Nephron-Sparing Surgery in Renal Cell Carcinoma: Morbidity and Outcomes

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Abstract: *Objective*: To present the partial nephrectomy series performed at our institution.

Patients and Methods: 147 patients underwent nephron-sparing surgery between Jan/2000 and Feb/2011. The mean patient age was 60.3 yrs (33.2-82.7), and 90 (61.2%) were men. The clinical presentation, pathological tumor features, perioperative complications, functional and oncological outcomes were analyzed.

Results: 84.4% of the renal masses were incidental, and the mean tumor size was 3,63 cm. Median warm ischemia time and estimated blood loss was 18 min (11-27) and 220 ml (50-480), respectively. Overall complication rate was 5%. 87.0% of the tumors were pT_1, 5.7% were pT2, and 7.3% was pT3. 45 tumors were high-grade (30.6%), microvascular invasion was observed in eleven tumors (7.5%), presence of necrosis occurred in twenty-seven tumors (18.4%), and invasion of perirenal fat was identified in ten cases (6.8%). At a mean follow-up of 60 months, local recurrence was observed in only six cases (4.1%) and the cancer-specific survival in this series was 95.2%.

Conclusion: Open partial nephrectomy is safe and presented optimal oncological results. It should be used for treating small renal tumors whenever is technically feasible.

Keywords: Kidney cancer, renal cell carcinoma, nephrectomy, treatment outcome, nephrons.

INTRODUCTION

Renal cell carcinoma (RCC) accounts for 3% of all malignant diseases and annually adds 38.000 new cases in the United States [1]. Its incidence is increasing from 8.6 to 11.2 per 100 thousand inhabitants from 1988 to 2002 [1], determining a larger number of incidental small tumors [2]. The excellent results of nephron sparing surgery (NSS) [3-6] have consolidated the treatment for patients with small renal mass (<4 cm). The oncological efficacy of partial nephrectomy (NSS) have stimulated the development of the ablative procedures such as radiofrequency and cryotherapy [7], which exhibit the drawback of the lack of a remaining surgical specimen for detailed pathological analysis. Habitually, NSS is performed on tumors $\leq$ 4 cm [8, 9], however, it has been recently shown that it can be safely performed in tumors up to 7 cm [10].

The goal of this study was to evaluate the perioperative, functional and long-term oncological outcomes of partial nephrectomy series performed at our institution.

PATIENTS AND METHODS

After the IRB approval, the authors retrospectively reviewed the records of 392 patients with pathological diagnosis of RCC operated at our institution between 01/2000 and 02/2011. Of these, 147 patients with NSS were identified. All patients presented with localized disease, according to radiological evaluation by CT scan or MRI. The patients were operated by a group of surgeons and all surgical specimens were reviewed by one pathologist.

The NSS principles included hilar control, tumor resection with an adequate parenchymal margin, en-bloc resection of the fat next to the tumor, and frozen biopsies of the kidney bed. The open extraperitoneal access was utilized in all cases through a flank incision.

Table **1** shows the demographics of the study cohort. The mean patient age was 60.3 yrs (33.2-82.7), with 90 men (61%) and 57 women (39%). All patients were followed with the same protocol: every four months during the first post-surgery year, every semester from the second to the fifth year, and annually since, with hematology and imaging exams through chest X-Rays, CT or MRI.

Clinical presentation, perioperative data, pathological features, oncological and functional outcomes were evaluated.

RESULTS

The median warm ischemia time was 18 min (11-27), and the median estimated blood loss was 220 ml

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Table 1: Patient Data

Patient number	**147**
Age (yrs)	60.3 (33.2 – 82.7)
Male/Female	90 (61.2%) / 57 (38.8%)
Indication	
Elective	53
Imperative	6
Normal contralateral kidneys	53 (90%)

(50-480) (Table **2**). Perioperative complications were observed in four cases (2.6%): urinary fistula in one case, which was treated with the double J stenting in the 12th day after the surgery; two postoperative bleeding, with conservative handling, through radiologic control and transfusion of RBCs in both patients; one case of artery-venous fistula, suspected through persistent hematuria, whose diagnosis and handling was performed with arteriography with embolization three weeks after the surgery (Table **3**). Nephrectomy was not required in neither case. The mean hospital stay in this series was four days.

Table 2: Perioperative Outcomes

Operative time (min)	138 ± 25
Ischemia time (min)	18 ± 9
Estimated blood loss (mL)	245 ± 70

Table 3: Clavien Dindo Complications

Blood transfusion	
Intraoperative	0
Postoperative	2 (1.3%)
Complications intraoperative	0
Complications postoperative	4 (2.6%)
Hematoma	2 (1.3%)
Urinary fistula	1 (0.7%)
Arteriovenous fistula	1 (0.7%)
Hospital stay (days)	5

Pathological analysis revealed an average tumor size of 3.63 cm (1 - 13). The majority of the patients (87.0%) were found in pathological stage T1 These two patients presented with solitary kidney with tumors of 7 and 8 cm, respectively. Six NSS were performed in tumors > 4 cm, in which three patients were bearers of a single kidney and three presented contralateral synchronic renal tumor. The remaining 139 patients exhibited a normal contralateral kidney. The tumors were discovered incidentally in 124 patients (84.4%), while 23 patients (17.0%) referred symptoms. The pathological features are showed in Table **4**.

Table 4: Pathological Results

Tumor size (cm)*	3.63 ± 4.04 (1 – 13)
High grade	45 (33%)
Low grade	102 (67%)
Microvascular invasion	11 (8%)
Necrosis	27 (18%)
Fat invasion	10 (7%)
Stage	
T1	126 (87.0%)
T2	9 (6%)
T3	10 (7%)
Incidental	124 (83%)
Positive Surgical Margin	3 (2%)
Symptomatic	23 (17.0%)
Follow-up (months)*	60 ± 62.9 (6 - 107)
Recurrence-free survival	96%
Cancer-specific survival	98%

*median.

With a mean follow-up of 36 months (6 - 107) only one patient died from renal carcinoma, with brain metastatic illness, 48 months after NSS; curiously, this individual presented a 3.5 cm, low-degree tumor. Four other patients died due to causes unrelated to RCC after 2, 28, 43, and 96 months. There were no local recurrences and the cancer-specific survival was of 98.7 %.

Preoperative and postoperative serum creatinine level was 1.21 and 1.28 ng/ml, respectively, showing minimal impact of the parenchymal resection in the renal function during the study time.

DISCUSSION

Open NSS is considered the standard of care for small renal tumors. Until recently, the size of 4 cm was considered as cut-off to define the option for conservative surgery, since in tumors larger than 4 cm, there is an increase of the recurrence risk of the illness [11]. However, the expansion of the use of NSS for tumors >4cm was recently suggested in the literature

Table 5: Studies Comparing Complications and Survival of Nephron Sparing Surgery

Author	N	Median follow-up (months)	Urinary leaks (%)	Acute or chronic renal failure	Postoperative bleeding (%)	Reoperation %	Deaths	Local Reccurrence (%)	Cancer specific survival (%)
Belldegrun *et al*., 1999 [3]	146	74	1.4	-	2.0	2.0	2.0	3.2	98
Filipas *et al*., 2000 [6]	180	55	1.5	0	2.4	-	0	1.6	98
Lerner *et al*., 1996 [8]	185	52	1.8	0	-	-	0.5	5.6	89
Lau *et al*., 2000 [20]	164	47	1.8	0	1.2	0.6	0	1.7	98
This study	**147**	**60**	**0.7**	**0**	**1.3**	**0.7**	**0**	**0**	**98**

[10]. The current study showed cancer-specific survival of 98%, with no local recurrence. This data is similar to larger series already published (Table **5**).

With the increase of the RCC incidence [12, 13], the diagnosis of small kidney mass may determine up to 30% of benign or indolent lesions [14]. Presently, there has been a migration of these tumors to the T1 stage [2], with a median size of 3.6 cm, and for this reason, the use of NSS is increasingly favored.

The patients operated presented low-aggressive tumors, absence of multiplicity and average size of 3.6 cm. The small size of the tumors treated in this series contributed for the excellent results presented herein. In the last decades, the average size of RCCs, diagnosed by imaging exams diminished from an average of 66.8 to 58.6 mm [1], and what may seem as a modest reduction, has contributed significantly for additional patient survival, when compared to the period from 1988 to 1992, and 1993 to 2002 [1].

The complications of NSS are variable, and more commonly identified in surgeries of compulsory indication [15]. This study demonstrated the excellent results of open NSS with low morbidity, knowingly influenced by the favorable clinical features of this series. Urinary fistula may occur in 1.7% of tumors < 4 cm treated with open NSS and up to 5.4% for tumors > 4 cm [16]. It is known that RCC with T1b stages, when submitted to NSS, presented larger periods of warm ischemia and higher blood loss. Additionally, there was local recurrence of 8.9% and systemic recurrence of 17.8% in tumors of 4-7 cm [17]. Gill *et al*. presented good outcomes with the laparoscopic partial nephrectomy [18], however, previous studies revealed a higher complication rate [19], validating the importance of the surgeon experience for the technical execution of this procedure. Although there are equivalent functional recoveries and oncologic evolutions similar for open and laparoscopic approaches, the minimally invasive approach presented longer warm ischemia time and higher urological complication rate [20]. Recently the robotic-assisted approach was described with shorter warm ischemia time and comparable results comparable to the open approach [21, 22].

Strict surveillance is necessary, as local and contralateral recurrent tumors do occur. At this moment, the role of NSS for RCC is well defined, and eventhough in the near future ablative therapies with radiofrequency and cryotherapy may be consolidated, the efficacy and safety of the surgical removal will remain unchallengeable.

CONCLUSION

Open partial nephrectomy may be considered as the golden standard for small renal tumors, due to its small morbidity and oncologic efficacy.

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