PROGRESSION AND LONG-TERM SURVIVAL AFTER SIMPLE ENUCLEATION FOR THE ELECTIVE TREATMENT OF RENAL CELL CARCINOMA: EXPERIENCE IN 107 PATIENTS

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ABSTRACT

Purpose: We present our findings in a series of T1a renal cell carcinoma treated with elective simple enucleation, specifically reporting the incidence of local recurrence, and progression-free and disease specific survival rates.

Materials and Methods: A total of 107 patients who underwent elective nephron sparing surgery performed with simple enucleation from January 1989 to December 2000 were studied retrospectively. None of the patients had preoperative or intraoperative suspicion of positive nodes. All patients were free from distant metastases before surgery (M0). Patient status was last evaluated in July 2004. Mean (median, range) followup was 88.3 (84, 44 to 175) months.

Results: Pathological review according to the 2002 TNM classification showed that 95% (102 of 107) of tumors were pT1a, 4% (4 of 107) pT1b and 1% (1 of 107) pT3a. Mean (SD, median, range) tumor greatest dimension was 2.7 (0.93, 2.5, 0.6 to 5) cm. None of the patients died in the immediate postoperative period (within the first 30 days). There were no major complications such as bleeding and urinary leakage/urinoma requiring reoperation. The 5 and 10-year cancer specific survival was 99% and 97.8%, respectively. The 5 and 10-year progression-free survival was 98.1% and 94.7%, respectively. Overall 3 patients had disease progression (2.8%) of whom 2 (1.9%) were local recurrence, 1 alone and 1 associated with distant metastases diagnosed 12 months earlier.

Conclusions: Simple tumor enucleation is a safe and acceptable approach for elective nephron sparing surgery. It provides excellent long-term progression-free and cancer specific survival rates, and is not associated with an increased risk of local recurrence compared with partial nephrectomy.

KEY WORDS: carcinoma, renal cell; surgery, nephrectomy; neoplasm recurrence, local

The widespread use of ultrasonography and computerized tomography (CT) has led to an increasing number of early detected/incidentally found renal tumors presenting with lower stage and grade, and without lymph node and distant metastases. Therefore, many patients are now diagnosed as having small renal masses (4 cm or less in greatest dimension) confined within the capsule (pT1a), potentially suitable for elective nephron sparing surgery (NSS). In the last 10 years many refinements and advancements have been made to improve technique, safety and results. Indeed several studies have showed NSS to offer equally effective local control as well as 5 and 10-year disease specific survival rates compared with radical nephrectomy.

To avoid the risk of local recurrence due to inadequate tumor excision or tumor multifocality closely related to the main tumor, a 1 cm margin of normal appearing parenchyma and perinephric adipose tissue superficial to the lesion are taken with the tumor. This is considered the treatment of choice in patients undergoing NSS. Nevertheless, the precise amount of healthy parenchyma necessary to avoid the risk of positive surgical margins and local recurrence is the subject of a prolonged debate. Several recent studies on the necessary amount of healthy parenchyma that should be removed with the specimen have shown that a normal tissue margin of at least 1 mm is adequate to prevent local recurrence from renal cell carcinoma (RCC). The simple enucleation technique has been reported in the treatment of benign looking tumors such as angiomyolipomas to preserve more kidney parenchyma, and avoid major bleeding and opening of the collecting system. The latter situation develops into urinary leakage/urinoma and urinary fistula if undetected and not repaired during surgery.

Only a few studies in the late 1980s and early 1990s have reported on the use of this technique for the treatment of small RCC and showed similar 5-year survival rates to partial nephrectomy. To our knowledge in the last 10 years no studies with extended followup have been published on the role of elective simple enucleation in the treatment of small renal masses. Thus, we report our findings in a series of 107 renal masses treated with simple enucleation and followed for a mean of more than 7 years. We specifically report on the incidence of local recurrence, and progression-free and disease specific survival rates.

MATERIALS AND METHODS

From January 1989 to December 2000 all patients suitable for elective NSS (preoperative tumor greatest dimension 4 cm or less) presenting to our institution were entered into a database to record patient details, operative and postoperative details. None of the patients had preoperative or intraoperative suspicion of positive nodes. All patients were free...
from distant metastases before surgery (M0). Preoperative evaluation included ultrasonography of the kidney, ureter and bladder, CT of the abdomen and chest x-ray in all patients. Overall 107 patients with pathologically confirmed RCC (80 men and 27 women with mean age 58.4 years, range 29 to 84) treated with simple enucleation were included in the study. The tumor was on the right side in 66 patients (62%) and on the left in 41 (38%).

Surgical technique: simple enucleation. All patients were treated with a lateral retroperitoneal approach. The patient is placed in an oblique position elevated approximately 75 degrees. The incision is made above the 11th intercostal space toward the umbilicus. The kidney is directly approached and completely separated from the perirenal fat to exclude satellite lesions not detected by the imaging technique. It is important to visualize the limit between the healthy renal parenchyma and the tumor, leaving the peritumoral fat in situ.

The renal pedicle is carefully isolated and usually controlled with vascular clamps before tumor enucleation. To prevent ischemic renal damage all patients are vigorously hydrated and infused with mannitol a few minutes before arterial occlusion to decrease intracellular swelling. Systemic or regional anticoagulation before clamping the renal vessels to prevent intrarenal vascular thrombosis is never used. Renal hypothermia with slush is adopted to minimize ischemic injury to the kidney when prolonged ischemia times, greater than 30 minutes, are anticipated, such as for intrarenal or perihilar lesions.

Then the kidney capsule is sharply incised starting a few millimeters away from the lesion toward the pseudocapsule, and when reached the tumor is enucleated without a rim of normal parenchyma, using the natural cleavage plane between the pseudocapsule and normal parenchyma by blunt dissection and scissors. The enucleation margins are meticulously inspected. Moreover, once the tumor is enucleated it is important to examine the renal surface to rule out possible infiltration of the enucleation bed. Intraoperative ultrasonography and biopsies of the enucleation bed are rarely used.

The visible bleeding vessels and incidental opening of the calices are ligated using a running or single suture with 4-zero monofilament. Then either diathermy spray coagulation or argon beam coagulation of the enucleation bed is used for hemostatic and oncological reasons. The parenchymal defect is closed with horizontal interrupted sutures such as Vicryl® or Vicryl Rapid® after fibrin glue or cyanoacrylate glue apposition. Then the vascular clamp is removed.

Histopathology. All cases were restaged according to 2002 TNM criteria, and patients with T1 disease were subdivided into T1a and T1b categories. Nuclear grading was assigned according to criteria proposed by Fuhrman et al. Histopathology was reviewed according to the new classification (UICC and American Joint Committee on Cancer 1997). Only patients with histologically confirmed RCC were included in the study.

Followup. Patient status was last evaluated in July 2004. The followup schedule included blood chemistries and chest x-ray in association with ultrasonography or CT of the abdomen, performed alternately every 6 months after surgery for the first 2 years and yearly thereafter. Bone scintigraphy was performed only in cases of clinical suspicion. In terms of statistical analysis the probability of survival was estimated by the Kaplan-Meier method using the whole number of events.

RESULTS

At diagnosis 93 of the 107 tumors were detected incidentally (87%) while 14 (13%) were associated with microscopic or frank hematuria. The tumor was in the upper pole in 41 cases (38%), mid kidney in 35 (33%) and lower pole in 31 (29%). Renal hypothermia with slush was adopted in 12 cases when prolonged ischemia times, greater than 30 minutes, were anticipated, but it was unnecessary in most patients. Indeed mean ischemic time was 26.3 minutes (range 19 to 41). Warm ischemia was used in 77 cases with a mean (range) ischemic time of 14.1 (10 to 19) minutes. A simple parenchymal compression avoiding clamping the renal pedicle was the technique adopted in 18 cases.

Mean (median, range) followup was 88.3 (84, 44 to 175) months. During the study period 11 patients died, of whom 2 died of RCC after 42 and 64 months, and 9 of causes independent from renal tumor. Mean (range) followup of the 96 patients who remained alive during the study period was 90.5 (44 to 175) months. Mean (range) time to tumor unrelated death was 72 (6 to 165) months. The pathological review according to the 2002 TNM classification showed that 95% (102 of 107) of tumors were pT1a, 4% (4 of 107) pT1b and 1% (1 of 107) pT3a. Mean (SD, median, range) tumor greatest dimension was 2.7 (0.93, 2.5, 0.6 to 5) cm.

On the basis of Fuhrman nuclear grading 39% (42 of 107) of tumors were G1, 45% (48 of 107) G2 and 16% (17 of 107) G3. The histopathological review according to the new classification (UICC and American Joint Committee on Cancer 1997) revealed 93 clear cell (86.9%), 9 papillary (8.8%) and 5 chromophobe (4.7%) RCCs.

None of the patients died in the immediate postoperative period (within the first 30 days). Of the 107 patients postoperative bleeding developed in 7 (6.5%), requiring transfusions, and 2 (1.9%) had postoperative prolonged urinary leakage from the drainage requiring double-J stent insertion. There were no major complications such as prolonged acute tubular necrosis/chronic renal insufficiency and bleeding or urinary leakage/urinoma requiring reoperation.

The 5 and 10-year cumulative survival was 95.1% and 89.6%, respectively. The 5 and 10-year cancer specific survival was 99% and 97.8%, respectively. The 5 and 10-year progression-free survival was 98.1% and 94.7%, respectively (see figure). Overall 3 patients experienced progressive disease (2.8%, see table) of whom 2 had local recurrence (1.9%) either alone or associated with distant metastases, while 1 patient had metastatic disease without local recurrence. Patient 1 had local recurrence alone detected 113 months after surgery. He underwent salvage nephrectomy that showed the recurrence elsewhere in the kidney indicating tumor multifocality, and he was free from distant metastases 9 months after surgery. Patient 2 had local recurrence detected 60 months after surgery with concurrent metastatic disease diagnosed 12 months earlier (48 months after surgery). Patient 3 had distant metastases with no evidence of local recurrence. Both patients with distant disease died of metastases a few months after diagnosis.

Cumulative, cancer specific and progression-free survival rates of 107 patients undergoing NSS by simple enucleation for RCC.
They concluded that when partial ne-
erative (SD, range) distance from the primary tumor being 0.5
with radical nephrectomy. Li et al found positive cancer
tissue preservation. Moreover, from a functional point of view, a narrower exci-
chyma that forms a pseudocapsule around it, allowing for
surgical margins, RCC tends to compress the normal paren-
the tumor represents the only strategy to ensure negative
conserving surgery is confirmed as an accepted alternative to
adequate for thin melanomas (1 mm thick or less), and breast
phrectomy is performeda5mm margin can be enough to
prevent a possible local recurrence.14 However, on the basis
of several recently published articles on the necessary
tion,4 the early detection of metastatic lesions after surgery,
The excellent progression-free and cancer specific survival rates similar to those of enucleo-resection and radical nephrectomy associated with minimal morbidity and maximal renal preservation clearly represent the rationale for adopting the simple enucleation technique as the standard procedure for the excision of clinically pT1a RCC. To our knowledge no other studies published to date have evaluated the long-term results of elective tumor enucleation for the conservative treatment of RCC.

REFERENCES


EDITORIAL COMMENT

This is an interesting study describing renal tumor resection by enucleation without the usually recommended rim of normal parenchyma and with additional biopsy of the tumor bed. Argon beam or cautery coagulation of the bed was performed. Of the 107 patients 14% had the indolent tumor subtypes of papillary or chromophobe carcinoma. However, the study did not include any benign lesions such as oncocytoma, angiomylolipoma and hemorrhagic or complex cyst, which now account for approximately 20% of lesions undergoing resection in recently published series. After a substantial followup of 84 months, the result of only 3 cancer recurrences (2 metastatic and 1 elsewhere in the kidney which was likely a new tumor occurrence) suggests that in this cohort of good prognostic cases only complete resection of tumor without a formal margin is sufficient to achieve local control. The additional therapeutic impact of coagulation to the tumor bed is not known.

The authors' data suggest that urologists evaluating a patient for partial nephrectomy may no longer be discouraged by the close proximity of the tumor to a critical renal vascular structure or the collecting system if complete resection is possible, even without a formal margin. Urologists have already accepted microscopically clear margins only during radical prostatectomy for prostate cancer so this concept should not be alien. It is now clear that prognosis is highly dependent on tumor histology. Even for small conventional clear cell cancer in this size range, the prognosis following complete resection is excellent. The default position to radical nephrectomy (by traditional open or newer minimally invasive methods) may be difficult to propose to patients when the benefits of excellent local tumor control, as again demonstrated in this study, and maximum preservation of renal function, are possible.

Studies such as this one provide insight into the good prognostic world of the incidental renal tumor which is increasingly being treated with kidney sparing surgery. Future advances in preoperative imaging and the molecular analysis of percutaneous biopsy material may distinguish between malignant, indolent or benign renal tumors. This information may allow for the safe expansion of kidney sparing surgery and the safe initiation of observation only strategies, particularly in elderly patients or those with serious comorbidities.

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