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The efficacy of open nephron-sparing surgery in the treatment of complex renal cell carcinoma

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Abstract. – OBJECTIVE: To analyze the efficacy of open nephron-sparing surgery (NSS) in the treatment of complex renal cell carcinoma.

PATIENTS AND METHODS: A total of 118 patients with complex renal cell carcinoma (T1N0M0, clear cell carcinoma) were included in this study, and assigned into open radical nephrectomy (RN) group (35 patients), open NSS group (45 patients) and laparoscopic NSS group (38 patients). After 3 years of follow-up, the clinical efficacy was analyzed.

RESULTS: Both the mean surgery time and ischemia blocking time in the open NSS group were comparable to those in the RN group, and significantly shorter than the laparoscopic NSS group, $p < 0.05$. The rate of positive margin in the open NSS group was significantly lower than the laparoscopic NSS group. The occurrence of total complications in the open NSS group was comparable to that in the laparoscopic NSS group and significantly lower than the RN group. The successful rate of surgery in the open NSS group was significantly higher than the laparoscopic NSS group, $p < 0.05$. The 75% survival was 30.0 months in the RN group, > 35.0 months in the open NSS group and 34.0 months in the laparoscopic NSS group, the difference was significant ($p < 0.001$). The mortality was similar in the open NSS group and the laparoscopic NSS group, and significantly smaller than the RN group, $p < 0.05$.

CONCLUSIONS: Open NSS was more safe and effective in the treatment of complex renal cell carcinoma than RN and laparoscopic NSS.

Key Words:
Nephron-sparing surgery, Complex renal cell carcinoma, Radical nephrectomy, Laparoscopy.

Introduction

Malignant renal cell carcinoma (RCC) is the most common type of kidney cancer in adults, accounting for 80-90% of primary malignant kidney neoplasms and are thought to be the 8th most common adult malignancy, representing 2% of all cancers[1,2]. RCC usually occurs in 50-70 year-old patients with a 2:1 ratio of males versus females.

Radical nephrectomy to resect the tumor completely is the chief treatment option of renal cell carcinoma. However, it may increase the occurrence of postoperative complications, chronic kidney disease and cardiovascular disease and decrease quality of life for patients[3]. In elderly patients or those with co-morbidities or smaller tumors, then organ-sparing treatment can be undertaken. Nephron-sparing surgery (NSS) has become an established surgical treatment for patients with renal cell carcinoma, particularly in cases where performing a radical nephrectomy would require subsequent dialysis. NSS can significantly improve the prognosis and kidney function without increasing the mortality or chance of recurrence. The indications of NSS had been extended to small renal cell carcinoma and complex renal cell carcinoma[4]. Currently, NSS could be performed in an open manner and with the assistance of laparoscopy as well as remote control manipulator[5]. The aim of the current study is to assess the efficacy of NSS in the treatment of complex renal cell carcinoma and provide evidence for clinical therapy.

Patients and Methods

Patients

118 patients diagnosed as complex renal cell carcinoma (T1N0M0, clear cell carcinoma, on the basis of imaging or pathology) were included in this study from January 2012 to January 2016.

Inclusion criteria: 1. 75 y > Age ≥ 18 y; 2. Maximal tumor size ≥ 4 cm; 3. Surgical indication and completion of surgery, with complete follow-up data.

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Exclusion criteria: 1. Solitary kidney, abnormal location of kidney, kidney abnormalities, renal trauma, concomitant primary kidney diseases, such as nephropathy, nephritis and abnormal creatinine; 2. Multiple kidney cancer, secondary kidney tumor or metastasis of occult renal cell carcinoma; 3. Concomitant underlying diseases for which surgery was intolerable, such as vascular and circulatory diseases, pregnant and lactating women, poor compliance, etc.

Successive patients were assigned into RN group (35 patients), open NSS group (45 patients) and laparoscopic NSS group (38 patients). As shown in Table I, the baseline information of these patients was not significantly different ($p > 0.05$).

Informed consent was obtained from all patients, and the study was conducted in accordance with the Declaration of Helsinki and approved by Ethics Committee of the hospital.

Methods

Surgery

Standard surgical procedures were performed in RN group. The procedures of open NSS were as follows: general anesthesia was performed; the patient was in lateral position. The lumbar bridge was elevated; a routine disinfection was performed and a sterile towel was prepared. Made an incision of 1.5 cm at 11th rib, opened the skin, subcutaneous tissues and muscles, dissected perineal fascia, detached perinephric fat, explored the size and shape of the tumor. Dissected the outer sheath of the renal artery, which was surrounded by fascicular tissues, and detached the trunk for 1.5 cm. In the same manner, detached the renal vein beneath renal artery, infused mannitol and systemic heparin 5 min before transient blocking renal blood flow, occluded renal artery and renal vein with a Bulldog clip, and recorded the blocking time. The perinephrium was placed in sterile ice for physical cooling. A circular incision was made in renal capsule 0.5 cm off the tumor border with an electric scalpel, detached and resected the tumor completely. Electrocautery was performed on the wound in kidney, hemostatic gauze was placed on the bottom of the wound, small extra peritoneal fat was applied; then, the wound was closed by the figure-of-8 suture with 2-0 liver suture. Vascular occlusion was removed, protamine was used against heparinization, the gauze was re-warmed with warm saline. Confirmed the absence of active bleeding and urine leakage, counted surgical instruments and gauze, indwelled a 16F perineal drainage tube, sutured the wound layer by layer, and packed the wound with a sterile dressing.

The procedures of laparoscopic NSS were as follows: Made an incision of 1.5 cm at posterior axillary line beneath 12th rib, opened the skin and subcutaneous tissue, the muscularis was opened by blunt dissection with hemostatic forceps. Placed in a balloon to dilate retroperitoneal space. With the guide of the index finger, placed a 5-mm Trocar in anterior axillary line under the costal arch, a 12-mm Trocar above the axillary line on the iliac spine, a 10-m Trocar in the 1st incision. The trocar above axillary line was connected to a laparoscope, the pressure in pneumoperitoneum was adjusted to 14 mmHg, the other 2 Trocar were used for medical instruments. Cleared extraperitoneal fat, dissected lateroconal fascia, detached along the anterior margin of the psoas muscle, detached and exposed renal artery out of renal fascia. Dissected perineal fascia, detached the kidney along with renal capsule, explored the size, shape and location of the tumor, occluded renal artery with a Bulldog clip, resected the tumor at renal

Table I. General information at baseline.

Group	N	Male/ Female	Mean age (y)	Mean tumor size (cm)	Central	Bilateral	Mean tumor number	RENAL score	Creatinine (μmol/L)
RN group	35	20/15	42.6 ± 7.3	6.2 ± 1.5	26 (74.3)	8 (22.9)	1.6 ± 0.5	6.3 ± 1.7	65.9 ± 15.2
Open NSS group	45	28/17	43.3 ± 7.4	6.2 ± 1.4	33 (73.3)	12 (26.7)	1.5 ± 0.4	6.5 ± 1.6	66.3 ± 16.3
Laparoscopic NSS group	38	22/16	43.5 ± 7.2	6.3 ± 1.6	30 (78.9)	9 (23.7)	1.6 ± 0.6	6.4 ± 1.5	65.7 ± 15.9
t (χ^2)		0.258	0.326	0.629	0.385	0.178	0.598	0.659	0.329
p		0.879	0.487	0.758	0.825	0.915	0.467	0.853	0.537

Table II. Surgery time, ischemia blocking time and the diameter of resected tumor.

Group	Surgery time (min)	Ischemia blocking time (min)	Diameter of resected tumor (cm)
RN group	56.4 ± 10.3	16.8 ± 4.2	8.3 ± 0.9
Open NSS group	62.3 ± 11.5	22.7 ± 4.5	6.8 ± 0.4
Laparoscopic NSS group	84.7 ± 16.8	33.2 ± 5.3	7.2 ± 0.5
t	5.628	5.947	5.714
p	0.033	0.027	0.031

parenchyma 0.5 cm around the tumor. Electrocautery was performed on the wound of the kidney; then, the wound was closed by continuous suture. Opened renal pedicle, confirmed the absence of active bleeding and urine leakage, applied hemostatic gauze on the wound, indwelled a perineal drainage tube. Collected the resected tumor, confirmed the absence of active bleeding, counted surgical instruments and gauze, indwelled a 16F perirenal drainage tube, exhausted gas, withdrew all Trocar, sutured the wound layer by layer, and packed the wound with a sterile dressing.

Observational Measurements

The surgery time, ischemia blocking time, the diameter of resected tumor, the rate of a positive margin, perioperative and postoperative complications and successful rate of surgery were analyzed between these patients. After 3-year follow-up, the differences in survival and survival rate were analyzed.

Statistical Analysis

SPSS 20.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Quantitative data was represented by mean±SD, one way ANOVA was used for comparing multiple-groups, independent samples *t*-test was used for inter-group comparison. Qualitative data was represented by number or rate. The chi-square test was used for inter-group comparison. Log-Rank test was used for comparing survival. $p < 0.05$ was considered statistically significant.

Results

Surgery Time, Ischemia Blocking Time and The Diameter of Resected Tumor

As shown in Table II, both the mean surgery time and ischemia blocking time in open NSS group were comparable to those in RN group, and significantly shorter than laparoscopic NSS group, $p < 0.05$. The diameter of resected tumor in open NSS group was similar to that in laparoscopic NSS group and significantly smaller than RN group, $p < 0.05$.

Rate of Positive Margin, Perioperative and Postoperative Complications, Successful Rate of Surgery

As shown in Table III, the rate of positive margin in open NSS group was significantly lower than laparoscopic NSS group, the incidence of total complications in open NSS group was comparable to that in laparoscopic NSS group and significantly lower than RN group, the successful rate of surgery in open NSS group was significantly higher than laparoscopic NSS group, $p < 0.05$. The patients in open NSS group whose resection was failed could transfer to RN group,

Table III. Rate of positive margin, perioperative and postoperative complications, successful rate of surgery [n (%)].

Group	N	Rate of positive margin	Bleeding	Transfusion	Urine leakage	Chronic kidney disease	Total complications	Successful rate of surgery
RN group	35	0	2	3	2	4	11 (31.4)	35 (100)
Open NSS group	45	4 (8.9)	2	1	1	1	5 (11.1)	41 (91.1)
Laparoscopic NSS group	38	10 (26.3)	1	1	2	1	5 (13.2)	28 (73.7)
χ^2		4.462					6.380	4.462
p		0.035					0.041	0.035

the patients in laparoscopic NSS group whose resection was failed could transfer to open NSS group or RN group.

Survival and Survival Rate

As shown in Figure 1, the 75% survival was 30.0 months in RN group, > 35.0 months in open NSS group and 34.0 months in laparoscopic NSS group, the difference was significant (χ^2 = 108.562, $p < 0.001$). There were 10 cases of death in RN group (28.6%), 4 cases in open NSS group (8.9%) and 4 cases (10.5%) in laparoscopic NSS group. The mortality in open NSS group and laparoscopic NSS group was comparable and significantly lower than RN group (χ^2 = 6.869, p = 0.032).

Discussion

Evidence-based medicine indicated that the efficacy of NSS and RN in control of renal parenchymal tumor was comparable, both the life quality and total survival in patients undergoing NSS were increased[6]. Recently, Huang et al[7] suggested 3 major therapeutic targets for NSS: negative margin of the tumor, minimum damage to renal function and the absence of urinary complications. Laparoscopic NSS was characteristic of small trauma and rapid recovery; it had been the standard surgery for T1a renal cell carcinoma[8]. However, laparoscopic NSS was difficult to perform for solitary kidney, renal cell carcinoma of large size, central, bilateral and multiple renal tumor[9].

NSS in the treatment of the renal cell carcinoma required more precise dissection, careful operation, complete resection of the tumor during the renal ischemia as fast as possible and decreased rate of positive margins. Therefore, the size, location and invading depth in renal parenchyma of renal cell carcinoma should be evaluated before surgery. In most cases, the option was retroperitoneal approach[10]. The retroperitoneal approach was characteristic of small peritoneal trauma, limited bleeding, and exudate. This approach could also be selected for large tumor or tumor at renal hilus or facies ventralis. Blood supply was adequate in a large tumor, the distance between tumor and renal sinus vessels as well as renal collecting system. The space required for NSS was larger for T1b-T2 renal cell carcinoma than T1a, leading to larger renal detachment surface, prolonged renal pedicle blocking time, more time required for hemostasis and revascularization, increased blood loss and incidence of perioperative complications. Although skilled operator could improve the efficacy of laparoscopic NSS, the duration of warm ischemia or cold ischemia was longer than that in open NSS, the incidence of reperfusion injury and long-term chronic kidney disease was significantly increased[11,12]. The surgical field in open NSS was more exposed, leading to more precise

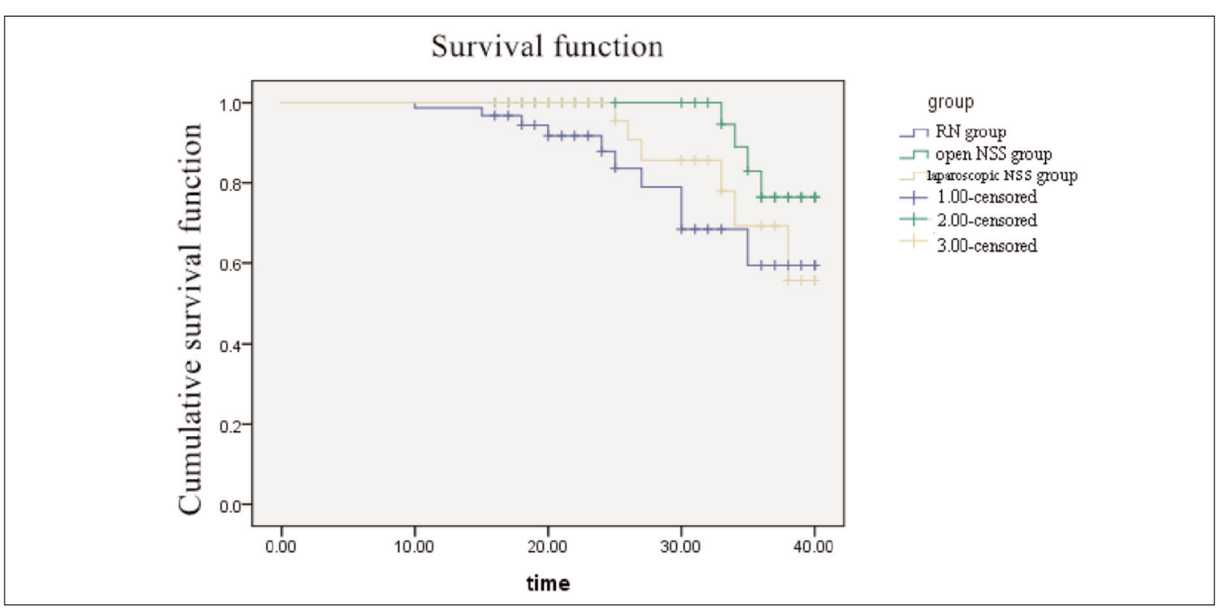

Figure 1. K-M method of survival time.

and accurate operation. Besides, cold ischemic vascular occlusion could be performed in the ice-cooling environment to increase the amount and quality of preserved nephron as far as possible[13]. For central renal cell carcinoma, which was in depth, completely, or partially embedded in the renal parenchyma, there was no tumor border or resection marker on the renal surface; thus, NSS was difficult to perform, renal collecting system was susceptible to damage, and the closure and remodeling were challenging. Therefore, NSS was a relative contraindication for this tumor type[14]. Laparoscopic NSS was suitable for peripheral renal cell carcinoma with superficial location, small size and outward growth. With the modification of vessel blocking technique and the development of novel hemostatic materials, the incidence of complications for laparoscopic NSS was higher than open NSS[15]. Open NSS was characteristic of large space, which allowed the exploration of location, depth and blood supply by ultrasound. Complete blockage of renal blood flow may eliminate backflow of renal vein blood, leading to nearly no blood on tumor bed wound, this facilitated precise recognition of renal parenchymal border, complete resection of tumor and affiliated renal tissues, and prevented positive margin[16].

This study demonstrated that both the mean surgery time and ischemia blocking time in open NSS group were comparable to those in RN group, and significantly shorter than laparoscopic NSS group, $p < 0.05$; the diameter of resected tumor in open NSS group was similar to that in laparoscopic NSS group and significantly smaller than RN group, $p < 0.05$. The rate of positive margin in open NSS group was significantly lower than laparoscopic NSS group, the incidence of total complications in open NSS group was comparable to that in laparoscopic NSS group and significantly lower than RN group, the successful rate of surgery in open NSS group was significantly higher than laparoscopic NSS group, $p < 0.05$. The survival in open NSS group was significantly prolonged, the mortality in open NSS group and laparoscopic NSS group was comparable and significantly lower than RN group, $p < 0.001$.

Conclusions

The open NSS was more safe and effective in the treatment of complex renal cell carcinoma than RN and laparoscopic NSS.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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