

Nephron-sparing surgery for small renal cell carcinoma

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Received 26 December 2008

Abstract

Objective: To investigate the method and effect of nephron-sparing surgery in the treatment of small renal cell carcinoma. **Methods:** From August 1997 to October 2008, 48 cases of small renal cell carcinomas were confirmed by surgery and pathology, and reviewed retrospectively. Of the 48 cases, there was 1 patient with bilateral tumors, 8 with solitary kidney tumors, 1 with unilateral tumor and a damaged contralateral kidney, and 38 with unilateral tumors and a normal contralateral kidney; 9 underwent tumor enucleation and the remaining patients received partial nephrectomy. **Results:** There were no local tumor recurrences and/or tumor metastasis at a mean follow-up of 60 months. **Conclusion:** Confirming conclusions from other centers, we have found that nephron-sparing surgery is an effective treatment for small renal cell carcinomas.

Keywords: small renal cell carcinoma; nephron-sparing surgery; kidney neoplasms

INTRODUCTION

With improvements of public health awareness, and advances in science and technology, and especially the progress in kidney imaging, the detection rate of small renal carcinoma is rising each year^[1]. From August 1997 to October 2008, a total of 396 renal carcinoma operations were performed at our hospital. Among these, 48 cases of small renal carcinoma underwent nephron-sparing surgery with a satisfactory outcome. These cases are reported below.

MATERIALS AND METHODS

Clinical data

The study group had a total of 48 cases, 32 males and 16 females, age 18–71yr with a mean age of 43.5yr. Thirty-four patients were asymptomatic and their tumors were found during physical examination, 9 patients experienced low-back pain, and 5 patients exhibited hematuria. Bilateral renal carcinoma in a patient was found contra-laterally 2 years after radical nephrectomy for renal carcinoma; congenital or acquired

solitary kidney renal carcinomas in 8 cases, among which, 5 cases involved the left kidney and 3 the right kidney; 1 renal carcinoma case with bilateral kidney cast-shaped stone; renal carcinoma with normal contralateral kidney in 38 cases. Fifteen patients were hypertensive, 8 had diabetes, and 6 had kidney cysts. The detected disease course was 3d–11m, with a mean of 3.8m. The pre-operative examinations of type B ultrasound, IVU and CT revealed tumors in the superior pole in 17 cases, the inferior pole in 23 cases, and the middle part of the kidney in 8 cases. The tumors had a diameter range of 1.2–4.0 cm, with a mean of 2.5 cm. None of the cases had intravenous tumor embolism of the inferior vena cava and kidney, and there was no renal pedicle lymph node, nor distant metastasis. **Surgical methods**

The XI intercostal or XII intercostal lumbar incision was adopted in 32 cases. The separation was performed within the Gerota's fascia. The para-renal fat of the tumor surface was totally resected with the tumor mass. In the remaining cases (16 patients) laparoscopic surgery was used. In most situations, the kidney blood vessels were blocked temporarily to reduce hemorrhage and tissue expansion. To prevent kidney ischemic injury, a

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sufficient volume of fluid was replenished and i.v. mannitol administered to promote a rapid diuresis at 5-10 min before the arterial blockage. When the expected blockage time was over 30min, it was necessary to cool down the kidney surface to reduce renal ischemic injury, and to administer 2.0 gram inosine by a rapid i.v. drip. In our case population, 9 patients underwent tumor enucleation, and the remainder underwent superior-pole or inferior-pole partial nephrectomy. At the time of tumor enucleation, special care was taken to avoid damaging the tumor-connected Gerota's fascia. The normal fat tissue at the surface of and around the tumor was resected. Then a circular incision was made at 0.5cm outside the tumor pseudo capsule and the tumor resected. During partial nephrectomy of either the superior pole or inferior pole of the kidney, the resection was made at least 0.5-1.0 cm away from the tumor tissue. In 36 of the cases, intra-operative tissue samples were sent for rapid pathological examination. These were definitively diagnosed as renal carcinoma with a negative cutting margin. At the kidney wound surface, 3-0 absorbable sutures were used to suture the exposed small blood vessels. With partial nephrectomy, where the margin of kidney reached the renal pelvis, 5-0 absorbable sutures were used to suture tightly, so as to avoid the postoperative leakage of urine. After the absorbable hemostasis gauze or gelatin sponge was cushioned into the kidney's wound surface, 1-0 absorbable sutures were used to suture the kidney parenchyma, and a para-renal irrigation tube was routinely inserted.

RESULTS

Pathological typing was as follows: Clear cell carcinoma, 34 cases; granular cell carcinoma, 9 cases; papillary carcinoma, 5 cases. Following surgery, there were no postoperative complications, such as hemorrhage, leakage of urine, infection, or kidney failure. The postoperative follow-up was from 3m-11yr, with a mean of 60 months. There was no tumor recurrence, the plasma creatinine and BUN were in normal range, and IVU showed that the kidney appeared to function quite well on the operative side.

DISCUSSION

In 1887, Czerny first applied partial nephrectomy to treat malignant kidney tumors, but the extremely high level of postoperative complications limited its application at that time. Radical nephrectomy has always been the gold standard for renal carcinoma surgery. In recent years, with the advances in imaging technology, refinements in surgical techniques and improvements in methods of preventing the kidney ischemic injury, nephron-sparing surgery for renal carcinoma has provided

long-term follow-up results of large groups of cases^[2]. Current surgical techniques can safely and effectively preserve kidney function. The mortality rate, recurrence rate and patient tumor-free survival rate are comparable to those of radical nephrectomy. Nephron-sparing surgery is now a safe surgical method^[3].

Surgical rationales

The major rationales of nephron-sparing surgery for small renal carcinoma are as follows^[4]: (1) renal carcinoma with a risk of bilateral occurrence; (2) contra-lateral kidney with a future risk of function loss through other diseases; (3) increased risks of proteinuria, hypertension and kidney insufficiency for uni-kidney patients as a possible result of high filtration after a reduced number of nephrons and glomerular sclerosis; (4) nephron-sparing surgery has been proven feasible, clinically and on a pathological basis.

Surgical indications

The present surgery had the following absolute indications: life-sustaining post-radical nephrectomy patients in need of blood dialysis or kidney transplantation, for example, anatomically or functionally solitary kidney and bilateral parenchymal kidney tumor^[5]. The present group had 9 such cases (19%).

Further absolute indications are unilateral renal carcinoma, contra-lateral lesions endangering the kidney function, such as contra-lateral kidney calculus, TB, chronic pyelonephritis, ureteral reflux, kidney arterial stenosis, diabetic nephropathy and kidney arterial sclerosis. The present group had 1 such case (2%).

Elective indications refer to those patients with focal small renal carcinoma and contra-lateral normal kidney^[6]. It is generally agreed that the tumor diameter should be ≤ 4 cm^[7]. The present group had 38 such cases (79%).

Surgical methods

The nephron-sparing surgery for renal carcinoma includes tumor enucleation, partial nephrectomy and autologous transplantation after ex vivo kidney partial nephrectomy^[8]. In renal carcinoma enucleation, a circular incision is made in the kidney parenchyma along the tumor margin. The tumor tissue, together with at least 0.5 cm of normal tissue, are enucleated together. After enucleation, a multi-site rapid biopsy is performed of the kidney wound surface. While the cutting margin is confirmed to be tumor-free, finger pressure is applied on the kidney parenchyma to control hemorrhage. A cross-locking U-shaped suture is made with absorbable suture. When enucleation is performed for a tumor in the middle part of the kidney, digital subtraction angiography (DSA) may be employed to determine the supply status of blood vessels, if necessary. The advan-

tages to this method include its ease and speed, the lack of a need to block the renal blood flow, and the fact that kidney tissue with normal functions can be saved maximally. The major disadvantage is that tumor enucleation has the risk of leaving a micro-tumor. In the present group, 9 cases underwent tumor enucleation.

In partial nephrectomy, the renal artery was exposed to prepare for controlling hemorrhage. One pole, or a part of the kidney over 0.5-1.0 cm away from the tumor, was resected. During the operation, hemostasis was best applied by pressure rather than by blocking the kidney blood vessel. If the renal pedicle was blocked, this should not occur for more than 20 min^[9]. The present group had 39 patients who underwent partial nephrectomy. An autologous transplantation after ex vivo kidney partial nephrectomy is indicated for a complex renal carcinoma involving the renal hilus. The present group had no such cases.

Surgical complications

The complications of nephron-sparing surgery, which may be as high as 10%-20%, are more common than those of radical or simple nephrectomy^[10]. The major complications are as follows: (1) Hemorrhage (1%-6%). When serious, the patients need to be surgically explored to search for hemostasis or manage any arterial embolism. The Argon ray laser knife is helpful in handling blood effusion at the surgical surface; (2) Leakage of urine (2%-15%). This is mostly related to the reconstruction techniques of the collection system. The intra-operative injection of methylene blue into the collection system will help to discover leakage of urine, which can be remedied by suturing tightly. Furthermore, if there is no obstruction, leakage of urine is mostly cured through such conservative methods as an indwelling catheter. (3) Ischemic RF. This is most commonly seen in ex vivo kidney surgical patients or with relatively large tumors, prolonged blockage of blood flow, and those in frequent need of temporary or permanent dialysis. Since no ex vivo kidney surgery was performed, the intra-operative hemostasis was thorough and the suturing was tight, such that the present group had no occurrence of these postoperative complications^[11].

Surgical outcome

Previously this surgery was applied for solitary kidney or bilateral renal cell carcinoma. It could spare the patients from blood dialysis therapy or kidney transplantation therapy. For the patients, there was no difference in postoperative survival rate when compared with radical nephrectomy, and both the local recurrence rate and distant metastasis rate were also quite low. Some scholars have discreetly employed the present surgery for localized renal cell carcinoma when the contra-

lateral kidney was normal^[12]. The short-term and long-term follow-up results were quite encouraging and the tumor-specific survival rate was as high as 72%-100%. The important influencing factors of survival rate are tumor grading, staging, unilateral/bilateral lesions and tumor diameter. Many studies retrospectively compared the outcomes of the present surgery with radical nephrectomy. In particular, Darmiento *et al*^[13] conducted a prospective comparative study with a mean follow-up time as long as 6 years. In terms of survival rate (both at 96%), local recurrence rate (both at 0%), or distant metastasis rate (both at 5.2%), the nephron-sparing surgery was not different from radical nephrectomy. In 2004, Manikandan *et al*^[14] reviewed the literature of patients with renal tumors up to 4 cm in diameter. There were a total of 797 cases in the radical nephrectomy group and 1,211 in the nephron-sparing surgery group. The parameters specifically evaluated were evidence of local recurrence, disease progression, and death within 33 months. Laparoscopic radical nephrectomy and laparoscopic nephron-sparing surgery articles were also reviewed. They considered that nephron-sparing surgery was as effective as radical nephrectomy in patients with renal cell tumors up to 4 cm. The present group had a mean follow-up of 60 months. There were no cases of recurrence or metastasis. Nephron-sparing surgery has become the standard operation in treating small volume (diameter \leq 4 cm) kidney neoplasms, and many research centers have successfully treated larger volume kidney tumors^[15].

Existing problems of surgery

For the nephron-sparing surgery, one major concern is with the local recurrence of operative surface with renal carcinomas in postoperative patients. In such cases, the tumor often lacks a complete pseudo-capsule, or the pseudo-capsule is attacked, or the tumor growth has caused perforation of the capsule. Therefore, partial nephrectomy (wedge-shaped nephrectomy: tumor enucleation within the normal kidney parenchyma or kidney polar resection) is superior to the tumor enucleation performed simply along the tumor pseudo-capsule. It was thought that the tumor should be resected together with normal kidney tissue 1 cm at the tumor margin. In fact, this is unnecessary. For the low-grade renal cell carcinoma, it is sufficient to perform partial nephrectomy several millimeters away from the tumor margin, as long as there is no residual tumor at the operative wound surface^[16]. A study by Li *et al*^[17] also showed that mini-margin nephron-sparing surgery was a safe and effective approach for treating early localized renal cell carcinoma of 4 cm or less. From 1998 to 2006, they treated 115 patients by nephron-sparing surgery using a mini-margin of less than 5 mm.

Another concern with the nephron-sparing surgery is the postoperative recurrence of tumors caused by the multi-focal tumors. This often occurs if small foci are left over or are operatively indistinguishable, or there are postoperative recurrent foci. The multi-focal renal carcinoma is commonly seen in von Hippel-Lindau syndrome and papillary renal cell carcinoma^[5]. For this type of patient, the possibility of both multi-focal disease and bilateral occurrence should be considered. As demonstrated by the results of pathological data of specimens from radical nephrectomy patients, the incidence rate of multi-focal renal carcinoma was as high as 25%, while reports in the literature showed that the recurrence rate of residual renal carcinoma after partial nephrectomy was quite low. This contradiction is seemingly hard to explain^[18]. For the present, the characteristics of the natural disease course for small and multi-focal low-grade renal cell carcinomas remains unclear. Some scholars think that, after the primary tumor foci is resected, the growth of residual and small secondary foci will be inhibited. But this is only a hypothesis which targets the immunological mechanism of tumors. Thus, the question is still moot as far as selecting nephron-sparing surgery for the treatment of multi-foci tumors^[19].

Postoperative follow-up

It has been found in most clinical trials that the staging and degree of cell differentiation of the primary tumor correlates with the local recurrence. The low-differentiated and high-grade tumor has a higher rate of local recurrence. The nephron-sparing surgery has the postoperative risks of local recurrence and distant metastasis. Prior to the operation, the patients should be fully informed and be closely followed up postoperatively for the rest of their life. Van Poppel^[3] suggested that the postoperative follow-up be conducted once every 3 months for the first year, once every 4 months for the second and third year, once every 6 months for the fourth and fifth year, and once yearly thereafter. Hafez *et al*^[20] summarized a total of 327 cases undergoing nephron-sparing surgery with a mean follow-up of 5 years, a local recurrence rate of 4.0% and no local recurrence of a T1 stage tumor. In addition, the size of the primary tumor is also correlated with the postoperative local recurrence. Tumors < 2.5 cm had no postoperative local recurrence, and for the 2.5-4.0 cm group, the postoperative recurrence rate was 2%(1/38). The most common metastasis sites are lung, skeleton and liver, in decreasing order. Thus it is suggested that the postoperative follow-up examination should be conducted differently based upon pathological staging. The patients should be followed up for at least once each year. If

kidney tumor recurrence is found, the physician may again perform either nephron-sparing surgery or renal carcinoma radical surgery. For those with distant metastasis, biotherapy may be complementary. Preventive biotherapy is not beneficial for small renal carcinomas. In the present group, the longest patient follow-up period was 11 years, and the patient remains alive.

In recent years, with the development and popularization of laparoscopic techniques, many renal cell tumors of less than 4 cm diameter have been treated by laparoscopic partial nephrectomy, with a tumor margin of less than 5 mm. Intraoperative biopsy was not recommended^[21]. A large number of clinical trials^[22,23] have shown that there were no significant differences between laparoscopic partial nephrectomy and open surgery on intraoperative and postoperative complication rates, cutting margin positive rates, and postoperative 5-year survival rates. Of the present group, 16 patients underwent retroperitoneal laparoscopic partial nephrectomy, all with a successful outcome.

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