

The curative effects of LPN combined LCA in treating with middle and advanced renal cancer

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Abstract. – OBJECTIVE: To discuss the curative effects of laparoscopy partial nephrectomy (LPN) combined with laparoscopy cryoablation (LCA) in treating renal cancer.

PATIENTS AND METHODS: A total of 58 patients that were diagnosed with phase III-IV renal cancer in the Hospital from February 2013 to October 2014 were enrolled in this study. After obtaining the approval of Ethics Committee of the Hospital as well as the informed consent of the patients and their relatives, the patients were randomly divide into two groups: control group consisted of 24 patients, who were treated with LPN + chemo radiotherapy and the observation group consisted of 34 patients, who were treated with LPN in combination of LCA + chemo radiotherapy.

RESULTS: The rate of successful operation was significantly higher in the observation group than in control group and the prevalence of per procedural complications in observation group was significantly lower than that of control group, and these differences had statistical significance ($p < 0.05$). Glomerular filtration rate (eGFR) after operation and 6-month follow-up in observation group was significantly higher than that in control group, and the level of serum creatinine (sCr) was significantly lower compared to the control group and the differences had statistical significance ($p < 0.05$). Follow-up survival rate of patients in the observation group was significantly higher than that of control group, recurrence rate and recurrence time of patients in the observation group was significantly lower than those of control group and the difference had statistical significance ($p < 0.05$).

CONCLUSIONS: LPN combined LCA therapy was quite effective in treating with middle and advanced renal cancer. Compared with pure LPN therapy, LPN combined LCA therapy could significantly improve the surgical effects, retain the functions of the renal unit and improve the patients' prognosis.

Key Words:

LPN, LCA, Middle and advanced renal cancer, GFR.

Introduction

The incidence of renal cancer accounts for about 2.1% of malignant tumors worldwide. It ranked the second among all male urogenital neoplasms. With the development of image technology and the improvement of early detective rate, minimally invasive surgery that could keep the renal unit has become the hot spot of research^[1]. Laparoscopic cryoablation (LCA) is combination therapy of laparoscopic and cryoablation. It could effectively avoid injuries on surrounding tissues incurred from puncture. It is not involved with renal artery and veins obstruction, so it was quite safe, effective and minimally invasive. Therefore, it was regarded as an important minimally invasive operation in renal cancer treatment². More and more studies have pointed out that³ LCA was safer and more effective than percutaneous cryoablation, radiofrequency ablation and laparoscopic partial nephrectomy. However, previous studies on LPN and LCA were mainly focused on renal tumors in the early period, and with relatively smaller diameter. In this study, we have tried to find out whether LPN combined LCA therapy was effective in treating the middle and advanced renal tumor, thus providing a new basis for the reveal of clinical indications and evaluation of curative effects.

Patients and Methods

Patients

A total of 58 patients who were diagnosed with phase III-IV renal cancer in the Hospital from February 2013 to October 2014 were enrolled in this study. All of the patients had been confirmed renal carcinoma staging through CT

or MRI. Inclusion criteria: (1) Patients with an age greater than or equal to 18 years old and less than 75 years old; (2) Patients that conform to 2004 WHO renal carcinoma diagnosis and staging criteria; (3) Patients undergoing the first-time treatment and had no history of operation, chemo radiotherapy and immunotherapy. Exclusion criteria: (1) Patients complicated by carcinomas in other organs; (2) Patients with other renal diseases, such as multiple cysts, stones, tuberculosis and so on; (3) Patients who were pregnant or had an infection, combined severe impairments in heart, liver, kidney and other organs, autoimmune disease, serious coagulation disorders and so on; (4) Patients with poor compliance and who refused the study.

After obtaining the approval of Ethics Committee of the hospital as well as the informed consent of the patients and their relatives, we divided the patients randomly into two groups: control group (n=24) and observation group (n = 34). In control group, there were 15 cases of male and 9 cases of female, being aged from 48-72 years old, on average (56.7 ± 12.6) years old; Out of these, 16 cases were in phase III and 8 cases were in phase IV; diameter was from 2.4-6.7 cm, on average (4.3 ± 1.1) cm; the number of bilateral renal tumor was from 1-5, on average (2.7 ± 0.6); 9 cases were accompanied with hepatic metastasis, 7 cases with osseous metastasis, 5 cases with pulmonary metastasis, and 3 cases with abdominal lymph metastasis. In the observation group, there were 21 cases of male and 13 cases of female, being aged from 46-74 years old, on average (54.9 ± 13.3) years old; Out of these, 23 cases were in phase III and 11 cases were in phase IV; diameter was from 2.5-7.2 cm, on average (4.6 ± 1.4) cm; number of bilateral renal tumor was from 1-4, on average (2.9 ± 0.7); 12 cases were accompanied with hepatic metastasis, 9 cases with osseous metastasis, 7 cases with pulmonary metastasis, and 6 cases with abdominal lymph metastasis. The differences in the baseline data between the two groups of patients had no statistical significance ($p > 0.05$).

Experimental Method

After relevant examinations had been completed, all of the patients were confirmed to conform to operative indications. Laparoscopic surgical access system (Advanced Surgical Concepts, Wicklow, Ireland), Endoscopic system: 30° Integrated digital laparoscopic system (EndoEye, Olympus Surgical, Orangeburg, NY,

USA). Patients in control group were treated with LPN + chemo radiotherapy, details were as follows: conducted general anesthesia on the uninjured side in lying position, and their waists elevated. Made a 2 cm incision on the twelfth rib of the posterior axillary line, bluntly separated retroperitoneal space, placed balloon dilator and inflate 600-800 ml air and keep for 3-5 min. Place 10 mm, 10 mm and 5 mm Trocar in 2 cm above the anterior superior spine of midaxillary line, 3 cm prone to abdomen side on the horizontal level, and under costal margin of the anterior axillary line, respectively. After pneumoperitoneum was successfully established, applied ultrasound knife, LigaSure, monopole electrode to open Gerota fascia, isolated renal artery from dorsal part of kidney, then used intraoperative interventional ultrasound to mark the tumor boundary, used Bulldog to obstruct segmental renal artery and finally cut off the tumor completely with cool knife at 0.5 cm-1 cm outside tumor border. Opened methylthioninium chloride to drop the solution and observe whether there was any methylthioninium chloride ooze. If there was, used 3-0 absorbable thread to suture the open renal collective system and then used hem-o-lock clamp to suture the renal parenchyma free of the knot. Pre-treatment and post-treatment chemo radiotherapy schemes could be subject to the recommendations of renal tumor treatment guideline.

Patients in observation group were treated with LPN combined LCA + chemo radiotherapy, Frozen operation system (Cryo-Care Surgery System, EndoCare Corporation, NY, USA). Details were as follows: LPN process was the same as described above. As for the tumor that was difficult to excise and that might result in excessive hemorrhage or that was easy to conduct radiofrequency ablation in advance, tumor puncture point could be defined and be isolated from peritoneal organs. Applied puncture needle to make needle biopsy (2-3 needles) on tumor under laparoscope monitoring and then sent for pathologic examination. Placed the laparoscopic ultrasound probe on contralateral tumor, carefully and slowly made puncture with cryoablation probe under the guidance of ultrasonoscopy till the border of deep tumor and made cryoablation so as to make the distal end of probe expand rapidly to form an ice ball. Kept the ice ball at an environment of -40°C for 10-15 minutes. The edge of ice ball had better exceed 10 mm of the tumor edge so that the tumor tissues could be de-

stroyed completely, then warm up to 30°C to make slow thawing till ice ball was melted completely, kept this state for 1-2 minutes. After the tumor was rewarmed, start the second freezing-rewarming process, the probe could not be taken out until the ice ball was completely melted. Avoid twisting force or violence in operation so as to prevent kidney rupture and massive hemorrhage.

Observation Indicator

To compare the successful operation rate and the prevalence of periprocedural complications between the two groups and analyze their differences. A successful operation was defined when the whole tumor as well as 0.5-1 cm of the tumor edge were successfully excised or the diameter of tumor was narrowed by over 85%; without massive hemorrhage or conversion to open surgery. Periprocedural complications included: massive hemorrhage, infection, injuries on surrounding tissues and deterioration of renal function. To analyze the differences on eGFR and sCr after the operation and after 6-month of follow-up. GFR formula ($\text{/ml/min/1.73 m}^2 = 186 \times \text{sCr}^{-1.154} \times \text{age}^{-0.203} \times [\text{female} \times 0.742] \times 1.233$). Collected venous blood, applied Hitachi 7600 autobiochemistry instrument to make analysis and picric acid rate method to measure sCr. To compare the differences on follow-up survival rate and recurrence rate.

Statistical Analysis

Statistical software package SPSS 20.0 (SPSS Inc., Chicago, IL, USA) was applied to process the data; measurement data was presented by means ± standard deviation; the *t*-test was applied in comparisons between groups; enumeration data was presented by percentage; the χ^2 test was applied in comparisons between groups. *p* < 0.05 was considered with statistical significance.

Results

Comparisons on Successful Operation Rate and the Incidence of Periprocedural Complication Between the Two Groups of Patients

Intraoperative pathologic results (under 2004 WHO Pathological classification Standard on Renal Cell Carcinoma) showed that there were 17 cases of renal clear cell cancer and 7 cases of polypoid adenocarcinoma in the control group while in observation group, there were 25 cases of renal clear cell cancer and 9 cases of polypoid adenocarcinoma. Differences between the two groups on pathological classification had no statistical significance (*p* > 0.05). Successful operation rate in the observation group was significantly higher than that in control group and the incidence of periprocedural complication in observation group was significantly lower compared to the control group, and differences had statistical significance (*p* < 0.05) (See Table I).

Comparisons on the Level of eGFR and sCr After Operation and 6-Month Follow-up

Differences in the level of eGFR and sCr between the two groups of patients before treatment had no statistical significance (*p* > 0.05). Compared with pre-treatment, eGFR in control group after treatment was reduced and rose again after 6-month follow-up and comparisons at different time points within the groups had no statistical significance (*p* > 0.05); compared with pre-treatment, eGFR in observation group after treatment was stable and rose up upon follow-up and comparisons had statistical significance (*p* < 0.05); the level of serum creatinine (sCr) in observation group after treatment was significantly lower than that in control group and difference had statistical significance (*p* < 0.05) (Table II).

Table I. Comparisons on successful operation rate and the prevalence of periprocedural complications between the two groups of patients [case (%)].

Group	Case	Successful operation	Death	Hemorrhoea	Infection	Surrounding tissue damage	Renal function deterioration	Incidence of complication
Control group	24	17	1	2	1	2	1	7
Observation group	34	29	1	0	1	1	0	3
χ^2		3.992						4.080
<i>p</i>		0.046						0.043

Table II. Comparisons on the level of eGFR and sCr after operation and 6-month follow-up.

Group	eGFR			sCr		
	Pre-treatment	Post-treatment	Follow-up for six months	Pre-treatment	Post-treatment	Follow up for six months
Control group	56.7 ± 5.5	48.3 ± 4.6	53.7 ± 3.8	115.4 ± 15.7	138.7 ± 12.4	106.6 ± 17.9
Observation group	54.2 ± 6.3	53.6 ± 5.2	60.5 ± 3.6	123.6 ± 13.9	127.9 ± 15.2	95.4 ± 18.3
<i>t</i>	0.527	2.417	4.529	0.674	2.659	4.759
<i>p</i>	0.326	0.043	0.037	0.419	0.041	0.034

Comparisons on the Follow-up Survival Rate and Recurrence Rate Between the two Groups of Patients

The survival rate of the observation group was significantly higher than that of the control group, the recurrence rate and recurrence time of the observation group were significantly lower than those of the control group and the difference had statistical significance ($p < 0.05$) (Table III).

Discussion

LCA used the cryoablation technology to ablate renal tumor tissue, thus leads to its necrosis. At the time of cryoablation, the water inside and outside the cells would freeze and results in damages on cells, organelle, and protein, and microtubule system, histocytes would have degenerative necrosis. Under the state of mild hypothermia, freezing could result in cell death through apoptosis, which was of great significance in reducing tumor residues⁴. Laparoscopic cryoablation had great advantages⁵: (1) Puncture could be guided more precisely under the monitoring of laparoscopic. It could locate the tumor that was positioned near great vessel better than ultrasound-guided percutaneous and it was especially favorable to be applied in exoge-

nous tumor. As for the tumor that was located near ureter and intestinal tube, under laparoscope guidance, the tumor body could be exposed completely, which could help reduce the risks of damages during cryoablation. (2) Laparoscope could help detect out the degree of tumor invasion, discover the tumor that could hardly be discovered by B-ultrasonic and CT and if necessary, enable us to implement lymph node dissection and biopsy. Intraoperative cholangiography inspection and position were the most commonly used and convenient methods and had quite significant effect in destroying tumor tissues precisely. To make cryoablation on focus under the guidance of laparoscope could significantly reduce the recurrence rate of tumors.

Nowadays, more and more authors have devoted themselves to studying the safety and curative effects of laparoscopic cryoablation. In 2008, Lehman et al⁶ treated 44 cases of renal tumor and divided the patients into two groups according to the size of tumor: the first group was composed of 23 cases with an average tumor size of 1.8 cm (0.7 cm-2.8 cm), after 9-month follow-up, no recurrence or complication was discovered; the second group was composed of 21 cases with an average tumor size of 4 cm (3.0 cm-7.5 cm), after 11-month follow-up, 13 cases (62%) were discovered with post-operative complications, among which hemor-

Table III. Comparisons on the follow-up survival rate and recurrence rate between the two groups of patients [case (%)].

Group	Case	Survival rate	Recurrence rate	Recurrence time (month)
Control group	24	9 (37.5)	13 (54.2)	3.5 ± 1.2
Observation group	34	23 (67.6)	9 (26.5)	5.2 ± 1.4
<i>t</i> (χ^2)		3.899	4.584	5.247
<i>p</i>		0.048	0.032	0.018

rhage was the most common one and one case (4.8%) had recurrence. Through an analysis of their curative effects, they concluded that LCA was quite effective in treating renal tumors those were less than 3 cm, but its effectiveness in treating relatively large tumors was not so favorable, which indicated that the efficacy of LCA was closely related to the size of the tumor. In 2010, Tsivian et al⁷ quantified this correlation based on experimental studies and they concluded that an 1 cm increase in the tumor size brought a 40% increase in the recurrence rate. They also insisted that LCA was quite effective in treating patients with multiple renal small tumors. However, for large or endogenous tumors, and those extensively contacted with renal sinus, LCA might increase the risk of recurrence.

LPN had many advantages in treating the localized renal tumor. It could effectively keep the normal renal unit and was characterized by less complication, short hospitalization time, and intraoperative blood loss. But the results of clinical studies conducted by medical centers at home and abroad⁸⁻¹⁰ have indicated that the influence of LCA and LPN on renal function, middle term tumor-specific survival were quite similar. Though LCA had the advantages of less complication, short hospitalization time, intraoperative blood loss. In this study, we have further analyzed the curative effects of LPN combined with LCA in treating with middle and advanced renal cancer. The results of this study: the successful operation rate in the observation group was significantly higher than that in the control group and the incidence of periprocedural complications in the observation group was significantly lower than that in the control group; the differences had statistical significance. Glomerular filtration rate (eGFR) after operation and 6-month follow-up in the observation group was significantly higher than those in the control group, and the level of serum creatinine (sCr) was significantly lower than that in the control group; the difference had statistical significance. The follow-up survival rate of the observation group was significantly higher than that of the control group, the recurrence rate and recurrence time of the observation group were significantly lower than those of the control group and the difference had statistical significance.

Conclusions

LPN when combined with LCA therapy was quite effective in treating with middle and advanced renal cancer. Compared with pure LPN therapy, LPN combined LCA therapy could significantly improve the surgical effects, retain the functions of renal unit and improve the patients' prognosis.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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