Nephron-sparing surgery for renal tumors

Abd El Hamid H. Ezzat *, Ahmed Helmy, Ashraf H. Ibrahim

Department of Surgical Oncology, National Cancer Institute, Cairo University, Egypt

Received 14 April 2011; accepted 7 May 2011
Available online 8 October 2011

KEYWORDS
Nephron sparing surgery (NSS); Renal tumors

Abstract Purpose: To report National Cancer Institute (NCI) experience in managing various benign and malignant renal tumors with nephron sparing surgery (NSS), and to assess its safety and feasibility.

Patients and methods: Literature review for NSS, and reviewing of the patients records who underwent NSS between the period from January-2000 to December-2009 at NCI-Cairo University was done. Tumor related characteristics, indication for NSS, operative techniques, postoperative complications, full histopathological data, and follow up results were reviewed.

Results: The total number of patients was 15. Median age at surgery was 32 years (range from 1.5 to 65 years). Five patients had bilateral tumors. The mean radiologic tumor size was 4.7 ± 5.2 cm. All patients had normal preoperative kidney functions. Six patients had an absolute indication for NSS, while 6 patients had a relative indication, and 3 patients were elective. All 5 patients with bilateral tumors underwent bilateral simultaneous surgery. Cold ischemia was used in 7 patients, 1 patient was exposed to warm ischemia. Manual compression was used in 2 patients, and no vascular control was applied in 5 patients. Complications were encountered in 2 patients, one of them had urinary leakage which needed reoperation, and the other had subcutaneous hematoma which was treated conservatively. Histopathological analysis revealed Wilm’s tumor (7 patients), angiomyolipoma (4 patients), renal cell carcinoma (RCC) (3 patients), and Hydatid cyst (1 patient). All patients had negative surgical margin. For patients with Wilm’s tumor, the median follow up

* Corresponding author. Mobile: +20 10 521 40 33.
E-mail address: hamidezzat@hotmail.com (A.H. Ezzat).

1110-0362 © 2011 National Cancer Institute, Cairo University. Production and hosting by Elsevier B.V. All rights reserved.

Peer review under responsibility of Cairo University.
was 24.4 months (range from 5 to 94 months), two patients had local recurrence, and 1 patient had distant metastasis. For patients with RCC, The median follow up was 14.7 months (range from 5 to 33 months) with no local recurrence or distant metastasis. All patients had normal kidney functions during postoperative and follow up periods.

Conclusion: NSS is a feasible safe procedure that could be done with acceptable complications. It provides a good solution for patients with bilateral benign tumors and early localized RCC.

© 2011 National Cancer Institute, Cairo University. Production and hosting by Elsevier B.V.
All rights reserved.

Introduction

Nephrectomy can be simple, radical or partial. In simple nephrectomy, only the kidney is removed. In radical nephrectomy (RN) the kidney with surrounding perinephric fat, Gerota’s fascia, adrenal gland, segment from the ureter and the regional lymph nodes are removed. In partial nephrectomy only part of the kidney is removed, sparing the rest of the kidney [1].

The history of renal surgery had an inauspicious beginning, following animal experiments and accidental removal of the kidney in humans during surgery for liver cysts [2]. The first scheduled nephrectomy was done by the German surgeon Gustav Simon in 1869 for treatment of urinary fistula [2,3]. In 1870, Simon performed the first partial nephrectomy (nephron sparing surgery) for a patient with hydronephrosis [2]. In 1884, Wells accidentally removed a third of a kidney during enucleation of a perirenal fibrolipoma [2,4]. The first oncologic nephron sparing surgery (NSS) was accomplished by Vizenz Czerny in 1887 as a therapy for renal malignancy (angiosarcoma) [2,4].

In 1950, Vincent Vermooten was the first to postulate the scientific rationale for NSS as an alternative to nephrectomy in the treatment of renal cell carcinoma [5]. “There are certain instances when for the patient’s well being it is unwise to do a nephrectomy, even in the presence of a malignant growth involving the kidney. It may also occur when the total renal function is such that nephrectomy for carcinoma would result in fatal uremia. If there is no evidence of metastasis and the neoplasm involves only the cortex of the kidney, excision of the tumor is unquestionably advisable. The question is, whether such a procedure is ever justifiable when the opposite kidney is normal. I am inclined to think that in certain circumstances it may be” [5].

The role of NSS was subsequently challenged by Robson et al. in 1969, who demonstrated that early ligation of the renal vessels decreased the risk of hematological spread when accompanied by removal of the perinephric fat and excision of all regional lymph nodes [4].

With the encouraging survival data reported by Robson and his colleagues, RN has been considered for many decades the standard treatment for renal cell carcinoma [4].

Through the encouraging survival data reported by Robson and his colleagues, RN has been considered for many decades the standard treatment for renal cell carcinoma [4].

The indications of NSS for renal tumors remained either absolute indication i.e. a solitary kidney (anatomical or functional), bilateral renal tumors that will leave the patient anephric, or relative indications i.e. impending or existing renal failure [6].

A second interest in NSS has been growing in localized renal tumors with normal contralateral kidney due to several developments; including advances in imaging techniques and its increased use, improved surgical techniques and methods to prevent ischemic renal injury, and reduced post operative complications due to better post operative care [7].

Various studies have proved that NSS is safe and cost effective. Moreover, NSS has shown effective local control and comparable five year cancer specific survival rate for localized renal tumors with normal contralateral kidney equivalent to RN [8].

These results, together with the impact of NSS on health-related quality of life, changed the indications of NSS to be elective in patients with normal contralateral kidney, where NSS is being increasingly used [9].

The aim of our study is to report National Cancer Institute (NCI) – Cairo University experience in managing various benign and malignant renal tumors with nephron sparing surgery (NSS), and to assess its safety and feasibility.

Patients and methods

This is a retrospective study of patients who underwent NSS at the National Cancer Institute (NCI) – Cairo University between the period from January 2000 to December 2009.

The records of the patients were reviewed and the following data were collected:

1. Epidemiologic data: age and sex.
2. Preoperative investigations: routine Labs and imaging.
3. Indication for NSS.
4. Aspects regarding operative techniques.

Operative details

The patient was placed in supine position, hyperextended over a folded towel or bag of sand. After induction of general anaesthesia, open transabdominal approach (midline, subcostal, or transverse) was used. After mobilization of the colon, the kidney was dissected within the Gerota’s fascia, while the perirenal fat around the tumor is left intact.

When vascular control was applied, the main renal artery was temporarily occluded using either nylon tape (Fig. 1) or vascular clamp while leaving the main renal vein patent (Fig. 2). The kidney was then surrounded by ice slush for 5–10 min before resection (Fig. 3). If manual vascular compression was used, the assistance compressed proximal to the tumor till hemostasis achieved. Combined blunt and sharp dissection (using cold scissors) was used during resection.

Hemostasis was achieved by either diathermy or suture ligations, but additional methods (Surgicel®, perinephric fat and Argon beam) were used in some patients. Whenever it was
opened, repair of the pelvicalyceal system was done using continuous sutures. The renal defect was closed using perirenal fat.

The kidney was then fixed to the posterior abdominal wall, and a closed suction drain was left in the retroperitoneal space.

(5) Post operative complications and post operative renal function which was assessed by measuring serum creatinine in mg/dl.

(6) Full histopathological data: tumor site, size, pathologic type.

(7) Findings during follow up period regarding local tumor recurrence and distant metastasis.

Results

Fifteen patients were included in the study. They were 4 (26.7%) male and 11 (73.3%) female. The mean age of patients at time of surgery was 30.4 ± 27.2 years and the median age was 32 years (range from 1.5 to 65 years). Seven patients were pediatrics (below the age of 18).

At the time of surgery, five out of 15 (33.3%) patients had bilateral tumors. The remaining 10 (66.6%) patients had unilateral tumors (5 on the right and 5 on the left).

Two patients had previous renal surgery, 1 of them had contralateral NSS and the other had contralateral RN. In both conditions, the first surgery was due to bilateral Wilm’s tumor.

All patients had normal preoperative kidney functions, and the mean preoperative serum creatinine was 0.7 ± 0.3 mg/dl.

Seven out of 15 (46.7%) patients received neoadjuvant chemotherapy (Wilm’s tumor) with a good response.

The mean tumor diameter by preoperative CT was 4.7 ± 5.2 cm. None of the patients in this study, had lymphadenopathy or adrenal involvement by preoperative imaging.

Regarding the indication for NSS in this review, 6 (40%) patients had an absolute indication (5 due to bilateral tumor and 1 due to solitary kidney), 6 patients had a relative indication (5 due to suspicious benign disease and 1 due to abnormal contralateral kidney “previous NSS”), and 3 (20%) patients were elective (tumor was ≤4 cm, normal contralateral kidney, and no medical diseases that predispose to renal failure).

Operative techniques

Bilateral synchronous surgery was done in 5 cases. 4 of them underwent bilateral NSS, and 1 patient underwent RN on one side (because of hilar tumor) and NSS on the other side. So the total number of tumors that was resected by NSS was 19 tumors in 15 patients.

Regarding tumor location, 8 out of 19 (42.1%) tumors were located in the upper pole, 8/19 (42.1%) tumors were in lower pole, and 3/19 (15.8%) tumors were in mid zone, and no tumor was found to be central (central tumor was defined as; (A) tumor that is surrounded by normal parenchyma and may not even be detectable on intraoperative inspection or palpation and (B) when the tumor develops into the renal hilum and contacts or invades the renal collecting system or major renal veins) [10].

Figure 1 Renal artery identified using a nylon tape.

Figure 2 Renal vein clamped at the hilum with a bulldog vascular clamp.

Figure 3 Renal hypothermia achieved by ice slush around the kidney.

During resection, 8 (53.3%) patients underwent vascular control of the main artery, manual compression was applied in 2 (13.3%) patients, and no vascular control was applied in 5 (33.3%) patients.
During resection, cold ischemia was used in 7 of 8 (87.5%) patients using ice slush, and only 1 (12.5%) patient was exposed to warm ischemia.

In all 15 patients, hemostasis was achieved by suture ligation and diathermy. Additional hemostatic measures were used in 13 (86.7%) cases as follows: argon beam was used in 2 (15.4%) cases, Surgicel® was used in 6 (46.2%) cases (Fig. 4), perinephric fat was used in 2 (15.4%) cases, Surgicel® and perinephric fat were combined in 1 (7.7%) case, argon beam and Surgicel® were used together in 1 (7.7%) case, and in 1 case argon beam, Surgicel®, and perinephric fat were all combined together.

Intraoperative frozen section from the tumor bed was used in 2 patients only, and the result was negative for both. Intraoperative ultrasound (US) was not used in our study (Table 1).

Histopathological results

Tumor types was found as follows; Wilm’s tumor in 7 patients, angiomyolipoma in 4 patients, renal cell carcinoma (RCC) in 3 patients, hydatid cyst in 1 patient. The mean pathological largest diameter of 19 resected tumors was 4.3 ± 4.7 cm. All cases had negative margin on the final pathological analysis (Table 2).

![Figure 4](image)

Hilar lymph nodes dissection was done in 8 patients. Seven (87.5%) of these patients had Wilm’s tumor, and 1 patient had angiomyolipoma. The total number of lymph nodes dissected was 20 (average 2.5 lymph nodes/patient), only 2 lymph nodes were positive for tumor cells in 2 different patients.

Postoperative complications and follow up results

Thirteen (86.7%) patients had an uneventful postoperative period. Complications encountered were urinary leakage (one patient), which did not resolve after conservative measure for 2 weeks, and was explored for repair and stent insertion, and subcutaneous hematoma (one patient), which was treated by conservative measures and did not require blood transfusion.

Immediate post operative serum creatinine was within normal for all patients, the mean was 0.8 ± 0.3 mg/dl.

The median follow up period for patients with Wilm’s tumor was 24.4 months (range from 5 to 94 months). For patients with RCC, it was 14.7 months (range from 5 to 33 months), and for patients with angiomyolipoma it was 5.5 months (range from 1 to 14 months). The follow up period for the patient with hydatid cyst was 1 month.

During the follow up period, the serum creatinine remained within normal for all patients. The mean was 0.8 ± 0.1 mg/dl.

For the patients with Wilm’s tumor, 2/7(28.6%) developed local recurrence (at 7 and 12 months), and 1/7(14.3%) patient developed distant metastasis (at 12 months). The 3 patients with RCC had free follow up period (Table 3).

Discussion

NSS is a surgical procedure which entails complete local resection of a renal tumor, while leaving the largest possible amount of normal functioning parenchyma in the involved kidney [3].

In addition to advances in surgical and imaging techniques which increased the interest in NSS [7], many factors expanded the indications for NSS from absolute indications (as in cases where RN would leave the patient anephric) to relative and elective indications [11]. These factors include: better understanding of the importance of preserving the renal parenchyma – even in cases with normal kidney functions [12,13], comparable oncological results “with certain criteria” to RN [14], and technical accessibility with accepted intraoperative and postoperative complications [15].

This study reviewed the experience of the National Cancer Institute with NSS during the period from January 2000 to December 2009.

In our study, we reviewed the data from 15 patients with different age groups who were subjected to NSS for different indications. Their mean age was 30.4 years. Kural et al. assessed

---

**Table 1** Important aspects regarding the operative technique.

<table>
<thead>
<tr>
<th>Vascular control</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main artery clamping</td>
<td>8</td>
<td>53.3</td>
</tr>
<tr>
<td>Cold ischemia</td>
<td>7</td>
<td>46.7</td>
</tr>
<tr>
<td>Warm ischemia</td>
<td>1</td>
<td>6.7</td>
</tr>
<tr>
<td>Manual compression</td>
<td>2</td>
<td>13.3</td>
</tr>
<tr>
<td>No vascular control</td>
<td>5</td>
<td>33.3</td>
</tr>
<tr>
<td>Intraoperative frozen section</td>
<td>2</td>
<td>13.3</td>
</tr>
<tr>
<td>Additional hemostatic measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Argon beam</td>
<td>2</td>
<td>13.3</td>
</tr>
<tr>
<td>Surgicel®</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>Perinephric fat</td>
<td>2</td>
<td>13.3</td>
</tr>
<tr>
<td>Mixed</td>
<td>3</td>
<td>20</td>
</tr>
</tbody>
</table>

*a* Additional hemostatic measures were used in 13 patients.

**Table 2** Histopathological findings.

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilm’s tumor</td>
<td>7</td>
<td>46.7</td>
</tr>
<tr>
<td>RCC</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>Angiomyolipoma</td>
<td>4</td>
<td>26.7</td>
</tr>
<tr>
<td>Hydatid cyst</td>
<td>1</td>
<td>6.7</td>
</tr>
<tr>
<td>Margin status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>15</td>
<td>100</td>
</tr>
<tr>
<td>Pathological tumor size in cm</td>
<td>Mean ± SD</td>
<td>Range</td>
</tr>
<tr>
<td></td>
<td>4.3 ± 4.7</td>
<td>1–8</td>
</tr>
</tbody>
</table>
the outcome of NSS in 76 patients with different indications, their mean age was 52.3 years [16], while Yip et al. reviewed 27 patients and their mean age was 54 years [17]. The lesser mean age in our study compared to the other mentioned studies could be attributed to the fact that 46.7% of our patients were below the age of 18 and all of them underwent surgery for Wilm’s tumor.

The largest mean tumor diameter by preoperative CT in our study was 4.7 cm, which was the same found by Agrawal and his colleagues [18]. The largest mean tumor diameter by pathological analysis in our experience was 4.3 cm. By comparing the radiographic size to the pathological size in this study, we found that 10 out of 19 resected tumors had lesser pathological size in comparison to radiographic one by about 1 cm. Five of these tumors were < 7 cm.

Schlomer et al. compared the radiographic to the pathologic size of renal tumors. They reported that the pathological size was found to be lesser than radiographic size by about 0.4 cm for tumors < 7 cm, which was more significant for tumors ranging from 4 to 5 cm [19]. Alicioglu et al. reported the same result for tumor < 7 cm, except for ill defined tumors which were larger by pathological assessment [20]. Alicioglu et al. attributed this difference to the effect of vasoconstriction during the temporary renal artery occlusion, surface hypothermia, and blood loss during the operation. They concluded that the radiographic size of renal tumors should be considered in staging and selecting the appropriate treatment for tumors [20].

Other factors, which may result in difference between radiographic and pathologic tumor size, may include: neoadjuvant chemotherapy (which occurred in 7 of our patients), the accuracy of imaging techniques, duration between imaging and surgery (the range in this study was 1–8 weeks, average = 4.4 weeks), and finally the nature of the tumor (either malignant or benign).

In this study, 6 of the enrolled patients had an absolute indication for NSS (5 due to bilateral tumors and 1 due to single kidney), 6 patients had a relative indication (5 due to possibility of benign disease and 1 due to abnormal contralateral kidney “previous NSS”). Three patients had an elective indication (tumor was ≤4 cm, normal contralateral kidney, and no medical diseases that predispose to renal failure). In Agrawal et al. 22 of 26 patients had an elective indication, 3 had an absolute indication (bilateral tumors), and 1 had a relative indication [18]. And in Yip et al. series 18 of 27 patients underwent NSS as an elective procedure for incidentally discovered renal tumors < 5 cm [17]. In our study, the small number of patients with elective indications could be attributed to the late presentation of our patients.

Five of the 7 (71.4%) patients under the age of 18 in this study had bilateral synchronous tumor, which represented all bilateral cases. Four (57.1%) patients underwent unilateral simultaneous NSS and 1 case had RN on one side with contralateral simultaneous NSS. In our study, one patient of the remaining 2 patients below the age of 18 had previous RN on the right side for Wilm’s tumor, and was subjected to NSS on the left side after 2 years for metachronous tumor. The last patient presented with bilateral renal tumors, underwent right NSS in April 1999 that was proved to be Wilm’s tumor by post-operative final pathology, and received postoperative chemotherapy. The tumor on the left side has regressed completely after treatment, thus was put under follow up. In May 2006, she developed recurrence on the left side and received further chemotherapy followed by left NSS. This patient was disease-free for 124 months of follow up.

In Fuchs et al. they reviewed 14 patients who underwent surgery for bilateral synchronous tumors, 9 of the 14 patients had bilateral simultaneous NSS and 5 patients had RN on one side with contralateral simultaneous NSS [21]. The indication for RN in our study was in accordance of the study done by Fuchs et al. (Presence of hilar tumor) [21]. In Davidoff et al. study, they reviewed 12 patients with bilateral Wilm’s tumor, 10 of them had bilateral simultaneous NSS, 1 had RN on one side (due to extensive tumor thrombus) with contralateral NSS, and 1 patient had bilateral RN (due to anaplastic histology and presentation with renal failure) [22].

In this study, we have noticed that the choice of applying vascular control as well as its technique and the type of ischemia used during resection were mainly affected by the surgeon preference, as there was no correlation between these items and the tumor size. On the other hand, Esteban et al. [23] reviewed 280 patients who underwent NSS and Huang et al. [24], who reviewed 83 patients who underwent NSS, found that arterial clamping (hypothermia was applied if ischemia time was anticipated to be more than 30 min) was standardly applied during resection and was only omitted in cases with small peripheral tumors.

Regardless of the technique used for vascular control, and the type of ischemia used with it, all patients in the present study had normal kidney functions during post operative and follow-up periods. Also, Gupta et al. in their study reviewed 36 patients who underwent NSS for elective indication. They did not report any change in kidney functions following NSS using either cold or warm ischemia (warm ischemia time range = 20–29 min) [6]. However, Agrawal et al. reported 2 patients who underwent bilateral NSS using cold ischemia, developed chronic renal failure [18].

Different ways were currently used to achieve hemostasis after NSS [12,25–27]. Richter et al. did not report postoperative bleeding following usage of FloSeal® for hemostasis during NSS in 25 patients [27]. In their study, Esteban et al. used different hemostatic measures (perinephric fat, Surgicel®, Tachosol®, and Tissucol®), and reported post operative bleeding in 4 patients of 83 [23]. Despite the different techniques in achieving hemostasis in our institute, no postoperative bleeding was encountered.

In the present study, intraoperative frozen section from the tumor bed was done for 2 patients only, and the results were negative for both of them. Furthermore, paraffin section

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Local recurrence</th>
<th>Distant metastasis</th>
<th>Follow up period in months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Percentage</td>
<td>Number</td>
</tr>
<tr>
<td>Wilm’s tumor</td>
<td>2</td>
<td>28.6%</td>
<td>1</td>
</tr>
<tr>
<td>RCC</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 3 Follow up results of patients with Wilm’s tumor and RCC.
confirmed these negative results. In their study Duvdevani et al. assessed the role of frozen section during NSS; positive margins were found in 2 patients by frozen section (both cases underwent immediate RN), but no residual tumor was subsequently found in the RN specimens. They also reported that paraffin sections disclosed positive margins in 4 patients, in which the frozen section analysis had shown negative margins [28]. Also, Kwon et al. studied factors that affect the surgical margin in NSS, and reported 7% positive surgical margin in the postoperative paraffin section of the final pathology despite the negative intraoperative frozen section results [29].

All the patients in the present study had no major postoperative complications except for a single patient (6.6%) who was complicated by urinary leakage, that did not improve after conservative management for 2 weeks. This patient was re-operated for ureteric stent application and repair of the pelvicyceal system. Similarly, Pasticier et al. reported urinary leakage in 13 of 127 patients (10.1%) [30], while Esteban et al. reported urinary leakage in 6 of 83 patients (8.8%) [23].

Conclusion

Nephron sparing surgery is a safe procedure that can be carried out with acceptable intraoperative and postoperative complications. It presents a good surgical alternative to patients whom RN would render anephric. It also provides adequate surgical margin in NSS, and reported 7% positive surgical margin in the postoperative paraffin section of the final pathology despite the negative intraoperative frozen section results [29].

Moreover, NSS may be considered as an adequate management for patients with benign renal tumors, avoiding a non-indicated aggressive type of surgery.

References