Long Term Results of Excision of Small Renal Cancer Surrounded by a Minimal Layer of Grossly Normal Parenchyma: Review of 94 Cases

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Abstract

Objective: To assess safety and effectiveness of excision of small renal cancer.

Methods: We reviewed the records of 94 patients, who underwent, from 1992 to 2001, excision of renal tumor leaving around it a thin layer of grossly normal parenchyma and adjacent perinephric fat. This technique has been called enucleoresection, as it is not a simple enucleation but neither a conventional partial nephrectomy. Patients were followed up mean routine blood examination, ultrasound and computed tomography scan every 6 months for 2 years and annually thereafter.

Results: Median age was 63 years (35–76). Median tumour size was 2.1 cm (1.1–4.5). Clamping of renal pedicle was performed in 54 cases. Major complications included 4 cases of haemorrhage; only 1 patient required surgical exploration. Pathological stage was pT1a in 87, pT1b in 4 and pT3a in 3 patients. Surgical margins were always negative. Median follow-up was 59 months (range 10–128). Eight patients died without evidence of tumour recurrence. One pT3a patient developed distant metastases and died 2 years after surgery. Five years survival rate was 95.7% (90/94 patients), cancer specific survival rate 98.9% (93/94) and disease free survival rate 98.9% (93/94).

Conclusions: Enucleoresection of small renal tumors surrounded by a minimal layer of grossly normal renal parenchyma reproduces the results of partial and radical nephrectomy with minimal morbidity.

Keywords: Kidney neoplasms; Renal cell carcinoma; nephrectomy; Postoperative complications; Survival rate

1. Introduction

Nephron-sparing surgery was initially indicated for patients with solitary kidney or bilateral tumors but recent studies suggested that small, solitary, unilateral lesions can be treated as well in those with normal controlateral kidney [1–5]. The widespread use of cross-sectional imaging has increased detection of incidentally discovered small renal cell carcinomas. Using ultrasound and computed tomography (CT) scan, asymptomatic lesions are detected at an earlier stage and are amenable to local excision with preservation of the normal adjacent parenchyma [6]. Thus, interest in nephron-sparing surgery for small localized renal tumors has increased. It is widely accepted that tumor excision with a surrounding margin of normal parenchyma is the safest approach to ensure no residual tumor in the renal remnant. However agreement on the optimal margin in nephron-sparing surgery has never been reached. From at least 1 cm margin of normal parenchyma around the tumour in the begining of
nephron-sparing surgery [7], it is now generally accepted, according to Herr [8], to leave no more than 5 mm around the tumour. As it is practically difficult, if not impossible, to measure intraoperatively how much tissue to leave around the tumor, we decided to leave the minimal layer of tissue technically feasible without ending in a simple enucleation. This technique may be also called enucleoresection as it is more than a simple enucleation. We report our series of 94 consecutive patients, who underwent enucleoresection of small renal cancer surrounded by a minimal layer of healthy tissue, which resulted to be only 2–3 mm.

2. Materials and methods

2.1. Patients selection and clinical staging

Patients with distant metastasis or with involvement of renal vein or vena cava or grossly extension into perirenal fat or beyond Gerota’s fascia were excluded. Patients with benign disease at pathological examination were excluded from the present review. Ninety-four patients with a contrast enhanced solid renal mass of less than 4 cm underwent tumor excision between February 1992 and December 2001. Median age was 63 (range 35–76). Fifty-four (57.4%) patients were males and 40 females (42.6%). Eleven patients (11.7%) had a solitary kidney and had a mean creatinine level (normal laboratory values from 0.5 to 1.2 mg/dl) of 1.4 mg/dl (range 0.7–1.6) before surgery. Median tumor size was 2.1 cm (range 1.1–4.5).

2.2. Surgical technique

All procedures were performed by the same surgeon (P.P.). It was always used an extrapleural extraperitoneal flank incision. Tumor was excised taking care of leaving around it a minimal layer of healthy renal tissue technically feasible. Perinephric fat covering the tumor was left intact (Figs. 1 and 2). Intraoperative frozen sections or biopsies of tumor margin or tumor bed were never carried out. Clamping of renal pedicle was carried out in 54 cases (57.4%). Median ischemia time was 18 minutes (range 14–32). Regional lymph node dissection was never performed.

2.3. Pathological diagnosis and staging

Pathological features were restaged and determined according to the new 1997 TNM classification system with the modification suggested by Guinan et al. [9]. Tumors were graded according to Fuhrman’s nuclear grade system [10]. The specimen was sectioned perpendicularly to the parenchymal margin at 5 mm intervals. Lesion size was reported as the longest dimension measured at pathological examination. Margin status was determined by submitting the whole margin for the histological evaluation. The shortest distance from the tumor to the inked margin was always reported.

2.4. Follow-up

Patients were followed with renal function test, chest X-ray, ultrasound and abdominal computed tomography at 6 months intervals for the first 2 years and annually thereafter.

3. Results

Eighty-seven tumors were pT1a (92.5%), 4 pT1b (4.3%) and 3 pT3a (3.2%). Grade was G1 in 14 (14.9%) cases, G2 in 53 (56.4%), G3 in 18 (19.1%), G4 in 9 (9.6%). Pathological T3a cases were determined by the invasion of the surrounding fat. Surgical margins were negative in all cases, even in pT3a stage. Mean and median shortest distance from tumor to inked healthy tissue margin was 2.4 mm and 1.9 mm respectively. Histological classification showed 77 (81.9%) cases of clear cell carcinoma, 14 (14.9%) of papillary carcinoma and 3 (3.2%) of chromophobe renal cell carcinoma. Early major complications were postoperative haemorrhage in 4 cases (4.3%), 3 were managed conservatively and 1 required surgical exploration but the kidney was anyway spared. No major late complications (more then 1 month after surgery) had been recorded in our registry. Median hospital stay was
5 days (range 4–14). Median follow-up was 59 months (range 10–128, interquartile range 33–90). Eight patients died for unrelated causes without evidence of tumor recurrence; 2 died the third year of follow-up (26th and 35th month respectively), 1 died the fourth year (in 44th month), 1 the fifth (in 57th month), 3 the sixth (in 62nd, 67th, 71st month), 1 the seventh (in 83rd month). One patient with a pT3a/G3 disease developed distant metastases after 1.5 year and died in 26th month after surgery. Actually, remaining 85 patients are alive without evidence of tumor recurrence as checked at follow-up examination. Five year survival rate (0–60 months interval) resulted 90/94 (95.7%, 95%CI 0.96 ± 0.04), five year disease free survival rate 93/94 (98.9%), five year cause specific survival rate 93/94 (98.9%). Renal function remained stable in solitary kidney patients with a mean creatinine level of 1.1 mg/dl (range 0.9–1.7).

4. Discussion

The interest in nephron-sparing surgery for renal cell cancer could date back to the late sixties when discussion was stimulated by papers showing tumor free survival rates after partial nephrectomy comparable to those reported by others after radical nephrectomy. Many early series were done in high risk cases in which nephron-sparing surgery was the only alternative to renal replacement therapy. Grabstald and Aviles reported first an excellent tumour free survival rate in 23 of 30 patients who underwent partial nephrectomy for renal cell cancer of a solitary or a single functioning kidney [11]. Jacobs et al. compared results of partial bilateral nephrectomy versus bilateral nephrectomy and dialysis for bilateral synchronous cancer and noted significantly improved survival after nephron-sparing surgery [12]. As more data emerged and technical success rates of nephron-sparing surgery improved, the role of partial nephrectomy for unilateral renal cell cancer expanded. To date, nephron sparing surgery is recognized as effective for renal cell cancer when preservation of renal function is necessary and also effective for small, incidentally discovered tumors, even when the contralateral kidney is normal [1–5]. The number of such tumors has increased in recent years due to increased use of non invasive radiological imaging techniques, especially ultrasounds and CT scan [6]. The efficacy of nephron-sparing surgery for such lesions in selected patients has been well documented with long term cancer free survival rate comparable to that after radical nephrectomy [1–5]. The major disadvantage of nephron-sparing surgery is the increased risk of local recurrence compared to radical nephrectomy. Van Poppel et al. reported of 76 patients who underwent kidney-sparing surgery from 1981 until the beginning of 1996. Fifty-one had a normal contralateral kidney. Mean follow-up was 75 months. None of the patients had local recurrence, although in 3 systemic disease developed [1]. Moll et al. reviewed 105 cases of nephron-sparing surgery for renal cancer with a contralateral healthy kidney. No patient had recurrence or metastasis [2]. Steinbach et al. experienced no local recurrence after a mean follow-up of 3.3 years in 72 cases of elective conservative resection of a renal tumor [3]. Fergany et al. reported a 10 years experience after partial nephrectomy [4]. The incidence and the mean time to recurrence for stage T1a (4 cm or less) was 4% at 70 months, for T1b (4 to 7 cm) 33% at 47 months, for T2 (greater than 7 cm) 20% at 91 months and 53% at 57 months for stage T3a. In all cases, a complete tumour resection was carried out and confirmed by pathological examination. One patient died of tumor metastases, and 2 (2.7%) had tumor recurrence in the kidney requiring nephrectomy and enucleation, respectively. The 5 year cause specific survival rate for the elective group was 84%. Uzzo and Novick [5] reviewed more than 1800 cases of nephron-sparing surgery in the literature and dated the risk of local tumour recurrence from 0% to 10% and it was clearly lowest in patients, who underwent elective nephron-sparing surgery for low stage lesions 4 cm or less. Local tumour recurrence after nephron-sparing surgery may be due to presence of occult multifocal lesions, incomplete resection of the primary tumour, the develop of a new primary or metastatic focus of renal cell carcinoma in the renal remnant, or tumour invasion beyond pseudocapsule when a margin is not resected enough [13,14]. The review article of Uzzo and Novick reported an incidence of multifocal disease of approximately 5% in almost 1000 combined cases of nephron-sparing surgery available in literature, when the primary or index tumour was 4 cm or less [5]. Moreover, multifocality seemed to be more frequent in patients with germ line mutations, such as those with von Hippel Lindau disease [15] and with larger tumors, especially, tumors that extended beyond the renal capsule [16]. However, the relationship of multifocality and local recurrence is neither linear nor predictable [5]. In the 1950s, Vermooten first suggested that peripheral renal neoplasms could be locally excised, leaving a margin of normal parenchyma around the tumor [7]. For many years, there has been a general agreement about the 1 cm margin of grossly normal parenchyma to include in the speci-
men to avoid local recurrence. Recently, the amount of normal tissue to excise with tumour has been object of controversies. Piper reported a multicenter review study of 67 patients who underwent nephron-sparing surgery. The mean follow-up was 60 months (range 5–124). Mean tumor size was 3 cm. Disease progression, margin status and the shortest distance of normal parenchyma around the tumor in the final pathologic specimen were together analyzed. 2/7 (28%) patients with a surgical positive margin progressed, 2/11 (18%) with a negative margin distance of less than 1 mm, none of the remaining 49. The conclusion was that 1 cm margin in nephron-sparing surgery is debatable [17]. Castilla et al. reviewed the resection margin, tumor size, TNM stage, and Fuhrman nuclear of 69 patients who underwent nephron-sparing surgery between 1976 and 1988 to determine whether they were associated with disease progression. The mean postoperative follow-up interval was 8.5 years and concluded that the width of the resection margin after nephron-sparing surgery for renal cell carcinoma does not correlate with long term disease progression. A histologic tumor free margin of resection, irrespective of the width of the margin is sufficient to achieve complete local excision of renal cell cancer [18]. Sutherland et al. studied 44 patients who had a median follow-up of 49 months. Three patients had positive surgical margins. No patient with negative parenchymal margins after nephron-sparing surgery for stages T1–2N0M0 renal cell carcinoma had local recurrence at the resection site at a mean follow-up of 49 months and margin size was irrelevant [19]. Herr et al. presented long term results of partial nephrectomy leaving no more than 5 mm of normal tissue at resection for unilateral renal tumours in 70 patients with a normal contralateral kidney. No local recurrence was registered. Only 2 patients died for metastatic disease [7]. More recently, Li et al. prospectively studied 82 kidneys in which renal cell carcinomas of 4 cm or less were resected by radical nephrectomy. The greatest distance between extra-pseudocapsule lesions and primary tumors was measured. The average distance between extra-pseudocapsule cancer lesions and primary tumors was 0.5 mm (range 0–5 mm). Their data suggest that when partial nephrectomy is performed for renal cell carcinoma of 4 cm or less, a 1 cm margin may be too much while enucleation alone may be associated with a significant risk of incomplete excision [20].

All these reports might suggest that renal tumors smaller than 4 cm in diameter have a “benign” behaviour and therefore the classical requirements of oncological surgery might be not entirely followed without significant risk. A histologic tumor-free margin of resection, irrespective of the width of the margin should be sufficient to achieve complete local excision of renal cell cancer [8,17–20]. In our series mean and median shortest distance from tumor to inked margin was 2.4 mm and 1.9 mm respectively. Intraoperative biopsy of the tumor bed was never performed but no positive margin was present at final pathologic examination. This might be due simply to serendipity but also in other series the positive margin rate was very low, varying from 0% [1] to 10.4% [17], and it has never been demonstrated that biopsy of the tumor bed may decrease positive margin rate. Indeed, technically, it is not easy and, if performed extensively, may increase the chance of complication. If performed formally, taking 1 or 2 small pieces of tissue, it could not be really helpful. Recommendation of biopsy of the tumor bed seems to be more a consequence of a consolidated surgical tradition that an evidence-based suggestion, at least for renal cancer. Our median follow-up (59 months) is shortest than the series described by Fergany [4] and Herr [8], but anyhow significant considering the local recurrence rate. It is now 9 months longer after the present paper has been written and no further local recurrence, distant metastasis or death have been recorded. None of the patients developed a local recurrence. Cancer specific survival rate is comparable to that of radical nephrectomy. The incidence of serious complications was considerably low, including only 4 cases of postoperative haemorrhage, 3 managed conservatively. In particular, no case of urinary fistula occurred. Our results confirm that enucleoresection of small renal tumors leaving only a minimal rim of grossly normal renal parenchyma is a safe and reliable surgical procedure which can be adopted without significantly increasing the oncological risk and surely minimizing the complication rate [8,17–19].

5. Conclusions

Recent long term data support the role of nephron-sparing surgery leaving less than 0.5 cm of normal parenchyma as an appropriate oncological procedure in properly selected patients. None of the patients of our series had positive surgical margins after surgery nor had local recurrence at excision site at median follow-up of 59 months. Excision of small renal tumours surrounded by 2–3 mm of grossly normal parenchyma and adjacent perinephric fat is a safe technique, which reproduces the results of radical nephrectomy with minimal morbidity and with preservation of renal function in patients with a solitary kidney.
References


