Nephron sparing surgery: A single institution experience

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ABSTRACT

Objective: To report our experience in managing various benign and malignant renal tumors with nephron-sparing surgery. Materials and Methods: Records of patients who underwent nephron-sparing surgery (NSS) either through open or laparoscopic approach between May 1997 and June 2006 at our institution were reviewed. Patient and tumor-related characteristics, treatment modality and complications were noted. Results: There were 26 patients (29 renal units), including three with bilateral lesions who underwent nephron-sparing surgery. Mean age at surgery was 47.0 years (range 16-67 years). Mean tumor size was 4.7 cm (range 2-7.5 cm). Mean warm ischemia time was 41 min and 32.5 min, operative time 158 min and 186 min and blood loss 200ml and 85 ml in open (n=24) and laparoscopic approach (n=2) respectively. Complications were seen in five (19.2%) patients of whom two had postoperative bleeding requiring nephrectomy in one and angioembolization in another. One patient with persistent urinary leak required intervention. Local wound infection in one patient and incisional hernia in another were surgically managed. Histopathological profile revealed 13 (44.8%) benign lesions which included angiomyolipoma (eight), simple cyst (two), cortical adenoma (one), metanephric adenoma (one) and myelolipoma (one). The remaining 16 (55.2%) malignant lesions included renal cell carcinoma (15) and metastatic adenocarcinoma (one). At a mean follow-up of 38.6 months (range 1-91) no patient had local recurrence or distant metastasis. Cancer-specific survival was 100% and overall survival was 92.3%. Conclusions: Nephron-sparing surgery is a safe and effective alternative to nephrectomy in both benign and malignant lesions of the kidney.

Key words: Kidney, kidney diseases, nephron sparing surgery

Enthusiasm for nephron-sparing surgery (NSS) has been stimulated by several trends, including advances in renal imaging, improved surgical techniques and methods to prevent ischemic renal injury, better postoperative management, such as renal replacement therapy and long-term prospective cancer-free survival data.[1] Nephron-sparing surgery may be performed safely and cost-effectively with low morbidity, preservation of renal function, a low local recurrence rate and high patient satisfaction.[2,3] In India, the rate of incidentally detected renal tumors is much lower that is 8% as compared to 50% in western countries because most of these cases present at an advanced stage.[4] Lack of regular health checkup as well as late consultation are the two main causes for not getting suitable cases for NSS. A survey of the existing literature revealed limited experience with NSS in India. Herein, we analyze our experience with nephron-sparing surgery with regards to the demographic profile of cases, clinical presentation, surgical and adjuvant therapy, complications and overall survival.

MATERIALS AND METHODS

Records of patients who had undergone NSS for various benign and malignant lesions between May 1997 and June 2006 were reviewed. Preoperative evaluation comprised urinalysis, chest radiograph, liver and renal function tests and abdominal CT. Magnetic resonance imaging (MRI), digital subtraction angiography [Figure 1], color Doppler scan and radionuclide imaging were obtained wherever indicated.

Operative technique

Open approach: An extraperitoneal flank approach through the 11th or 12th rib bed was preferred. Extra-gerotals dissection was performed. Renal artery and vein were mobilized separately. After clamping renal artery, ice slush was placed around the kidney for 15 min to obtain regional hypothermia. Gerotas fascia and renal capsule were sharply incised around the lesion leaving a 0.5 to 1.0 cm margin of normal appearing parenchyma beyond the visual limits of the tumor. Frozen
section of the tumor bed was obtained in cases of suspected RCC in the initial eight cases and later on this practice was abandoned due to a low yield. Segmental renal vessels were individually ligated with 5-O’ prolene. Disruptions in the collecting system were detected by instilling dilute solution of methylene blue through a preplaced ureteric catheter and oversewn with 4-O’ vicryl or polydioxanone suture. Surgicel and gelfoam spongstran bolster were then placed on the cut surface and 2-O’ vicryl sutures were used to approximate the remaining renal parenchyma. A double J stent was placed in cases where the pelvicalyceal system was opened.

**Laparoscopic approach:** For laparoscopic partial nephrectomy 4-port technique was used. Hilar control was obtained with the help of vascular loops (SURG – I - LOOP; SCANLAN International, Netherlands) placed around the artery and vein. These loops were brought out extracorporally through small incisions and traction was applied to occlude the vessels [Figure 2]. No regional hypothermia was attained.

Patients were followed up with serum creatinine, urinalysis and renal sonography or computerized tomography scan.

**RESULTS**

Table 1 lists the demographic and operative data of the patients’ cohort. There were 26 patients (29 renal units), including three with bilateral lesions who underwent nephron-sparing surgery. Of 26 patients, 24 underwent NSS by open technique and two by laparoscopic technique. Mean age at surgery was 47.0 years (range 16-67 years). Mean tumor size was 4.7 cm (range 2-7.5 cm). Of the 26 patients, 18(69.2%) had symptomatic lesions and the remaining eight (30.8%) were incidentally detected. Partial nephrectomy was performed as an elective procedure in 22 (84.6%) cases while one case had a relative indication for NSS – renal tumor with contralateral pelvi-ureteric junction obstruction with mild impaired renal function. Three patients with bilateral synchronous renal tumors warranted a nephron-sparing approach on each side. Nephron-sparing surgery was performed as a staged procedure (with a minimum duration of one month) with the less involved side done first to obviate the need for temporary dialysis if acute tubular necrosis developed after NSS.

Table 2 reveals the histopathological profile of 29 surgically removed specimens. There were 13 (44.8%) benign lesions which included eight angiomyolipomas. Two young patients...
with complex, polar, Bosniak Type III cysts, with calcifications and irregular margins were operated upon for suspected malignancy, but they revealed to be simple cysts in each. The remaining 16 (55.2%) specimens were compatible with malignant lesions, in which renal cell carcinoma (RCC) accounted for 15 cases. Clear cell carcinoma was the commonest histological cell type. There was one case of metastatic adeno-carcinoma whose origin could not be detected as the case was lost to follow-up.

The majority – 11 (73.3%) of the RCC were less than 4 cm in size. Seven of RCC were located at the upper pole, four at lower pole, while four were found to be in central position. Pathological tumor staging was determined according to the 1997 TNM classification. All the 15(100%) cases of RCC were of low stage (T1) and 13 (86.7%) had a favorable Fuhrmann’s grade (GD II or less). None of the specimens revealed positive surgical margins or evidence of vascular invasion.

Minor to major complications were seen in five (19.2%) patients. Two of the cases had postoperative bleeding. One was reactionary bleeding for which re-exploration was done and nephrectomy performed in view of persistent intraoperative hemodynamic instability. The other case had hemorrhage from pseudo-aneurysm arising from the lobar artery, which was managed by angioembolization [Figure 3]. One case had a prior history of gallstone pancreatitis with diabetes and hypertension died four months later of hepatic encephalopathy. Another patient with bilateral large renal tumors, who for the purpose of renal preservation, underwent simultaneous radical nephrectomy on one side and bench partial nephrectomy for complex, lower and mid-polar tumor invading into pelvicalyceal system near hilum on the opposite side, subsequently died of acute tubular necrosis with acute respiratory distress syndrome and multi-organ failure. Overall survival was 92.3% and cancer-specific survival was 100%.

DISCUSSION

Standard indications for NSS fall into three categories, i.e. absolute, relative and elective. Absolute indications include circumstances where radical nephrectomy would render the patient anephric, with a subsequent immediate need for dialysis. This includes patients with bilateral RCC or RCC involving a solitary functioning kidney. Three of our patients had bilateral renal tumors. Relative indications for NSS include patients with unilateral RCC and a functioning contralateral kidney when the contralateral kidney is affected by a condition that threatens its future function, e.g. calculus disease, chronic pyelonephritis. It also includes patients with hereditary forms of RCC such as von Hippel-Lindau disease (VHL). Elective indications for NSS include patients with localized unilateral RCC and a normal contralateral kidney. The role of partial nephrectomy in angiomyolipoma and oncocytoma has already been established.

Nephron-sparing surgery is a technically advanced procedure requiring considerable expertise. Intraoperative issues may be attributable to time limitations caused by warm ischemia, wherein the tumor must be excised and precise hemostatic repair performed expeditiously, especially when considering laparoscopic approach. Our modest surgical experience regarding NSS compares favorably with the other series reported so far[8] regarding estimated blood loss, operative time, convalescence and hospital stay. After having accrued sufficient experience with the open approach, laparoscopic partial nephrectomy in two patients was successfully performed with good oncological (negative surgical margin) and functional outcome.
Although radical nephrectomy remains the standard treatment for localized RCC, different series have reported similar cancer-specific survival or progression-free interval at five or 10 years in patients who underwent radical nephrectomy or NSS for localized RCC. In a recent study from the Memorial Sloan-Kettering Center, Herr et al. reported the 10-year results of elective NSS for patients with a normal contralateral kidney. With a mean tumor size of 3 cm and with predominantly low-grade, low-stage tumors, 69 of the 70 patients (98.5%) had no local recurrence and 68 (97%) survived free of metastasis. Thus our series comprise majority - 22/26 (84.6%) of NSS, performed as an elective procedure. Although the long-term functional advantage of NSS when there is a normal contralateral kidney remains to be definitively shown, the benefits might include a decreased risk of progression to chronic renal insufficiency and end-stage disease. The oncological results presented in our series are encouraging. None of the specimens was found to have a positive margin on final histopathological analysis. Cancer-specific survival and overall survival at a mean follow-up of 38.6 months (range 1-91) was 100% and 92.3% respectively. Overall negative tumor margin status along with the relative majority of patients with low-grade 13 (86.7%) and a favorable tumor stage 15(100%), would suggest durable outcome even during longer follow-up. For tumors smaller than 4 cm, the local recurrence rate has been estimated between 1.5-4%.[11] Prior series assessed the prognostic significance of tumor stage, grade, size, laterality and margin status on the long-term outcomes of open NSS. In the absence of cancer recurrence or cancer-related death as an end point, the present study could not analyze the factors affecting disease outcome. Similarly, given the lack of cancer mortality, estimates of actuarial five-year survival in this series are not warranted.

Prolonged acute tubular necrosis with or without clinically overt renal failure may occur in 6.3% (range 0.7-7.3%) of patients.[13] In the current series, two patients who developed chronic renal insufficiency had bilateral renal masses. Considering the relatively short cold ischemia time of 38 and 32 min respectively, it is unlikely that ischemic insult per se had a major role in the gradually worsening renal function in these patients. Excisional loss of functioning parenchyma is probably the cause for deteriorating renal function. Long-term efficacy of NSS in preserving renal function is evident by the fact that none of the patients in the present series required renal replacement therapy.

Despite reconstructing renal remnant over a hemostatic agent, such as oxidized cellulose (surgicel), bleeding is an important complication. Van Poppel et al. reported hemorrhage in 7.9% of 76 patients and suggested that larger tumor size and a central location correlated with the risk of postoperative hemorrhage. In the present series, two of 26 cases required re-exploration and underwent nephrectomy in one and angioembolization in the other.

The cumulative incidence of urinary fistula following partial nephrectomy is reported as 6.5%.[6] In the current series urinary leakage developed in only one case which resulted possibly due to down migration of the stent causing obstruction.

Review of the literature reveals that when NSS is performed with attention to excising a perimeter of grossly normal-appearing parenchyma, sending specimens for intraoperative frozen section may result in an unnecessary expense without providing meaningful and reliable information.[15] Hence, except in the initial few cases, no attempt was made to routinely obtain frozen section from the tumor bed.

We also recognize the shortcomings of our study – mainly the relative scarcity of numbers, inherent indolent nature of the favorable stage and low-grade renal tumors detected and the need for larger follow-up of 10 years to document definitive oncological outcome. However, our experience reaffirms the clinical relevance of nephron-sparing surgery with significant but manageable complications.

**CONCLUSION**

Nephron-sparing surgery is a safe and effective alternative to nephrectomy in both benign and malignant lesions of the kidney. Overall functional and oncological outcomes are quite encouraging. Patients with NSS performed for bilateral renal masses should be followed closely for possible renal deterioration. Though technically feasible, it needs reasonable expertise to achieve the best functional and oncological outcome with minimal complications.

**REFERENCES**

1. Fergany A, Khaled S, Hafez, Novick AC. Long term results of Nephron sparing surgery for localised renal cell carcinoma: 10-year follow up. J Urol 2000;163:442-5.
2. Clark PE, Schover LR, Uzzo RG, Hafez KS, Rybicki LA, Novick AC. Quality of life and psychological adaptation following surgery for localized renal cell carcinoma: Impact of the amount of remaining renal tissue. Urology 2001;57:252-6
3. Uzzo RG, Wei JT, Hafez K, Kay R, Novick AC. Comparison of direct hospital costs and length of stay for radical nephrectomy versus nephron-sparing surgery in the management of localized renal cell carcinoma. Urology 1999;54:994-8.
4. Srivastava A, Mandhani A, Jain M, Kapoor R, Srivastava A, Dubey D, et al. Prognostic factors in patients with renal cell carcinoma: Is TNM (1997) staging for renal cell carcinoma relevant in indian subpopulation? Indian J Cancer 2004:41:99-103.
5. Guinan P, Sobin LH, Algaba F, Badellino F, Kameyama S, MacLennan G, et al. TNM staging of renal cell carcinoma: Workgroup no 3. Cancer 1997:80:992-3.
6. Novick AC, Derweesh I. Open partial nephrectomy for renal tumors: Current status. BJU Int 2005;95:35-40.
7. Leach GE, Lieber MM. Partial nephrectomy: Mayo clinic experience 1957-1977. Urology 1980;15:219-28.
8. Winfield HN, Donovan JF, Lund GO, Kreder KJ, Stanley KE, Brown BP, et al. Laparoscopic partial nephrectomy: Initial experience
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Commentary

Nephron sparing surgery: Is here to stay

While radical nephrectomy is still the gold standard of treatment for renal cell carcinoma, its role is now being seriously challenged. As one surveys world literature, it has become evident that numerous articles have shown the long-term safety both surgically and oncologically of nephron sparing surgery (NSS).

What does one mean by the term “Nephron Sparing Surgery.” Loosely it could be used to include any surgical procedure that preserves nephrons. This includes a whole list of procedures for both benign and congenital anomalies. I believe we need to restrict the use of the term NSS for the treatment of renal cell carcinoma when conventionally we have all been doing a radical nephrectomy. For example, removal of a non-functioning duplex moiety should not be classified as NSS.

There are two articles in this issue of the journal that report single center experience of NSS.

Complications of nephron sparing surgery for renal tumors. J Urol 1994;151:1177-80.
14. Van Poppel H, Bamelis B, Oyen R, Baert L. Partial nephrectomy for renal cell carcinoma can achieve long-term tumor control. J Urol 1998;160:674-8.
15. Kubinski DJ, Clark PE, Assimos DG, Hall MC. Utility of frozen section analysis of resection margins during partial nephrectomy. Urology 2004;64:31-4.

Additional in our country, when treatment and follow-up costs are invariably borne by the patient, it might seem prudent to offer a radical nephrectomy for the “elective NSS” at least in the older population. In our enthusiasm to perform NSS we should also be focused on local patient demographics. Certainly in the younger patient NSS is a strong option. One cannot predict in the absence of a strong family history if a younger person will develop hypertension and/or diabetes in later life. We need to remember that soon the Indian subcontinent will have the largest number of diabetes in the world (International Diabetes Federation Report).

At this time, a maximal amount of nephron mass is important to reduce the effects of target organ damage. The oncological safety of NSS for a < 4 cms renal neoplasm is now fairly well established in the category of elective NSS. The five-year cancer specific survival of a 97.8% for tumor < 4 cm treated by partial nephrectomy compares with a similar survival when treated with radical nephrectomy. The articles in this issue have addressed this modality of treatment with good short-term outcome. I believe we need longer follow-up. The controversy is the role of NSS for tumors between 4-7 cm. These articles do not address this issue. Literature while suggesting the successful use of partial nephrectomy for such lesions, is limited by small numbers and short-term follow-up.

In the subgroup univariate and multivariate analysis, the most important predictor of outcome was tumor size. In my opinion, measurement of tumor size by imaging or at surgery and by the pathologist on the specimen are quite in variance with one another and could make a difference at the upper end of the spectrum. Similarly some large tumors could also be undersized. Unfortunately these corrections are not taken into our analysis.

At this time, I believe that we need to remember the facts while offering treatment for patients with renal cell carcinoma.