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ORIGINAL ARTICLE

Nephron sparing surgery for renal cell carcinoma in a solitary kidney

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Abstract To determine functional and oncological outcomes of nephron sparing surgery (NSS) for renal cell carcinoma (RCC). We identified from our kidney database 103 consecutive patients undergoing NSS for solid renal tumors in a solitary kidney. After excluding 17 patients (16.5%) undergoing NSS with palliative intent in presence of preoperatively diagnosed metastatic disease ($n = 15$) or positive lymph nodes ($n = 2$) and 6 patients (5.8%) who turned out to have benign tumors, the remaining 80 patients with RCC were analyzed. Mean follow-up is 8.0 years (range: 0.1–25.8). Mean tumor size was 4.2 cm (range 1.2–11 cm). Chronic renal failure requiring hemodialysis developed after NSS in nine patients (11.2%). In the remainder, serum creatinine was 1.72 mg/dl (range: 0.45–4.6 mg/dl) at latest follow-up. The cancer specific survival rates at 1, 5 and 10 years were 97.2, 89.6 and 76%, respectively. The estimated local recurrence free survival rates at 1, 5 and 10 years were 97.8, 89.4 and 79.9%, respectively. Univariate analysis of correlation between clinical and pathologic features with death from RCC showed significant associations for grading and tumor size. The long-term data of our series support the concept of organ-sparing surgery for RCC in a solitary kidney since it provides excellent local tumor control and cancer specific survival and preserves renal function renal function so that 89% of patients remained free of dialysis in the long-run.

Keywords Nephron sparing surgery · Renal cell carcinoma · Solitary kidney

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Introduction

Surgery is the gold standard for treating renal cell carcinoma. Nephron sparing surgery (NSS) has become a standard strategy for treating selected renal tumors [1–3]. Elective NSS for renal cell carcinoma (RCC) in presence of a normal contralateral kidney has become accepted for small, incidental tumors. The outcome of patients with RCC treated with cone resection, wedge resection or partial nephrectomy in the elective setting is excellent and comparable with results obtained by radical nephrectomy [4–6]. Imperative NSS is the method of choice for treatment of tumors in a solitary kidney and for bilateral tumors when radical nephrectomy would render the patient anephric and subject him to renal replacement therapy. In patients with a tumor in a solitary kidney, preservation of renal parenchyma is mandatory and must be weighed against the risk of compromising the oncological efficacy in NSS of very large or centrally localized tumors. As a consequence, RCC in a solitary kidney poses unique challenges of surgical and clinical management. We wanted to study functional and oncological long-term outcomes of patients treated at our institution by NSS for RCC in a solitary kidney under curative intent.

Methods

We identified from our kidney database 103 consecutive patients undergoing NSS for solid tumors suspicious for renal cancer in an anatomically or functionally solitary kidney. Patients with synchronous bilateral renal cell carcinoma (RCC), transitional cell carcinoma and Wilms tumor were excluded from this analysis. From 103 patients with NSS in a solitary kidney, another 17 patients (16.5%) were

excluded who underwent NSS with palliative intent in presence of preoperatively diagnosed metastatic disease ($n = 15$) or positive lymph nodes ($n = 2$) and 6 patients (5.8%) who turned out to have benign tumors. The remaining 80 patients undergoing NSS for RCC with curative intent were followed-up and analyzed. Mean age at surgery was 62.6 years (range: 41.6–79.3). Fifty (62.5%) patients were male. Forty-eight patients (60%) had had previous nephrectomy of the contralateral kidney, 26 of them (54.2%) because of RCC, seven patients (14.6%) because of sepsis, five patients (10.4%) because of a non-functioning kidney and another ten patients (20.8%) because of other reasons (transitional cell carcinoma, oncocytoma, trauma, stone disease, tuberculosis). Twelve patients (15%) had a congenital solitary kidney and 20 patients (25%) had a scintigraphically proven non-functioning contralateral kidney. The time interval in patients with metachronous bilateral RCC for radical nephrectomy for treatment of RCC and NSS for treatment of RCC in the remaining contralateral kidney was at mean 9.35 years (range: 1.2–26.9).

The surgical technique of NSS has been described in detail previously [7]. Surgical access is gained by an extraperitoneal flank incision. Intraoperative ultrasound is since the 1980's routinely performed to determine the tumor extension. The renal artery is occluded after furosemide is given intravenously and slush ice is applied to the surface of the kidney. The tumor is resected with a surgical margin of a few millimeters of renal parenchyma if possible. The choice of the surgical strategy depends on the size and location of the tumor and number of tumors per kidney. Peripherally localized tumors are treated by cone resection, wedge resection or partial nephrectomy [7]. Central tumors were resected as described in detail previously [8]. Renal segmental arteries are localized by Doppler ultrasound [9]. Multiple biopsies are obtained from the renal margins of resection and are sent seperately with the resected complete tumor for frozen sections to determine surgical margins. This is particularly important for large and centrally localized tumors. The argon beam and infrared coagulators are used for hemostasis. The infrared coagulator has the advantage to provide an additional safety margin by denaturization of 2 to 3 mm of the surrounding parenchyma [3].

All patients were postoperatively at regular intervals reevaluated for local cancer recurrence using imaging studies such as renal ultrasound, computerized tomography (CT) or magnetic resonance imaging (MRI) of the kidney and abdomen, and chest X-ray or CT. In our retrospective analysis, we reviewed these data and completed follow-up studies where necessary. Our analysis included clinical and pathological features such as histological subtype, tumor size, tumor stage as assessed by the actual TMN classification (2003) and grading of tumors using the classification of Thoenes et al. [10]. Mean follow-up is 8.0 years (range: 0.1–25.8 years). The oncological outcome calculation was performed cancer specific for renal cell carcinoma. The Kaplan–Meier analysis was used to estimate overall survival, cancer specific survival, local recurrence-free survival and metastasis free survival. Univariate Cox proportional hazards regression models were fit for assessment of an association between clinical and pathological features and outcome. The relationships between clinical and pathological features and outcome were characterized by risk ratios and their 95% confidence interval (CI). Significance was regarded at $P < 0.05$. All statistical analyses were performed using SPSS statistical software (SPSS Inc., Chicago, USA).

Results

Pathologic features of NSS in a solitary kidney are summarized in Table 1. Of the 80 patients with RCC, 64 patients (80%) had clear cell RCC, 12 (15%) had papillary RCC, and 4 (5%) had chromophobe RCC. Mean tumor size was 4.2 cm (range 1.2–11). Forty-five patients (56.3%) had stage pT1a, 22 patients (27.5%) pT1b, five patients (6.3%) pT2 and seven patients (8.6%) pT3. Among the pT3 tumors, four tumors did infiltrate perirenal fat (pT3a) and three tumors (pT3b) did infiltrate the renal vein ($n = 2$) and the adrenal gland ($n = 1$). Sixteen patients (20%) had grade 1 RCC, 50 (62.5%) grade 2 and 14 (17.5%) grade 3 tumors.

Three patients (3.2%) died within the first 30 postoperative days because of myocardial infarction (two patients) and pulmonary embolism (one patient). The most frequent postoperative complication after NSS in a solitary kidney was acute renal failure (Fig. 1) with consecutive need for temporary hemodialysis in ten patients (12.5%). Renal

Table 1 NSS in a solitary kidney: pathologic features of RCC ($n = 80$)

Mean tumor diameter	4.2 cm	(range: 1.2–11.0 cm)
Tumor stage	*n*	
pT1a	45	(56.3%)
pT1b	23	(28.7%)
pT2	5	(6.3%)
pT3	7	(8.7%)
Grade	*n*	
I	16	(20.0%)
II	50	(62.5%)
III	14	(17.5%)
Histologic subtype	*n*	
Clear cell	64	(80.0%)
Papillary	12	(15.0%)
Chromophobe	4	(5.0%)

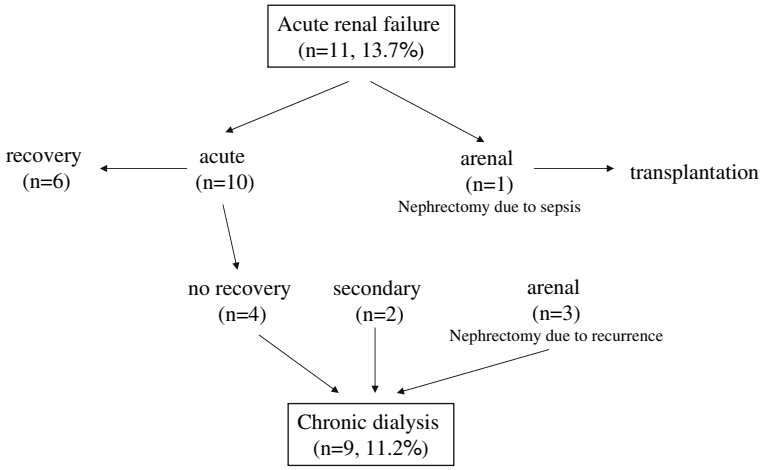

Fig. 1 NSS in a solitary kidney: renal failure ($n = 80$)

function recovered after a mean of eight weeks in six of these ten patients. Mean tumor size in patients with acute renal failure was 4.9 cm (range 3.0–8.0 cm) as compared to 4.2 cm (range: 1.2–11.0 cm) in the remaining patients. In four patients, nephrectomy was performed because of postoperative sepsis in one case and for treatment of local tumor recurrence after 4, 5 and 13 months in the three other patients. One of these patients underwent renal transplantation three years after nephrectomy. Chronic renal failure requiring hemodialysis developed in nine patients (11.2%) after a mean of three months including 4/10 patients with acute renal failure postoperative, in whom kidney function did not recover (Fig. 1). Serum creatinine in the remainder (no dialysis) was 1.72 mg/dl (range: 0.45–4.6 mg/dl) at the latest follow-up. Urinary extravasation was a postoperative complication in six patients (7.5%) and was treated in all cases with retrograde insertion of a ureteric catheter and—when necessary—with percutaneous drain insertion ($n = 4$). The above mentioned nephrectomy because of sepsis became necessary in one of these patients. Postoperative hemorrhage required in two further patients open surgical reintervention and superselective arterial embolisation in another two patients, which is now the treatment of choice for hemorrhage.

At the time of review, a total of 37 patients had died, 14 patients from to tumor progression of RCC. The estimated overall survival rates at 1, 5, 10 were 93.6, 80.1, and 54.1%, respectively. The mean time from NSS to death from RCC in 14 patients was 3.7 years (range 0.7–6.7). The cancer specific survival rates at 1, 5 and 10 years were 97.2, 89.6 and 76.0%, respectively (Fig. 2a). When stratified between patients without or with previous RCC before NSS, cancer specific survival at 1, 5 and 10 years was 96.1, 85.0 and 74.3% for patients without previous RCC, and 100, 93.3 and 78% for patients with metachronous bilateral RCC. Local tumor recurrence occurred in 13 patients. Mean time from nephron sparing surgery to local tumor recurrence was 4.7 years (range: 0.4–15.9 years). The estimated local recurrence free survival rates at 1, 5 and 10 years were 97.8, 89.4 and 79.9%, respectively (Fig. 2b). Six patients of the 13 patients with local tumor recurrence were treated with repeat NSS after a mean of 6.7 years (range: 1.4–13.7 years). Three patients underwent radical nephrectomy after a mean of 0.6 years (range: 0.4–1.1 years). In the

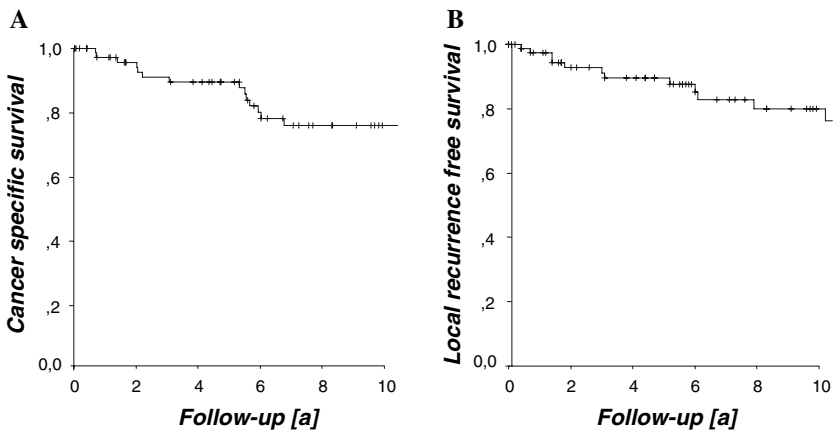

Fig. 2 Oncological outcome of patients with a solitary kidney undergoing NSS for RCC. **a** Cancer specific survival for patients with a solitary kidney undergoing NSS. The cancer specific survival rate at 1, 5 and 10 years were 97.2, 89.6 and 76.0%, respectively. **b** Local recurrence free survival for patients with a solitary kidney undergoing NSS. The estimated local recurrence free survival rate were 97.8, 89.4 and 79.9%, respectively

remaining five patients, no further surgery was employed because of distant metastases formation. The metastasis free survival rates at 1, 5 and 10 years were 98.6, 88.5 and 75.0%, respectively. Univariate analysis of an association between death from RCC and clinical and pathologic features revealed significant association for tumor size and grading. The hazard ratio for tumor size (>4 cm) was 2.64 (95% CI: 1.07, 6.24, $P < 0.05$) and for tumor grading 4.75 (95% CI: 1.65, 13.67, $P < 0.05$).

Discussion

Elective NSS for renal tumors results in excellent local tumor control with disease-free survival rates comparable to those of radical nephrectomy [4, 5]. In addition, a lower long-term risk of chronic renal failure as compared to patients treated with radical nephrectomy has been reported [11, 12]. The surgical safety and reproducibility of NSS has been proven by low complication rates [8, 13, 14]. However, imperative NSS for renal tumors in a solitary kidney faces different problems. When in elective NSS selection for organ preservation is by tumor features such as size, location and safe respectability, in a solitary kidney imperative NSS even of tumors, which do not favour local resection due to their size and/or location can be indicated by mandatory preservation of renal parenchyma to avoid subsequent hemodialysis and transplantation. The surgical and oncological risks of NSS in a solitary kidney must be weighed against morbidity and mortality of hemodialysis and transplantation. However, there are little contemporary data on the subpopulation of patients with solitary kidney and renal cell carcinoma [14–16].

Improvements in surgical technique have decreased the early surgical complication rates of NSS [13]. However, NSS in a solitary kidney poses unique surgical challenges because many of these tumors do not lend themselves for NSS. Postoperative complications requiring intervention (percutaneous drainage, ureter catheter placement, arterial selective embolisation, open surgical revision) in this series included urine extravasation (7.5%), hemorrhage (5%) and sepsis (1.1%), which is comparable to other series of imperative NSS [13] in a solitary kidney [14, 16].

Oncological efficacy, and long-term renal function are the major concerns in patients with NSS of RCC in a solitary kidney. The most significant risk factor for acute renal failure after NSS is a solitary kidney [17]. In a consecutive series of 64 patients undergoing NSS, a ≥ 0.6 mg/dl increase in postoperative serum creatinine was observed in 10 of 28 patients (35.7%) with a solitary kidney, while no increase occurred in 23 patients with a normal contralateral kidney [18]. In our series, the risk of acute renal failure was 13.2% and of chronic renal failure 11.2% including the cases of secondary nephrectomy which is comparable to other series of NSS in a solitary kidney [14, 16]. Adequate hydration, use of diuretics, minimizing the duration of renal ischemia and the interdisciplinary management of patients involving nephrologists are the key issues to prevent chronic renal failure. Alternatively, radical nephrectomy would render the patient anephric and the morbidity and mortality of hemodialysis and renal transplantation with subsequent immunosuppression facilitating tumor progression has to be account for.

The major issue for justifying NSS in the treatment of RCC in a solitary kidney is the oncological safety of the strategy. In our series disease specific survival rates at 5 and 10 years are 89.6 and 76%, respectively. Cancer specific survival rates in imperative NSS are generally lower than in elective NSS [13]. The reason is the positive selection bias of tumors of mostly small size and peripheral location for elective NSS. Some of the patients in this series of imperative NSS in a solitary kidney represent a rather negative selection in terms of oncological safe resectability with tumor size ≥ 7 cm in 12 cases and centrally localized tumors in 23 cases. Cancer specific survival was better in patients who had metasynhronous RCC. However, not significant, this issue is related to a higher stage of metasynhronous RCC. However, the oncological outcome of our series compares well to other series of NSS in patients with RCC in solitary kidney. The Cleveland Clinic series of 107 patients, most of them (90%) undergoing NSS for imperative indications, report a cancer specific survival rates of 88 and 73% at 5 and 10 years, respectively [19]. The Mayo Clinic series of 63 evaluated patients reports cancer specific survival rates of 81 and 64% at 5 and 10 years, respectively [14]. In another recent study from the Memorial Sloan-Kettering Cancer Center of 54 patients including synchronous bilateral RCC, the 5-year cancer specific survival rate was 88% [16]. The local recurrence rates our series were 10.6 and 20.1% at 5 and 10 years, respectively. The Mayo Clinic series of RCC in a solitary kidney yielded after NSS similar local recurrence rates of 11 and 20% at 5 and 10 years, respectively [14].

In conclusion, nephron-sparing surgery for the treatment of renal cell cancer in a solitary kidney is feasible, safe and associated with acceptable morbidity and reduction of renal function. The oncological safety is acceptable, but inferior to elective NSS in patients with a normal contralateral kidney.

References

1. Novick AC, Stewart BH, Straffon RA et al (1977) Partial nephrectomy in the treatment of renal adenocarcinoma. J Urol 118:932–936
2. Marberger M, Pugh RC, Auvert J et al (1981) Conservation surgery of renal carcinoma: the EIRSS experience. Br J Urol 53:528–532

3. Bazeed MA, Scharfe T, Becht E et al (1986) Conservative surgery of renal cell carcinoma. Eur Urol 12:238–243
4. Butler BP, Novick AC, Miller DP et al (1995) Management of small unilateral renal cell carcinomas: radical versus nephron-sparing surgery. Urology 45:34–40
5. Lerner SE, Hawkins CA, Blute ML et al (1996) Disease outcome in patients with low stage renal cell carcinoma treated with nephron sparing or radical surgery. J Urol 155:1868–1873
6. Filipas D, Fichtner J, Spix C et al (2000) Nephron-sparing surgery of renal cell carcinoma with a normal opposite kidney: long-term outcome in 180 patients. Urology 56:387–392
7. Pahernik S, Gillitzer R, Thuroff JW (2004) Surgical atlas. Cone/wedge resection of renal cell carcinoma. BJU Int 93:639–654
8. De la Rosette J, Sternberg CN, van Poppel HPA (eds) (2007) Renal cell cancer: diagnosis and therapy. Springer, Heidelberg (in press)
9. Thuroff JW, Frohneberg D, Riedmiller R et al (1982) Localization of segmental arteries in renal surgery by Doppler sonography. J Urol 127:863–866
10. Thoenes W, Storkel S, Rumpelt HJ (1986) Histopathology and classification of renal cell tumors (adenomas, oncocytomas and carcinomas). The basic cytological and histopathological elements and their use for diagnostics. Pathol Res Pract 181:125–143
11. Lau WK, Blute ML, Weaver AL et al (2000) Matched comparison of radical nephrectomy vs nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. Mayo Clin Proc 75:1236–1242
12. McKiernan J, Simmons R, Katz J et al (2002) Natural history of chronic renal insufficiency after partial and radical nephrectomy. Urology 59:816–820
13. Uzzo RG, Novick AC (2001) Nephron sparing surgery for renal tumors: indications, techniques and outcomes. J Urol 166:6–18
14. Ghavamian R, Cheville JC, Lohse CM et al (2002) Renal cell carcinoma in the solitary kidney: an analysis of complications and outcome after nephron sparing surgery. J Urol 168:454–459
15. Novick AC, Gephardt G, Guz B et al (1991) Long-term follow-up after partial removal of a solitary kidney. N Engl J Med 325:1058–1062
16. Saranchuk JW, Touijer AK, Hakimian P et al (2002) Partial nephrectomy for patients with a solitary kidney: the Memorial Sloan-Kettering experience. BJU Int 94:1323–1328
17. Campbell SC, Novick AC (1995) Surgical technique and morbidity of elective partial nephrectomy. Semin Urol Oncol 13:281–287
18. Duque JL, Loughlin KR, O'Leary MP et al (1998) Partial nephrectomy: alternative treatment for selected patients with renal cell carcinoma. Urology 52:584–590
19. Fergany AF, Hafez KS, Novick AC (2000) Long-term results of nephron sparing surgery for localized renal cell carcinoma: 10-year followup. J Urol 163:442–445