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Laparoscopic simple enucleation and coagulation on tumor bed using argon beam coagulator for treating small renal cell carcinomas: An animal study followed by clinical application

Changwen Zhang^{BCEF}, Yong Xu^{AG}, Zhihong Zhang^E, Baomin Qiao^D, Kuo Yang^G,
Ranlu Liu^E, Baojie Ma^E

Department of Urology, Second Hospital of Tianjin Medical University, Tianjin Institute of Urology, Tianjin, China

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Background:

The aim of our study was to evaluate the feasibility and clinical effect of laparoscopic simple enucleation and coagulation on tumor bed using an argon beam coagulator for treating small renal cell carcinomas.

Material/Methods:

The animal experiments of coagulation therapy on the wound tissue bed during partial nephrectomy with an argon beam coagulator were performed on 16 rabbits, which were randomly divided into 4 groups. Groups A and B had renal artery occlusion; the treatment time of coagulation was 4 seconds and 6 seconds, respectively. Groups C and D did not have renal artery occlusion; the treatment time of coagulation was 2 seconds and 4 seconds, respectively. Then 30 clinical operations of laparoscopic simple enucleation and coagulation on tumor bed using an argon beam coagulator were performed.

Results:

All 16 rabbits successfully underwent the operation. By the histological examination, the scab depth of the wound tissue bed in groups A, B, C, and D were 2.76 ± 0.17 mm, 3.15 ± 0.15 mm, 2.28 ± 0.16 mm and 2.75 ± 0.06 mm, respectively. Group A differed significantly from groups B and C ($P=0.012$, 0.007), and group D differed significantly from groups B and C ($P=0.002$, 0.002). In the clinical study, all 30 patients successfully underwent the operation. The mean operative time was 182 minutes, and the mean blood loss was 280 ml. With a median follow-up time of 37 months, neither local recurrence nor distant metastasis was found by computerized tomography scan.

Conclusions:

Laparoscopic simple enucleation and coagulation on tumor bed using an argon beam coagulator can be considered for treating small renal cell carcinomas. However, the indication of this procedure should be highly selected.

key words:

renal cell carcinoma • simple enucleation • laparoscopy • animal experiment • clinical study • argon beam coagulator

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Author's address:

Yong Xu, Department of Urology, Second Hospital of Tianjin Medical University, Tianjin Institute of Urology, Tianjin, China, e-mail: xuyong8816@sina.com

BACKGROUND

Renal cell carcinoma (RCC) accounts for 2% of all solid tumors and is the urologic malignancy associated with the highest mortality rate due to the lack of efficient systemic therapy [1]. In recent years, with the increasing number of asymptomatic, small, lower-stage, and incidentally detected renal tumors, laparoscopic nephron-sparing surgery (LNSS) has been widely accepted and has emerged as a minimally invasive alternative treatment for small RCC with a normal contralateral kidney. Early studies showed NSS could offer equally effective local control and a similar disease-specific survival rate compared with radical nephrectomy (RN) for treating RCC of <4 cm in their greatest dimension [2,3]. Many studies have shown that a certain amount of normal tissue should be excised along with the tumor to avoid the risk of local recurrence. However, Sutherland et al. [4] argued that the margin width was irrelevant to the possibility of local recurrence if the tumor was completely resected. Some researchers challenged the accepted wisdom, and proposed simple enucleation to the patients who followed surgery indication. However, due to the risks, such as local tumor recurrence and excessive bleeding from the renal parenchyma, simple enucleation is still confronted with technical challenges. Some ablative technology instruments, such as ultrasonic shears, microwave tissue coagulator, argon beam coagulator and bipolar electrocautery, have been used with solid vascular organs (e.g., liver, spleen and kidney) to control parenchymal bleeding, and were reported to be useful and less invasive [5,6]. However, some complications (e.g., urinoma and renal arteriovenous fistula) were reported with the application of these instruments in NSS [6]. There is no established method that is widely accepted and applied.

We think that tumor size, location, and proper coagulator devices should be considered to avoid these complications. Recently, we succeeded in ablating the wound tissue bed during NSS using argon beam coagulator in an animal experiment. Additionally, 30 small RCC patients underwent laparoscopic simple enucleation and tumor bed ablation with an argon beam coagulator from June 2006 to April 2011. The patients were followed up for a median time of more than 37 months, with very positive outcomes in most cases.

MATERIAL AND METHODS

Animal experiment

The care and treatment of the experimental animals conformed to the guidelines for the ethical treatment of laboratory animals of the Tianjin Medical University animal laboratory.

Sixteen rabbits weighting 2~3 kg were obtained from the animal laboratory of Tianjin Medical University (Tianjin China), and housed in a controlled environment with an ambient room temperature of 24°C. The rabbits were randomly divided into 4 equal groups. Group A was without renal artery occlusion, the wound tissue bed was ablated with an argon beam coagulator (Beamer plus, Conmed Corporation, USA) during NSS by the standard of stopping bleeding, and the treatment time was 4 seconds. In Group B, on the basis of group A, the wound tissue bed was re-ablated for 2 seconds with an argon beam coagulator. Group C had renal artery

occlusion, the wound tissue bed was ablated with an argon beam coagulator by the standard of stanching bleeding, and the treatment time was 2 seconds. In Group D, upon the basis of group C, the wound tissue bed was re-ablated for 2 seconds with an argon beam coagulator.

After the preparation, the rabbits were placed in the supine position throughout the operation. Pentobarbital sodium 3% (1 ml/kg) was injected via the ear vein. Surgery was performed through an abdominal mid-line incision 15 cm in length, and the left kidney was exposed. In Group A, after the upper or lower pole of the kidney had been enucleated about 1 cm³, the wound tissue bed was ablated using an argon beam coagulator for stanching bleeding, with argon flow rate was 6.0 L/min, the power was 90 w, and the treatment time was 2 seconds. In Group B the wound tissue bed was re-sprayed for 2 seconds after stanching bleeding with an argon beam coagulator, and other procedures were the same as that of Group A. In Group C, after blocking the renal pedicle with an arterial clip clamp, we enucleated the tissue about 1 cm³ in the upper or lower pole of the kidney, then ablated the wound tissue bed with an argon beam coagulator. When there was no bleeding, we removed the arterial clip clamp, and the renal pedicle blocking time was <30 minutes. The ablation time was 2 seconds. In Group D the wound tissue bed was re-sprayed for 2 seconds with the argon beam coagulator after stanching bleeding following group C (Figure 1A). Three weeks later, all the renal wound-tissue specimens were harvested and examined under an optical microscope after being fixed, embedded, sectioned and stained by HE.

Clinical study

Thirty patients underwent laparoscopic simple enucleation and tumor bed ablation using the argon beam coagulator from June 2006 to April 2011. The basic operative indications were small and incidentally detected renal tumors which were solitary, located peripherally, well demarcated, exophytic and no less than 1 cm away from the kidney collecting system on computerized tomography (CT) scan (Figure 1B). The preoperative diagnosis was T1N0M0 renal cell carcinoma in all patients. Preoperative patient characteristics are shown in Table 1.

Under general anesthesia and with 16F urethral catheter being inserted, patients were placed in a lateral decubitus position, securing both arms on the sides; proper padding was placed at all pressure points. A 2 cm incision was made on the posterior axillary line across the twelfth rib costal margin in the left lumbar region and the peritoneum was pushed away using a finger, to expose to the perirenal space. A balloon device for the dilation of retroperitoneum was inserted into the perirenal space, and the perirenal space was enlarged with 800 ml air pumped into the balloon. After the pneumoperitoneum was created, a 25° laparoscope was inserted above the midaxillary line, across the spina iliaca. Additional working ports (5 mm) were placed under the anterior axillary line across the eleventh rib costal margin. The kidney was exposed by the opening of Gerota's fascia. After enucleating the tumor about 1 cm margin away from the capsular using an ultrasonically activated scalpel (UAS), we ablated the tumor bed with an argon beam coagulator for 6~10 seconds, and then secured the wound tissue bed with assimilable gauze (Ethicon, Somerville, NJ).

Figure 1. (A) The demonstration of coagulation therapy on the wound tissue bed using an argon beam. (B) CT scan demonstrated a renal cell carcinoma, which was in the lateral portion of the kidney (arrow). (C) Compact structure in the area of scab, and the granulation tissue was found between renal tissue and scab (HE $\times 40$). (D) Calcification was found in the area of necrosis (HE $\times 40$).

Table 1. Patient characteristics.

Sex	16 men, 14 women
Age (yr)	Median 57.2 (range 42~65)
Tumor size (mm)	Median 28 (range 15~38)
Tumor laterality	Right 18, left 12
Tumor location	Upper pole 7 Upper portion 3 (lateral 2, anterior 1) Middle portion 10 (lateral 6, anterior 4) Lower portion 6 (lateral 2, anterior 4) Lower pole 4

Statistical analysis

SPSS Statistics 17.0 was applied to analyze data. The difference between 2 groups was assessed using the independent t-test and $P < 0.05$ was considered statistically significant.

RESULTS

Animal experiment

All 16 rabbits survived the operation and healed satisfactorily. By the histological examination, calcification was

Figure 2. The scab depth of the 4 group rabbits' kidneys. Group A differed significantly from group B & C ($P=0.012$, 0.007), as well as group D from group B & C ($P=0.002$, 0.002), but no significant difference between group A and group D ($P=0.915$).

found inside the area of necrosis, and compact structure in scab. Moreover, granulation tissue was found between the scab and the renal tissue (Figure 1C,D). The scab depth of the rabbits' kidneys in Groups A, B, C and D was 2.76 ± 0.17 mm, 3.15 ± 0.15 mm, 2.28 ± 0.16 mm and 2.75 ± 0.06 mm, respectively. Group A differed significantly from groups B and C ($P=0.012$, 0.007), and group D differed significantly from groups B & C ($P=0.002$, 0.002), but there was

no significant difference between group A and group D ($P=0.915$) (Figure 2).

Clinical study

All 30 patients successfully underwent laparoscopic simple enucleation and tumor bed ablation with an argon beam coagulator. The mean operative time was 182 minutes (range from 100 to 252 minutes), and the mean blood loss was 280 ml (range from 100 to 400 ml). Urine leakage persisted for 16 days in 1 patient, and was managed conservatively. Another patient showed allergy to assimilable gauze, and the fluid effused via catheter drainage, which was taken away 1 month later, while the median duration of catheter drainage was 4 days (range from 3 to 6 days) in other patients. There were no other postoperative complications (e.g., hemorrhage, urinoma, renal function insufficiency and infection) recorded during the early postoperative period (within the first 30 days). No patients required blood transfusion. Postoperatively, all patients could eat and walk on day 2. The median time of full convalescence was 10 days (range from 6 to 30 days).

Histopathological diagnosis showed renal cell carcinoma in all 30 patients, including clear cell renal cell carcinoma in 21, papillary renal cell carcinoma in 5, chromophobe renal cell carcinoma in 2, multilocular cystic renal cell carcinoma in 1, and mucinous tubular and spindle cell carcinoma in 1. All the patients were followed up and the median time was 37 months (range from 8 to 54 months). One patient died of unrelated cancer causes 15 months after kidney surgery, without any evidence of tumor recurrence. None of the other 29 patients with renal cell carcinoma treated laparoscopically showed local recurrence or distant metastasis when examined by CT scan. Renal functions were stable in all patients during the whole follow-up period, with a median postoperative creatinine level of 92 $\mu\text{mol/l}$ (range from 75 to 104 $\mu\text{mol/l}$).

DISCUSSION

Historically, RN as described by Robson et al. has been the gold standard for patients with localized RCC [7]. However, the number of asymptomatic, small, lower-stage, and incidentally detected renal tumors greatly increased as a result of the wide-spread usage of ultrasound and CT scan for evaluating other abdominal processes. Other therapeutic approaches have been explored, such as cryoablation, high-intensity focused US, radiofrequency ablation, and simple enucleation [8]. Meanwhile, the long-term effectiveness of these emerging technologies remains to be determined, and there is controversy regarding how these patients should be treated. With the development of laparoscopic technique, laparoscopic surgery has been widely used in many diseases, such as ovarian endometriomas, adrenal gland neoplasms and renal carcinomas [9–11]. It was reported that LNSS was easier and safer than RN, and its oncological results appeared to be equal with RN for small localized tumors. Meanwhile, the application of UAS, laser, microwave coagulator and Water Jet Cutting System promoted the development of LNSS [6,12,13]. The choice of the patients for NSS had been changed from the cases with solitary kidney or bilateral renal carcinoma before to those with a normal contralateral kidney [14]. Lapini et al. [15] found that

simple enucleation was a safe and acceptable approach. In the present study we successfully performed an animal experiment of ablating the wound tissue bed during NSS with an argon beam coagulator. More importantly, 30 small RCC patients underwent laparoscopic simple enucleation and tumor bed ablation with an argon beam coagulator, with very good outcome in most cases.

Simple enucleation has been regarded as a challenging surgery because of its associated complications (e.g., hemorrhage) local recurrence, urinary fistula and renal dysfunction. Uzzo et al. [16] reported that the rate of acute or delayed hemorrhage ranged from 1.3–7.9% in simple enucleation. In our study, after enucleating the tumor, we widely ablated the tumor bed using the argon beam coagulator, which caused little blood loss in the tumor bed, and no delayed hemorrhage complications were found during the early postoperative period. Thus, the argon beam coagulator may be a good technique for stanching in simple enucleation. Until recently, surgical practice for NSS is to have a >1 cm margin of normal tissue around the tumor. However, the optimal resection margin is still under discussion because satellite lesions can be found more than 1.0 cm beyond the primary tumor [17]. Some recent studies showed that the width of the margin seemed less important, and NSS with a smaller margin was also safe and effective in tumor control [18]. During the operation, we enucleated the tumor with a 1 cm margin away from the capsular, and then coagulated all resection beds routinely using an argon beam coagulator. During a long follow-up, no recurrence was found. Lapini et al. [15] similarly used diathermy spray coagulation or argon beam laser on the tumor bed, and also achieved good results. More importantly, coagulation destroyed another rim of parenchyma up to 2–3 mm in our study, which caused the residual tumor to be necrotic. This might explain why simple enucleation provides the same results as NSS, which needs a larger rim of healthy tissue to be resected together with the tumor. Urinary fistula is one of the most common complications after NSS, with a reported rate of 6.5% [16]. The low rate of morbidity in our study may be due to the strict patient selection criteria and more renal parenchyma left with the technique of enucleation.

Kane et al. [19] reported that with temporary renal artery occlusion, the average warm ischemia time was 43 ± 10 minutes (range from 25 to 65 minutes), and the serum creatinine increased after surgery, but the differences from the preoperative value were not statistically significant. They also found that there were no differences in blood loss, operative time, or margin status between the occlusion and non-occlusion patients. Nevertheless, Campbell et al. [20] concluded that the rates of postoperative acute renal failure after open partial nephrectomy can approach 14% with artery occlusion. Regarding the safety of arterial occlusion and warm ischemia, some investigators have been prompted to study non-ischemic hemostatic techniques, including cable tie tourniquet, radio frequency ablation and so on. Despite these efforts, the techniques are still unproved. In our study, we coagulated the tumor bed with an argon beam coagulator without blocking the artery, which not only limited the tissue injury during the exposure of the renal pedicle, but left wider adjacent normal parenchyma tissue. More residual renal function could be compromised, which is important, especially for the patients with only 1 kidney.

The present studies in patients with T1 tumors revealed that NSS could be safely performed and resulted in a very low percentage of progression (4.5%) and renal cancer-related death (3%) [21]. Roos et al. [22] reported that NSS could be considered as the standard care for most RCC masses when feasible, and they pointed out that the tumor location, not the tumor size, appeared to be the limiting factor for NSS. Until now, there has been no definite evidence of a theoretical advantage of NSS over simple enucleation. The research by Pertia et al. nicely provides additional evidence in favor of simple enucleation in cT1a and cT1b RCC. In their limited series of 30 patients, the complication rate was very low, with only 1 urinary leakage, and no hemorrhagic complications. Five- and 7-year cancer-specific survival rates were impressive, at 100% and 96.5%, respectively [15], similar to our study. During the long follow-up period, we did not observe any local recurrence, and we also got high cancer-specific and recurrence-free survival rates.

CONCLUSIONS

Simple enucleation and coagulation on the tumor bed using an argon beam coagulator has the advantage of preserving more kidney parenchyma and avoiding major bleeding and the opening of the collecting system, which is also associated with a reported long-term incidence of local recurrence similar to that of partial nephrectomy [18]. However, the indication should be strictly restricted to renal tumors that are small, solitary, well-demarcated, located peripherally, exophytic and no less than 1 cm away from the kidney collecting system on CT scan, in order to minimize serious complications secondary to unexpected collateral damage to surrounding structures.

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