Non-ischemic Nephron-sparing Surgery for Small Renal Cell Carcinoma: Complete Tumor Enucleation Using a Microwave Tissue Coagulator

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Received August 9, 2001; accepted December 27, 2001

Objective: To determine the methodological usefulness of non-ischemic complete enucleation for small renal cell carcinomas (RCC) using a microwave tissue coagulator (MTC).

Methods: Fifty-nine patients (61 kidneys) underwent non-ischemic complete tumor enucleation by MTC. Of the 59 patients, 46 had an elective indication and 15 kidneys of 13 patients had an imperative indication. RCC was exposed with minimal peri-renal detachment. The demarcation line, 7–10 mm from the tumor, was coagulated at 8–10 mm intervals with a microwave antenna needle for 30–40 s at 50–60 W. The renal tumor was excised along the coagulated zone with normal surrounding tissue. The enucleation bed was covered with fibrin glue or fat tissue without approximation.

Results: The operations were successfully completed in all intended cases. The mean operation time was 160 ± 43 (median: 160) min and the mean blood loss was 313 ± 370 (median: 158) ml. No major bleeding or urine leakage from the enucleation bed was observed in 62.2 and 88.5% of cases, respectively. The minor bleeding and urine leakage were controlled easily with absorbable sutures. None of the cases presented with postoperative bleeding or urine leakage from the enucleation bed. Severe impairment of the renal function was not observed in any case evaluated by means of serum creatinine, creatinine clearance and radioisotope examination. The 5-year overall survival rate was 87% without recurrence up to 23.1 ± 19.5 months of the mean follow-up.

Conclusion: Non-ischemic complete tumor enucleation using MTC constitutes a simple, reliable and less invasive alternative to ordinary nephron-sparing surgeries for small RCC.

Key words: renal cell carcinoma – non-ischemic procedure – complete enucleation – microwave tissue coagulator

INTRODUCTION

Recent advances in diagnostic imaging have led to an increase in asymptomatic small RCC over the last two decades. While the prognosis for patients with asymptomatic small RCC was excellent when they underwent radical nephrectomy (1–4), an excellent prognosis was also reported in imperative indication patients who underwent nephron-sparing surgery (5–8). Although partial nephrectomy for RCC in patients with a normal functioning contralateral kidney was first reported by Vermooten (9), radical nephrectomy has still been the gold standard for all types of RCC based on the propriety of Robson et al.’s report (10). Recently there have been several reports indicating that nephron-sparing surgery in elective cases with a normal functioning contralateral kidney may be acceptable as an alternative procedure to radical nephrectomy under specific eligibility criteria (11–14). Thus, the indication of nephron-sparing surgery has become very controversial in the treatment of small RCC in patients with a normal functioning contralateral kidney: is radical nephrectomy necessary or is nephron-sparing surgery sufficient?

Besides the controversy around the indication, the technical factors for nephron-sparing surgery remain problematic, including the possibility of local recurrence, the management of perioperative bleeding and impairment of renal function caused by renal ischemia. With the increase in the chance to treat asymptomatic small RCCs, simple, reliable minimally invasive techniques of partial nephrectomy or tumor enucleation by using a microwave tissue coagulator (MTC), for exam-
ple, without renal ischemia have been anticipated. An MTC (Microtaze OT-110M, Aswell, Osaka, Japan) was developed in Japan for partial hepatectomy (15) and it allows partial resection of parenchymal organs without ischemic procedure. Tissue coagulation by MTC is achieved by heat that derived from the rapid oscillation of H\textsubscript{2}O particles at a rate of 2450 million per second. The thermal effect by microwaves is limited only to the area where the microwave reaches with H\textsubscript{2}O particles immersed. If the entire circumference of an RCC can be coagulated by MTC, complete enucleation can be achieved, thereby minimizing cancer cell dissemination without clamping vessels.

In this paper, we report the surgical procedure, technical feasibility and early clinical outcome of the non-ischemic complete enucleation for small RCC using MTC.

PATIENTS AND METHODS

Between September 1993 and May 2000, 59 patients (61 kidneys) underwent non-ischemic complete enucleation of small RCC using MTC in Nara Medical University Hospital and its affiliated hospitals. Patients with a minimum of 3 months’ follow-up included 47 men and 12 women with an average age of 60.5 (37–80) years. The average patient age in the elective indication and imperative indication groups was 59.7 ± 11.3 and 62.8 ± 10.8 years, respectively. Of the 61 kidneys of the 59 patients, 46 had an elective indication and 15 kidneys of 13 patients had an imperative indication; metachronous bilateral RCC in six cases, synchronous bilateral RCC in three cases (two cases underwent bilateral enucleations and one underwent enucleation with contralateral lower pole resection) and a single kidney after nephrectomy in four cases individually due to multiple renal cysts, von Hippel–Lindau disease, atrophic kidney and renal pelvic tumor.

The indications for this procedure constituted two conditions: the tumor itself and the patient’s status. To meet the indication for this operation, tumors should be (1) solitary and round or oval shaped, (2) smaller than 50 mm maximum diameter (preferably 40 mm for elective cases), (3) expanding outer growth with a clear margin and (4) clear enhancement under CT scan. The patient should (1) be in a tolerable physical condition for standard nephrectomy, (2) have no symptoms associated with RCC and (3) give informed consent based on an understanding of the risks and benefits of this treatment.

The maximum diameter of RCC on CT scan averaged 25.9 ± 9.9 (10–50) mm in elective cases and 28.1 ± 10.2 (10–48) mm of cases: patients/kidneys

<table>
<thead>
<tr>
<th>Indication</th>
<th>No. of cases</th>
<th>Average tumor size (range) (mm)</th>
<th>Average operative time (median) (min)</th>
<th>Average blood loss (median) (ml)</th>
<th>Overall 5-year survival rate (%) (average follow-up, months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>59/61</td>
<td>26.5 ± 9.9 (10–50)</td>
<td>160 ± 43 (160)</td>
<td>313 ± 370 (158)</td>
<td>87* (23.1 ± 19.5)</td>
</tr>
<tr>
<td>Elective</td>
<td>46/46</td>
<td>25.9 ± 9.9</td>
<td>159 ± 45</td>
<td>333 ± 396</td>
<td>91</td>
</tr>
<tr>
<td>Imperative</td>
<td>13/15</td>
<td>28.1 ± 10.2</td>
<td>165 ± 38</td>
<td>254 ± 265†</td>
<td>83†</td>
</tr>
</tbody>
</table>

*There was no recurrent case. †Statistically not significant.
in imperative cases (Table 1). Thirty-three tumors were in the right kidney and 28 were in the left. Tumors were in the upper pole of 12 kidneys, in the middle of 21 and the lower of 20. The remaining eight tumors were located across two poles. Six tumors were located near the renal hilus and the remaining tumors were in the peripheral area.

The MTC is made up of a surgical hand-piece, a coaxial cable and a generator console with a 180 W maximum output. A needle antenna is adjustable in length from 10 to 40 mm with pliers and a circle electrode, 10 mm in diameter, is placed at the base of the needle antenna (Fig. 1). The needle can be bent corresponding to the round margin of a tumor. The process and extent of coagulation are demonstrated using the albumen (Fig. 2). The coagulated zone grows rapidly around the needle, forming a cone shape. The extent of the coagulation area reaches a plateau after 30–40 s of microwave transmission: 3–4 mm at the apex and 10–12 mm at the base (Fig. 2).

Postoperative renal function damaged by enucleation was evaluated with serum creatinine, creatinine clearance and radioisotope renogram. Anatomical alteration of the enucleated-tumor bed was usually evaluated by CT scanning 1–2 and 6 months after operation and by renal scintigraphy according to the circumstances.

**SURGICAL PROCEDURE**

The kidney was exposed extraperitoneally via a flank incision with minimal peri-renal detachment. The location and shape of the tumor, and the presence of satellite tumor nodules, were examined with *in situ* ultrasonography. After excision of the peri-renal fat tissue over the tumor, a demarcation line, 7–10 mm away from the tumor edge, was defined measuring the angle and depth with ultrasonography to avoid damaging the underlying collecting system and large vessels. The circumference was coagulated at 8–10 mm intervals along the demarcation line with a microwave needle of suitable length according to the tumor diameter and the depth to the renal sinus. We used a needle of 15 or 20 mm in length, taking the insertion angle carefully so as not to penetrate the calyceal mucosa or cause excessive coagulation of the intervening normal parenchyma below the tumor. Each coagulation process constituted 30–40 s of coagulation at 50–60 W and subsequently 10–15 s of dissociation. When coagulation around the tumor was completed, the coagulated zone was cut sharply and dissected bluntly. The concept of this surgical procedure is presented as a schema (Fig. 3). Since the coagulated tissue was not carbonized, dissection was achieved cautiously with clear recognition of the tubular structure in the bloodless field without pushing the ischemic time. The tumor base was dissected carefully because the main tumor vessels and collecting system were in this deep area. Marginal histopathological diagnosis was also performed on the enucleated tumor bed to ensure complete enucleation. A visible vessel-like structure larger than 2 mm in diameter was ligated with an absorbable suture. Indigocarmine was injected intravenously to detect whether or not urine leakage during dissection was present. Accidental impairment of the collecting system occurred but was repaired with an absorbable suture after removal of frail coagulated tissue and dissection of the collecting system. The enucleated tumor bed was covered...
with fibrin glue without approximation (16). For a large defect, the bed was filled with peri-renal fat tissue. A drainage tube was left near the enucleation site.

RESULTS

Non-ischemic complete enucleation for small RCC using MTC was achieved as intended in 61 kidneys of 59 patients. No conversion from enucleation to nephrectomy or additional surgical procedures were required in any cases.

The operation time averaged 160 ± 43 min, ranging from 80 to 253 min. There was no significant difference in the average operation time between elective cases (159 ± 45 min) and imperative cases (165 ± 38 min) (Table 1). Blood loss averaged 313 ± 370 ml, ranging from 30 to 1915 ml. There was also no significant difference in blood loss between elective cases (333 ± 396 ml) and imperative cases (254 ± 265 ml) (Table 1). The mean blood loss was 313 ± 370 ml in the total number of cases and a blood transfusion was performed in five patients (8%). During the operation, no major bleeding from the enucleated-tumor bed was observed in 38 kidneys (62.2%) whereas minor venous and arterial bleeding occurred in 10 and six kidneys, respectively. At the start of this series, two initial patients required a blood transfusion owing to uncontrollable bleeding from the enucleated tumor bed. However, the blood loss has decreased significantly with increase in the various experiences of the medical team. Clamping of renal hilar vessels was unnecessary to control the bleeding, except for the two patients mentioned. Urine leakage from the enucleated tumor bed was not observed in 54 kidneys (88.5%). However, closure of the damaged collecting system was required for urine leakage in the remaining seven kidneys. There was no patient who needed nephrostomy and a ureteral stent to keep the damaged collecting system as dry as possible. Hemostasis and repair of the renal collecting system were achieved easily with 4–0 absorbable sutures.

Histopathological diagnoses of enucleated tumors revealed that RCCs were surrounded by normal parenchyma with a thickness of 3–5 mm. Heat degeneration induced by MTC did not extend to the renal parenchyma more than 2–3 mm from the surgical margin. In the microscopic findings of enucleated kidneys (Figure 4), the surgical margins were free of tumor and clear from the surrounding renal tissue.

Table 2. Serum creatinine level and creatinine clearance before and after enucleation

<table>
<thead>
<tr>
<th>Indication (n = 59)</th>
<th>Mean creatinine level (mg/dl)</th>
<th>Mean increase in creatinine (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before enucleation</td>
<td>After enucleation</td>
</tr>
<tr>
<td>Elective</td>
<td>0.82 ± 0.24</td>
<td>0.87 ± 0.26*</td>
</tr>
<tr>
<td>Imperative</td>
<td>1.06 ± 0.31</td>
<td>1.66 ± 1.69*</td>
</tr>
<tr>
<td>Indication (n = 40)</td>
<td>Mean creatinine clearance (ml/min)</td>
<td>Mean decrease in creatinine clearance (ml/min)</td>
</tr>
<tr>
<td></td>
<td>Before enucleation</td>
<td>After enucleation</td>
</tr>
<tr>
<td>Elective</td>
<td>89.3 ± 28.3</td>
<td>74.2 ± 26.1*</td>
</tr>
<tr>
<td>Imperative</td>
<td>73.1 ± 30.6</td>
<td>69.5 ± 29.0*</td>
</tr>
</tbody>
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Postoperative creatinine and creatinine clearance were evaluated 2–3 weeks after the operation. *Statistically not significant (before vs after). †Statistically not significant (elective vs imperative).
not interfere with the accurate histopathological diagnosis of frozen or paraffin sections. The changes in the margins were mainly hemorrhagic necrosis in the limited coagulation zone (Fig. 4). The enucleated tumor bed was also examined histopathologically and found to be negative for residual cancer tissue in all cases. Vascular invasion or cancer cells in the marginal tissue were not observed in any cases. There were no postoperative major complications, such as bleeding or urosepsis, in any cases. Only one patient had a minor urine leakage, which was treated conservatively by continuous suction drainage around the leak point and disappeared 2 weeks later. One imperative case with chronic renal failure of a single kidney was inducted into hemodialysis therapy due to progressing renal failure. Variations of postoperative renal function in the elective indication and imperative indication groups are summarized in terms of mean serum creatinine and creatinine clearance in Table 2. There was no significant difference in the mean values of serum creatinine and creatinine clearance between the preoperative and postoperative values in both indications. Although the mean increase in creatinine and decrease in creatinine clearance were higher in the imperative cases and in the elective cases, respectively, there was no statistical significance in the alteration of renal function between the elective and imperative cases. Postoperative renal failure due to enucleation did not occur in any patients. The radioisotope absorption of the enucleated kidney was well maintained, except for the marginal area of the enucleated site. Renogram patterns were found to be normal with minimum loss of function when compared before and after the operation, even in a patient with bilateral RCC (Fig. 5). Loss of effective renal plasma flow depended on the impaired normal tissue volume and ranged from 5 to 30% of the preoperative values evaluated in 37 cases. One case had a renal arteriovenous fistula treated by transarterial embolization. The adjacent zone of the enucleated tumor bed was visualized as a low-density area, with poor enhancement of 5–10 mm in thickness by CT scans and MRI. Severe deterioration or obvious infarction in the remaining parenchyma was not observed by CT scanning (Fig. 6). Local recurrence was not observed in any cases and the 5-year overall survival was 87% at 23.1 ± 19.5 months (3–72 months) of the mean follow-up (Table 1). One imperative case, a metachronous RCC with small lung metastasis, died 23 months after the operation. Two elective cases died of corresponding rectal cancer and primary lung cancer 14 and 23 months after the operation.

**DISCUSSION**

Recently, nephron-sparing surgery has been selected not only for imperative cases, but also for elective cases. The operative technique has been developed paying attention to both complete resection and the preservation of renal function using
local cooling or extracorporeal surgery (17–19). Even if 25–75% of the solitary kidney is excised, long-term renal functions remain stable in most patients without hemodialysis (20). The imperative indication for nephron-sparing surgery is no longer controversial if the disease extension and the patient’s physical condition permit the surgical indication (7,8,13,21).

As for the elective indication, the risks of local recurrence, which may result from remnant cancer cells on the margin due to incomplete resection and multicentricity of RCC or microscopic intravascular invasion or intra-renal metastasis, must be considered (22). The incidence of undetected satellite tumors in nephrectomy specimens is 19.7% for all sizes of RCC (23) and 7% in RCC smaller than 8 cm (24). Although multiple RCCs in the ipsilateral kidney were observed in 13–14% of 216 cases that underwent nephron-sparing surgery, no local recurrence was observed in patients with unilateral, stage I tumors smaller than 4 cm in the same series (14). The local recurrence rates in elective cases ranged from 0 to 3.3% in patients with RCC smaller than 3.5 cm and 3-year disease-specific survival rate ranged from 90 to 100% (21).

Simple tumor enucleation can be done to resect tumors, keeping its thin capsule intact when the tumor is small and superficial (25). However, ordinary simple tumor enucleation, dissecting right along the pseudocapsule, has a higher risk of generating remnant cancer cells on the margin (22). Complete tumor enucleation can be achieved only with en bloc resection with 4–7 mm of surrounding normal tissue as reported by Steinbach et al. (13). Although asymptomatic small RCCs have less malignant biological potential (8,13,14,26), it is also well known that there are some cases with metastasis from small RCC at the time of diagnosis or immediately after nephrectomy. The prognosis for RCC patients depends on whether it has already metastasized at the time of surgery, but not on the modality of tumor resection.

The following strategies are required for ordinary nephron-sparing surgery: (1) early control of the main renal blood vessels, (2) minimizing the ischemic time, (3) meticulous hemostasis and (4) complete closure of the urinary collecting system (27). These operative techniques sometimes require complex surgical procedures such as renal surface cooling and cold perfusion when renal ischemia is prolonged more than 30 min (21) and the perioperative complications of nephron-sparing surgery are still substantial even when performed on a patient with asymptomatic small RCC (28). The major complications after nephron-sparing surgery are bleeding, fistula formation and loss of renal function. Major complications in total patients were observed in 15% of patients who underwent partial nephrectomy and 12% of patients who underwent enucleation (8). The complication rate was significantly higher in imperative cases (13%) than elective cases (5.2%) (13). Thus, nephron-sparing surgery is not always safe and substantial complications may occur even when conducted by experienced and skilled surgeons.

Figure 6. A CT scan of the bilateral RCC after non-ischemic complete enucleation for small RCC after 4 weeks (the same case as in Fig. 5). The upper half shows the preoperative scan and the lower half shows the postoperative scan. Dotted lines in the upper pictures represent demarcation lines of coagulation and resection.
With increase in asymptomatic small RCC, a novel surgical technique that is simple and reliable without requiring control of the main renal blood vessels is warranted. To adapt the primary objective of nephron-sparing surgery to small RCC, operative techniques must conform to the following principles: (1) complete resection of the tumor with adequate normal surrounding tissue, (2) minimal chance of cancer cell dissemination during manipulation, (3) minimal loss of renal function and (4) minimal incidence of complications.

To reduce bleeding from the enucleated tumor bed, various techniques have been reported for partial nephrectomy and tumor enucleation. The simplest technique is to control bleeding from the cut surface by denaturing an Nd:YAG laser (31), are still in preliminary use. Although an techniques, including an ultrasonic surgical aspirator (30) and Steinbach et al. (13), and a kidney tourniquet such as the tumor enucleation. The simplest technique is to control bleeding from the cut surface without clamping the hilar vessels via manual compression of the renal parenchyma, described by Steinbach et al. (13), and a kidney tourniquet such as the rubber tubing reported by Goldwasser et al. (29). Novel techniques, including an ultrasonic surgical aspirator (30) and an Nd:YAG laser (31), are still in preliminary use. Although an argon beam coagulator is an effective tool to control minor bleeding from the cut surface of the parenchyma by denaturing for a depth of 2–3 mm (13,32), dissection in a bloodless field cannot be achieved.

The usefulness of MTC in partial nephrectomy was determined using experimental animals to reduce perioperative blood loss, the operation time and the thermal damage around the coagulating point when compared with an electric coagulator (33). The major advantages of this procedure are mainly derived from the non- ischemic technique: (1) cautious and reliable tumor enucleation cutting into the surrounding normal tissue in the bloodless field without trying to shorten the ischemic time, (2) avoidance of unnecessary skeletonization of renal hilar vessels that makes the operation simple and have less morbidity, (3) reduction of the possible impairment in the remaining renal tissue due to renal ischemia, subsequent microthrombus and vascular injury and (4) the more practical use of surgical pathology. Nonetheless, we consider that a tumor larger than 5 cm in diameter or seated deeply in the thin parenchyma adjacent to the renal hilus without adequate intervening normal tissue as far as the collecting system, particularly the renal pelvis, is an inappropriate indication for non-ischemic enucleation by MTC because of complications such as incurable urine fistula or trunk vessel bleeding.

This novel procedure can be achieved easily by a urological surgeon who can perform nephrectomy and is especially suitable for the younger generation of urologists who have trained in the era of endourology and ESWL, because they have less experience in renal parenchymal surgery. In the future, the clinical usefulness of this procedure must be further clarified regarding the risk of local recurrence and the effect on renal function over the long term. This non-ischemic complete enucleation technique has potential for use in laparoscopic surgery and is largely experimental at present.

References