment protocols for such patients.

Methods

General data

A total of 116 patients with large-volume renal carcinoma were selected as the subjects, including 65 males and 51 females aged 41-72 years old, with (54.1±9.9) years old on average. Inclusion criteria: patients definitely diagnosed with renal carcinoma (tumor diameter >7 cm) by means of B-mode ultrasound, computed tomography (CT) and pathology, those with indications of laparoscopic radical resection for renal carcinoma, and those with a clinical TNM stage of T2 or T3. Exclusion criteria: patients who had hepatic insufficiency, inferior vena cava thrombosis, distant tumor metastasis or lymph node metastasis, or those complicated with connective tissue disease or coagulation abnormality. The differences in baseline data such as age, gender, tumor site, tumor number, tumor size, clinical stage of tumor and complications were not statistically significant before operation between the two groups ($p>0.05$) (Table 1). This study was approved by the Ethics Committee of the First Affiliated Hospital of Soochow University. The *Declaration of Helsinki* was followed, and the duty of disclosure was performed. All the patients enrolled signed the informed consent.

Operative methods

The patients receiving retroperitoneal laparoscopic operation were generally anesthetized after tracheal

Table 1. Baseline demographic and clinical characteristics of the studied patients

Indicators	Retroperitoneal group (n=58) n (%)	Abdominal group (n=58) n (%)	p
Age, years	53.68±10.04	54.52±10.51	0.661
Gender			0.455
Male	35 (60.3)	30 (51.7)	
Female	23 (39.7)	28 (48.3)	
BMI (kg/m ²)	21.23±2.11	21.79±1.88	0.134
Tumor side			0.452
Left kidney	31 (53.4)	36 (62.1)	
Right kidney	27 (46.6)	22 (37.9)	
Tumor location			0.276
Upper pole or renal hilum	41 (70.7)	38 (65.5)	
Inferior pole of kidney	10 (17.2)	14 (24.1)	
Perinephrit tissue	7 (12.1)	6 (10.3)	
Tumor diameter (cm)	7.52±1.46	7.66±1.34	0.592
Pathological type			0.473
Clear cell carcinoma	47 (81.0)	51 (87.9)	
Papillary cell carcinoma	7 (12.1)	10 (17.2)	
Chromophobe renal carcinoma	3 (5.2)	7 (12.1)	
Collecting duct carcinoma	1 (1.7)	0 (0)	
Systemic disease			0.635
Hypertension	11 (19.0)	15 (25.9)	
Diabetes Mellitus	7 (12.1)	8 (13.8)	
Heart Disease	6 (10.3)	4 (6.9)	

BMI: body mass index.

intubation. In the lateral position on the uninjured side, 3 puncture points were determined on the posterior axillary line below the costal margin, the anterior axillary line below the costal margin and the midaxillary line at 2 cm above iliac crest, where a 2 cm-long incision was made separately. After the incision at the puncture point on the posterior axillary line below the costal margin was cut open, the fascia of the back was bluntly dissected using big vascular forceps first, and the peritoneal space was expanded by injecting 500 mL of water. Then 12 mm, 5 mm and 10 mm Trocar were punctured into the 3 puncture points, respectively, the dorsal perirenal fascia was isolated to the diaphragm and iliac vessel, and the renal artery and vein were dissociated and processed. Later, the ventral surface of the kidney was separated, the ureters were dissociated to the bifurcation of the abdominal aorta and then dissected, and the kidney and surrounding tissues were resected completely. Finally, the lymph nodes were dissected, and the specimens were put into specimen bags and taken out. After operation, a drainage tube was placed, and the incision was sutured.

As for the patients undergoing laparoscopic operation through transperitoneal approach, they lay in the lateral position on the uninjured side after tracheal intubation and general anesthesia, and 3 puncture points were determined in the paraumbilical region, on the anterior axillary line at the level of the umbilicus and on the outer margin of rectus abdominis or at 2 cm below the costal margin. Then an incision (1 cm) was made at the paraumbilical puncture point, and the pneumoperitoneum was constructed first. The 10 cm Trocar was used for puncture, and then the other 2 puncture points were punctured by 5 cm and 10 cm Trocar, respectively. Later, the paracolic sulcus was cut open, the colon and mesentery were dissociated downward, and the medial renal fascia was cut off. Subsequently, the renal vein and artery were severed, the ureters were dissociated and dissected, and the upper pole of kidney was dissociated upward, followed by en bloc resection of the kidney and surrounding tissues. Finally, the lymph nodes were dissected, and the specimens placed into specimen bags were taken out. After that, a drainage tube was placed, and the incision was sutured.

Observation indexes

Related clinical operation indicators such as operation time, intraoperative blood loss (amount of aspirated liquid in aspirator - amount of flushing liquid), blood transfusion rate, length of hospital stay after operation and time of postoperative intestinal exhaust were recorded and compared between the two groups of patients. Moreover, the levels of interleukin-6 (IL-6), IL-12 and IL-1 β were detected before and after operation via enzyme-linked immunosorbent assay. Besides, 5 mL of fasting peripheral venous blood was separately collected from the patients before operation and at 4 weeks after operation, and the levels of carbohydrate antigen 50 (CA50), CA125 and carcino-embryonic antigen (CEA) in the serum were measured. The incidence of postoperative complications, including pancreatic fistula, retroperitoneal hematoma, delayed wound healing, intestinal obstruction and pulmonary infection, was compared between the two groups of patients.

The parameters of blood routine, urine routine and renal function of the enrolled patients were followed up every month during treatment, and adverse reactions to treatment were inquired. In addition, the patients were reexamined every 3 months within 2 years and then every 6 months within 3 years, and chest imaging examination, B-mode ultrasonography of upper urinary tract and CT scan of pelvic cavity were performed every year. The tumor recurrence was followed up and compared between the two groups, and the time to recurrence was recorded if the tumor recurred in patients. The survival of all the patients was recorded.

Statistics

SPSS 22.0 statistical software (IBM, Armonk, NY, USA) was adopted for statistical analyses. The measurement data were expressed by mean \pm standard deviation, and two-sample t-test was performed for inter-group comparison. The enumeration data were presented as ratio (%), χ^2 test was conducted for inter-group comparison, and $p < 0.05$ suggested that the difference was statistically significant. Kaplan-Meier method and log-rank test were utilized for survival analyses, and $p < 0.05$ suggested statistically significant differences.

Table 2. Comparison of perioperative indicators

Indicators	Retroperitoneal group (n=58)	Abdominal group (n=58)	p
Operation time (min)	114.6 \pm 13.3	130.2 \pm 14.8	0.001
Renal artery occlusion time (min)	20.1 \pm 5.7	21.8 \pm 5.1	0.039
Blood loss (ml)	155.7 \pm 9.4	178.4 \pm 6.1	0.001
Intestinal exhaust after surgery (day)	1.7 \pm 0.5	2.3 \pm 0.6	0.001
Blood transfusion (Cases), n (%)	2 (3.4)	3 (5.2)	0.648
In-hospital time after surgery (day)	5.2 \pm 1.9	6.3 \pm 2.2	0.005
Complications, n (%)	6 (10.3)	8 (13.8)	0.569
Delayed wound healing	2 (3.4)	1 (1.7)	
Retroperitoneal hematoma	2 (3.4)	1 (1.7)	
Intestinal obstruction	1 (1.7)	3 (5.2)	
Pulmonary infection	0 (1.7)	3 (5.2)	
Pancreatic fistula	1 (1.7)	0 (0)	

Results

Comparison of relevant operative conditions between the two groups of patients

Retroperitoneal group had an evidently shorter operation time [(114.6±13.3) min vs. (130.2±14.8) min, $p<0.001$], time of renal artery occlusion [(20.1±5.7) min vs. (21.8±5.1) min, $p=0.039$], time of intestinal exhaust [(1.7±0.5) d vs. (2.3±0.6) d, $p<0.001$] and length of hospital stay after operation [(5.2±1.9) d vs. (6.3±2.2) d, $p=0.005$] as well as smaller intraoperative blood loss [(155.7±9.4) mL vs. (178.4±6.1) mL, $p<0.001$] than Abdominal group. No statistically significant difference in the blood transfusion rate was observed between the two groups ($p=0.648$). Different degrees of complications emerged in both groups after operation, including delayed wound healing, retroperitoneal hematoma, intestinal obstruction, pulmonary infection and pancreatic fistula. Furthermore, the total incidence rate of complications was 10.3% (6/58) in Retroperitoneal group and 13.8% (8/58) in Abdominal group, without a statistically significant difference ($p=0.569$) (Table 2).

Comparisons of IL-6, IL-12 and IL-1 β levels before and after operation between the two groups of patients

The levels of IL-6, IL-12 and IL-1 β displayed no statistically significant differences before op-

eration between the two groups ($p=0.472$, $p=0.651$, $p=0.193$). After operation, the IL-6 level rose from 12.81±5.61 pg/mL to 27.65±8.78 pg/mL in Retroperitoneal group and from 13.65±6.87 pg/mL to 30.39±8.97 pg/mL in Abdominal group, the IL-12 level was increased from 30.13±5.65 ng/mL to 40.08±6.76 ng/mL in Retroperitoneal group and from 30.66±6.89 ng/mL to 42.12±6.90 ng/mL in Abdominal group, and the IL-1 β level was elevated from 3.47±0.72 pg/mL and 3.63±0.59 pg/mL to 4.22±1.06 pg/mL and 4.68±1.57 pg/mL in Retroperitoneal group and Abdominal group, respectively. The levels of serum IL-6, IL-12 and IL-1 β were raised remarkably after operation in both groups in comparison with those before operation ($p<0.05$), and they were lower in Retroperitoneal group than those in Abdominal group, but the differences were not statistically significant between the two groups ($p=0.099$, $p=0.111$, $p=0.067$) (Figure 1).

Comparisons of tumor markers in peripheral blood between the two groups of patients

There were no statistically significant differences in the concentrations of serum CA50, CA125 and CEA before operation between the two groups ($p=0.650$, $p=0.614$, $p=0.384$). After operation, however, the CA50 level declined from 20.68±5.15 U/mL to 11.63±2.87 U/mL in Retroperitoneal group

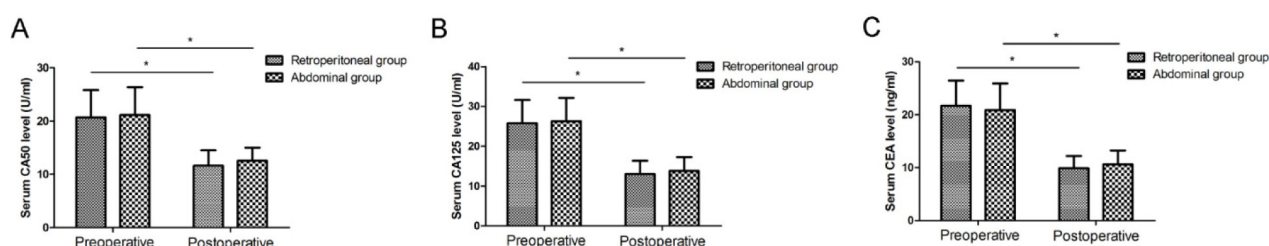


Figure 2. Comparison of serum CA50, CA125 and CEA levels between the two groups of patients. Pretreatment CA50 (A), CA125 (B) and CEA (C) levels of patients had no significant difference between Retroperitoneal group and Abdominal group. Posttreatment serum AFP (A), CEA (B) and CA199 (C) levels of patients in both groups significantly decreased after treatment. The difference between posttreatment serum AFP (A), CEA (B) and CA199 (C) levels of patients in Retroperitoneal group and Abdominal group had no statistical significance (* $p<0.05$).

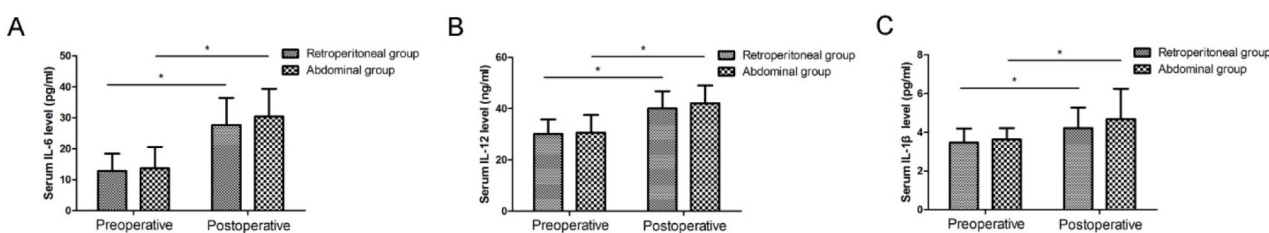


Figure 1. Comparison of serum IL-6, IL-12 and IL-1 β levels between the two groups of patients. Pretreatment IL-6 (A), IL-12 (B) and IL-1 β (C) levels of patients had no significant difference between Retroperitoneal group and Abdominal group. Posttreatment serum IL-6 (A), IL-12 (B) and IL-1 β (C) levels of patients in both groups significantly increased after treatment ($p<0.05$). The differences in posttreatment serum IL-6 (A), IL-12 (B) and IL-1 β (C) levels of patients between Retroperitoneal group and Abdominal group had statistical significance (* $p<0.05$).

and from 21.12 ± 5.25 U/mL to 12.56 ± 2.43 U/mL in Abdominal group, the CA125 level was decreased from 25.77 ± 5.86 U/mL to (13.01 ± 3.35) U/mL in Retroperitoneal group and from 26.32 ± 5.84 U/mL to 13.83 ± 3.44 U/mL in Abdominal group, and the CEA level was lowered from 21.69 ± 4.76 U/mL and 20.90 ± 4.98 U/mL to 9.89 ± 2.32 U/mL and 10.62 ± 2.64 U/mL in Retroperitoneal group and Abdominal group, respectively. In short, the concentrations of serum CA50, CA125 and CEA were markedly lower after treatment than those before treatment in the two groups ($p < 0.05$), while no statistically significant differences in those concentrations were observed between the two groups after treatment ($p = 0.062$, $p = 0.196$, $p = 0.117$) (Figure 2).

Comparison of renal function recovery between the two groups of patients

The differences in renal function indicators [blood urea nitrogen (BUN) and serum creatinine (Scr)] were not statistically significant before operation between the two groups ($p = 0.236$, $p = 0.749$). The level of BUN was increased from 21.32 ± 6.55

mmol/L and 22.76 ± 6.46 mmol/L to 25.10 ± 7.65 mmol/L and 26.16 ± 7.08 mmol/L in Retroperitoneal group and Abdominal group, respectively, after operation, and that of SCr was raised from 78.18 ± 20.32 mmol/L and 76.92 ± 21.96 mmol/L to 84.24 ± 23.83 mmol/L and 86.70 ± 22.69 mmol/L in the two groups, respectively. Retroperitoneal group exhibited lower levels of both BUN and SCr than Abdominal group after operation, but the differences were not statistically significant ($p = 0.440$, $p = 0.570$) (Figure 3).

Comparison of survival during follow-up between the two groups of patients

All the patients were followed up for 6-36 months, with an average of 23.3 ± 4.4 months. There were 6 and 7 cases of distant metastasis in Retroperitoneal group and Abdominal group, respectively. Specifically, 2 cases of metastasis to the lung, 2 cases of metastasis to the liver, 1 case of bone metastasis and 1 case of abdominal lymph node metastasis were detected in Retroperitoneal group. In Abdominal group, there were 3 cases of metastasis

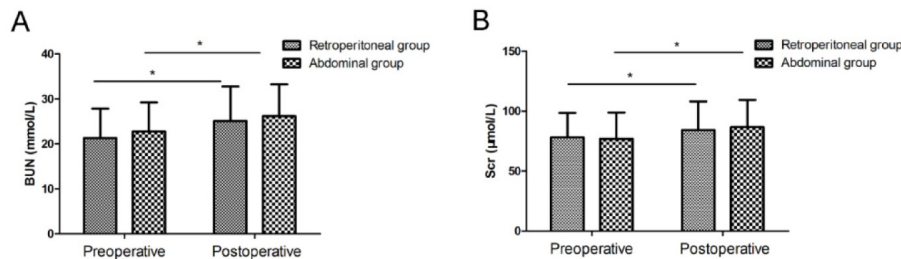


Figure 3. Comparison of serum BUN and Scr levels between the two groups of patients. Pretreatment BUN (A) and Scr (B) levels of patients had no significant difference between Retroperitoneal group and Abdominal group. Posttreatment serum BUN (A) and Scr (B) levels of patients in both groups significantly increased after treatment. The difference between posttreatment serum BUN (A) and Scr (B) levels of patients in Retroperitoneal group and Abdominal group had statistical significance. (* $p < 0.05$).

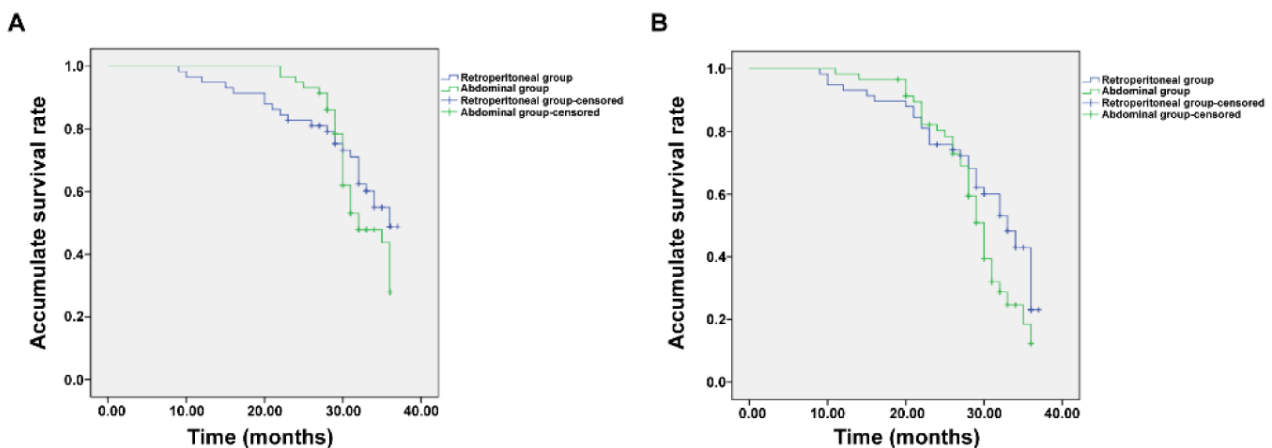


Figure 4. Kaplan-Meier survival curves of patients in Retroperitoneal group and Abdominal group. The differences in overall survival rate (A) and progression free survival rate (B) of patients between Retroperitoneal group and Abdominal group had statistical significance. (* $p < 0.05$).

to the lung, 2 cases of metastasis to the liver, 2 cases of bone metastasis and 1 case of abdominal lymph node metastasis. Both groups had no local recurrence. At the end of follow-up, the average survival and progression-free survival were 18.3 months and 16.0 months, respectively, in Retroperitoneal group, and 19.1 months and 16.8 months, respectively, in Abdominal group. The survival curves were plotted by Kaplan-Meier method (Figure 4), and the results of log-rank test showed that there were no statistically significant differences in the overall survival rate and the progression-free survival rate between Retroperitoneal group and Abdominal group ($p=0.217$, $p=0.064$).

Discussion

Surgery is the primary means to treat renal carcinoma, and traditional laparotomy has been gradually substituted with minimally invasive laparoscopic operation due to large operative trauma, slow recovery of patients, etc. Currently, laparoscopic operation is fairly mature in the treatment of renal carcinoma in the T1 stage, and a growing number of studies have elaborated that laparoscopic operation is not prominently different from open operation in terms of perioperative safety and therapeutic effect in treating large-volume renal carcinoma, while it is superior to open operation in the aspects of operative trauma and postoperative recovery [9-12]. Pierorazio et al [9] reported that 200 renal carcinoma patients with a tumor diameter >7 cm were all treated by laparoscopic operation through transperitoneal approach. Among them, 138 patients had a tumor diameter of 7-10 cm, 62 patients had a tumor diameter larger than 10 cm, and favorable therapeutic effects have been obtained. However, it was noted that larger tumors (>10 cm) are associated with greater intraoperative blood loss and higher rate of conversion to open surgery, and the experience of operators is correlated with the incidence rate and severity of complication at the same time.

There are mainly 2 approaches of laparoscopic operation in clinic at present: retroperitoneal approach and transperitoneal approach [13]. Currently, the retroperitoneal approach is more widely applied in clinical practices because of such merits as early exposure of renal pedicle, rapid processing of renal artery and vein, mild interference of operation in abdominal viscera and small intraoperative injury [14]. Nevertheless, it still possesses disadvantages, including limited operation space, unclear anatomical landmarks, great influence from peritoneal fat and difficulty in exposing lesions, which immensely increase the operative risk for

large-volume renal carcinoma with abundant blood supply and close relation to surrounding tissues [15]. Nambirajan et al [16] prospectively compared laparoscopic radical nephrectomy between retroperitoneal approach and transperitoneal approach, and they held that the differences in various indexes such as operation time, blood loss and postoperative recovery were not statistically significant between the two approaches. Fan et al [17] retrospectively reviewed the case data of laparoscopic radical nephrectomy through retroperitoneal approach or transperitoneal approach and found that the retroperitoneal approach had a shorter operation time, shorter time for controlling renal pedicle and lower total incidence rate of postoperative complications than transperitoneal approach. Ha et al [6] compared the case data of laparoscopic radical nephrectomy from 23 medical centers, including 472 cases of transperitoneal approach and 108 cases of retroperitoneal approach, and the results indicated that the overall survival and recurrence-free survival manifested no statistically significant differences between the two approaches. However, they did not carry out research on the subgroup of large-volume renal carcinoma.

According to the results of the present study, the operation time, gastrointestinal function recovery time after operation and length of hospital stay in Retroperitoneal group were notably shorter than those in Abdominal group ($p<0.05$). Meanwhile, the difference in the incidence rate of complications was not statistically significant between the two groups (10.3% vs. 13.8%, $p>0.05$), suggesting that the two approaches of laparoscopic operation have equivalent safety. Nevertheless, the major complications were retroperitoneal hematoma and delayed wound healing in Retroperitoneal group, while postoperative intestinal obstruction and pulmonary infection were the main complications in Abdominal group. These results imply that patients with weak gastrointestinal function and poor body immunity should select the retroperitoneal approach, while those with obesity and tumor that is complexly correlated with surrounding tissues should choose the transperitoneal approach [7,18]. The results of follow-up revealed that the differences in overall survival rate and progression-free survival rate were not statistically significant between the two groups of patients ($p=0.217$, $p=0.064$).

In this study, the levels of tumor markers in the serum of the patients with renal carcinoma were further compared between the two approaches, which revealed that there were no statistically significant differences in the levels of serum CA50, CA125 and CEA between Retroperitoneal group and Abdominal group before and after operation

($p > 0.05$). It was also discovered that the levels of pro-inflammatory cytokines IL-6, IL-12 and IL-1 β in the serum were elevated distinctly in both groups after operation compared with those before operation ($p < 0.05$), suggesting that the two approaches of operation cause certain damage to the body. However, Retroperitoneal group had lower levels of serum IL-6, IL-12 and IL-1 β than Abdominal group after operation, without statistically significant differences ($p > 0.05$), indicating that the transperitoneal approach causes greater operative injuries and adverse effects to the body. The reason may be that the research sample size is relatively small, so a larger sample size is needed for further investigation.

To sum up, either transperitoneal or retroperitoneal approach is safe and feasible in treating large-volume renal carcinoma if the experienced operators select patients carefully, and choosing appropriate approaches for different patients is more conducive to making best use of the advantages and avoiding the disadvantages as well as maximizing patient's benefits. There are certain limitations in this single-center retrospective study. For example, the sample size was not big enough, the follow-up time was not long enough, and the follow-up

content was not comprehensive enough. Therefore, more rigorous and scientific large-sample, multi-center, prospective randomized controlled studies need to be designed in the future to confirm the results, thus providing references for selecting treatment protocols for patients.

Conclusions

The retroperitoneal laparoscopic radical resection possesses exact therapeutic effects in treating large-volume renal carcinoma, and it has shorter operation time, less blood loss, fewer impacts on inflammatory responses in patients and higher safety than transperitoneal laparoscopic radical resection.

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Conflict of interests

The authors declare no conflict of interests.

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