Original article

Clinical characteristics and functional and oncologic results of patients with kidney tumors that underwent partial nephrectomy

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Abstract

Background: Partial nephrectomy has become standard treatment for T1 tumors (≤ 7 cm), solitary kidney, bilateral tumors, and hereditary cancer. There are few studies in Mexico that report on said procedure.

Aim: To know the clinical characteristics, perioperative morbidity, and functional and oncologic results of partial nephrectomy at the Instituto Nacional De Cancerología

Materials and methods: A retrospective, analytic study was conducted on patients that underwent partial nephrectomy within the time frame of 2000 to 2018, reporting the oncologic and perioperative results.

Results: Seventy-nine patients that underwent partial nephrectomy were analyzed. A total of 82 procedures were performed. Mean patient age was 52 years. Clinical stage was T1a and T1b in 62 (74.6%) and 20 (24.4%) cases, respectively. Warm ischemia was utilized in 39 (47.6%) patients and n ischemia was used in 35 (42.7%). Mean surgery duration was 162 min, mean blood loss was 449 ml, and mean hospital stay was 2.1 days. Open surgery was performed on 70 (85.4%) patients and 12 (14.6%) patients underwent the laparoscopic procedure. There were early complications in 17 (20%) patients that included 9 (11%) transfusions. Clear cell renal cell carcinoma was reported in 66 (80.5%) cases and surgical margins were negative in 73 (89%). Cancer-specific survival was 100% and overall survival was 92% at five years. The mean preoperative estimated glomerular filtration rate was 88 ml/min and it was 79 ml/min at one year. Renal ischemia influenced the decrease in the glomerular filtration rate.

Conclusions: The results of the present study are similar to those reported in other international referral centers, making the performance of partial nephrectomy in T1 tumors a safe procedure in our population.

Keywords:
Partial nephrectomy; Survival; Renal ischemia; Glomerular filtration rate.

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Introduction

The estimated worldwide incidence of kidney tumors is 300,000 per year and over 50% are diagnosed incidentally.[1] Partial nephrectomy (PN) is the standard procedure for the treatment of T1 lesions (£ 7 cm) and in cases of anatomic or functional solitary kidney, bilateral tumors, hereditary kidney cancer, and chronic kidney disease.[2-3] Good results have also been reported in some T2 tumors.[4] A smaller decrease in glomerular filtration rate and lower incidence of cardiovascular disease has been shown with PN, compared with radical nephrectomy (RN), with comparable oncologic results.[5-6]

Different scores have evaluated the complexity of partial nephrectomy, including the Preoperative Aspects and Dimensions Used for an Anatomical score (PADUA), the C index, and the RENAL nephrometry score, which is the most widely used.[2,7]

The success of PN has been assessed through the "trifecta" concept. It consists of negative margins, the absence of complications, and warm ischemia time under 25 min, and is reported in 44 to 68% of cases.[7-8] Positive margins are described in 4-7% of the procedures and are associated with central tumors or highly complex lesions.[9] Some authors have associated them with local or distant recurrence, especially with adverse factors, such as T3 or nuclear grade III or IV,[10] but the recommendation continues to be strict surveillance.[2,9,11] As in other types of surgeries, the Clavien-Dindo system [12] classifies complications in PN, reported at approximately 14%, and they are associated with preoperative comorbidity, multiple tumors, and larger tumors.[13] The main complications are transfusion, urine leaks, bleeding, and acute kidney injury.[13-15] Knowledge about ischemia was originally obtained from animal models, with a limit of 25 to 30 min for warm ischemia and 60 to 90 min for cold ischemia. However, the quantity and quality of the renal parenchyma has recently been described as having the greater impact on kidney function.[16-17] The current tendency is to not utilize ischemia, resulting in long-term improvement in the GFR and delayed progression to chronic kidney disease.[18]

Since 2000, a delay in the progression to kidney failure has been reported with the performance of PN, compared with RN.[19] A decrease in the incidence of chronic kidney disease [20-21] and in death from a cardiovascular event, as well as improved overall survival, were later established as satisfactory results of PN.[5,22]

The most widely performed approach worldwide is open partial nephrectomy (OPN), but the advent of minimally invasive surgery has brought adequate results through the laparoscopic and robotic-assisted approaches. [23-24] Although it produces excellent results in experienced hands,[25] laparoscopic partial nephrectomy is a technical challenge with a long learning curve and has been associated with prolonged ischemia times. Robotic-assisted partial nephrectomy with the da Vinci system has gained ground, thanks to its three-dimensional vision, ergonomics, and wrist movement, producing results in relation to the trifecta similar to those of open surgery.[26-27]

There are few Mexican studies on the results of PN,[28] therefore the present study reporting the clinical characteristics and perioperative, functional, and oncologic results of the procedure at a high-volume hospital center in Mexico provides an evaluation of our management, with respect to that of international specialized centers.

Materials and methods

A retrospective, descriptive, and analytical study was conducted on 79 patients in whom 82 partial nephrectomies were performed within the time frame of January 2000 and June 2018. The following clinical and perioperative characteristics were collected: age, sex, comorbidities, clinical stage, RENAL nephrometry score, surgical approach, type of procedure performed, type of renal ischemia, renal ischemia time, surgery duration, intraoperative blood loss, transfusion rate, days of hospital stay, early complications classified using the Clavien-Dindo system, and late complications.

The oncologic characteristics collected were: histologic type, nuclear grade, presence of positive margins, recurrence-free survival (RFS), progression-free survival (PFS), cancer-specific survival (CSS), and overall survival (OS). The relation of positive margins, histologic type, and nuclear grade to recurrence and progression was analyzed.

With respect to the functional results, preoperative GFR, postoperative GFR at 3 months, and postoperative GFR at one year were collected. The abbreviated version of the Modification of Diet in Renal Disease (MDRD) equation with the variables of sex, creatinine, race, and age was employed. The role of ischemia in relation to the GFR was analyzed.

The statistical analysis was carried out using the SPSS and GraphPad Prism 7 programs. The qualitative variables were analyzed using the Pearson chi-square test and the quantitative variables were analyzed using the Student's t test and the Mann-Whitney U test.

Results

Seventy-nine patients, 49 men and 30 women, underwent partial nephrectomy, with a mean patient age of 52 years. A total of 82 procedures were performed and there were 3 cases of synchronous tumors. Regarding the indications for PN, almost 30% were elective surgeries, 7% were absolute indications (anatomic or functional solitary kidney), and the rest were relative indications (associated comorbidity). The most common clinical stage was T1a (75%). According to the RENAL nephrometry score, the most common level of complexity (64%) was mild (4-6 points). The most widely used approach was the open procedure (85%), albeit there has been an increase in the laparoscopic approach with no conversions in the last 2 years. The most commonly used surgical procedure was enucleation (73%), followed by partial or wedge resection (22%), predominantly used in the first 17 procedures, and finally polectomy (5%). Ischemia was utilized in 47 (57.3%) interventions and it was not carried out in 35 (42.7%). There was no ischemia in 11 patients (91.7%) that underwent the laparoscopic approach. Mean blood loss was higher in the open approach surgeries, compared with the laparoscopic procedures (409 vs 205 ml) ($p = 0.02$) (Table 1). There were early complications (< 90 days) in 17 (20%) procedures and they included nine transfusions, two urine leaks treated with percutaneous drainage and double-J catheter, one drain retention that required reintervention, one patient with postoperative fever, two patients with ileus, and two urinary tract infections. The late complications were three post-incisional hernias.

The most frequent histology was clear cell renal cell carcinoma (80.5%). Even though, cli-

nically, all the patients that underwent PN had T1a or T1b disease, the histopathologic report stated T2a or T3a in 12.2%. Eleven percent of the patients had positive margins (Table 2). Upon analysis, neither pathologic stage (p = 0.6) nor RENAL score complexity grade (p = 0.5) were factors for the presence of positive margins. There were positive surgical margins in 2 of the LPNs, compared with 7 (10%) of the OPNs, with no statistically significant difference (p = 0.04).

Six patients had local recurrence and RFS was 98% and 89.3% at 12 and 36 months, respectively (Figure 1). Four of those patients had been treated with radical nephrectomy, one with tumorectomy, and one with radiofrequency. None of the patients with local recurrence had a history of positive margins. Five patients presented with disease progression; two to the lung, two to the central nervous system (CNS), and one to the liver. PFS was 96.5% at 2 and 5 years (Figure 2). Another patient presented with progression at the 10th year of follow-up. Nuclear grade was the factor associated with disease progression (two patients had grade 4; p = 0.02).

Six patients died during follow-up. Three of the deaths were from kidney cancer and two of those patients had presented with progression to the SNC. CSS was 100% at 24 and 60 months, 80% at 96 months, and 64.3% at 120 months (Figure 3). The other three deaths were due to kidney failure, second primary cancer (sarcoma), and valvular heart disease. OS was 98, 92, and 53% at 2, 5, and 10 years, respectively (Figure 4).

The functional results of all the PNs were a mean GFR of 88 ml/min, 82 ml/min at three months, and 79 ml/min at one year. Upon comparing clinical stage with the GFR, there were no differences in relation to stage T1a, but there were with clinical stage T1b (preoperative 87 ml/min vs 76 ml/min at one year), albeit with no statistically significant differences (p = 0.4) (Table 3).

In the analysis of ischemia as a factor influencing GFR, the percentage of decrease in GFR in the surgeries with ischemia was greater at months three and twelve, than in the surgeries with no ischemia (Table 4).

Table 1 Clinical characteristics

	n = 82
Age	(SD)
	52 (±12)
Sex	Men: 49
	Women: 30
	(%)
Comorbidities	
None	24 (29.3)
DM2	17 (20.7)
HBP	20 (24.4)
Solitary kidney	6 (7.3)
VHL	4 (4.8)
CKD	2 (2.4)
Heart disease	1 (1.2)
Second cancer	13 (16)
Clinical stage	
T1a	62 (74.6)
T1b	20 (24.4)
Approach	
Open	70 (85.4)
Laparoscopic	12 (14.6)
Conversion	0 (0)
Renal score	
4-6	53 (64.7)
7-9	25 (30.4)
10-12	4 (4.9)

	n = 82
Ischemia	
Warm	39 (47.6%)
Cold	8 (9.8%)
No ischemia	35 (42.7%)
Surgery duration (min)	(SD) 162 (±44)
Ischemia time (min)	
Warm	19 (± 8)
Cold	33 (±18)
Blood loss (ml)	449 (±395)
Open surgery	490 (±406)
Laparoscopic surgery	205 (±189)
Hospital stay (days)	2.1
Transfusion	(%) 9 (11)
Early complications (< 90 days)	
Clavien I	17 (20)
Clavien II	3
Clavien III	11 (9 transfusions) 3
Late complications (> 90 days)	3 (3.6)

SD: standard deviation

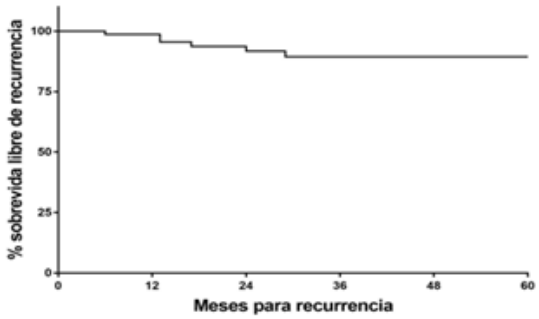

Figura 1: Sobrevida libre de recurrencia.

Table 2 Oncologic results

	(%)
Histology	
Clear cell	66 (80)
*Grade 1	13 (15)
*Grade 2	39 (47)
*Grade 3	9 (11)
*Grade 4	5 (6.1)
Chromophobe	7 (8.5)
Papillary	2 (2.4)
Angiomyolipoma	5 (6.1)
Oncocytoma	2 (2.4)
Pathologic stage	
T1a	53 (64.6)
T1b	19 (23.2)
T2a	5 (6.1)
T3a	5 (6.1)
Positive margins	9 (11)
Laparoscopy	2 (16.7)
Open surgery	7 (10)

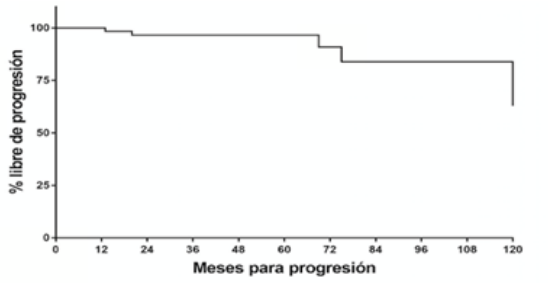

Figura 2: Sobrevida libre de progresión.

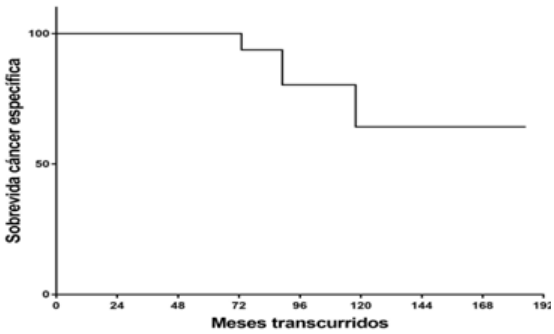

Figura 3: Sobrevida cáncer específica.

Table 3: GFR based on stage

	Partial nephrectomy	*T1a partial nephrectomy*	*T1b partial nephrectomy*
Preoperative GFR	(SD) 88 (± 24)	88.5 (±23)	87(±30)
Postoperative GFR at 3 months	82 (± 22)	82 (±21)	84 (±29)
Postoperative GFR at 1	79(±24)	80 (±26)	76 (±20)

GFR: glomerular filtration rate; SD: standard deviation

Table 4: GFR in PN performed with or without ischemia

	With ischemia (n=47)	*Without ischemia (n=35)*
Preoperative GFR (ml/min)	(SD) 92 (±28)	(SD) 83 (±16)
Postoperative GFR at 3 months (ml/min)	84 (±25)	79 (±18)
Postoperative GFR at 1 year (ml/min)	78 (±29)	79 (±16)
% of change in GFR at 3 months	9 %	5 %
% of change in GFR at 1 year	15%	5%

GFR: glomerular filtration rate; SD: standard deviation

Discussion

Our case series of 82 PNs, albeit small when compared with those published in the international literature, is the largest series reported in Mexico. In the majority of studies, PN was performed on tumors with T1a and T1b clinical stages, coinciding with our study.[1,3] A Mexican study conducted at the *Hospital General* analyzed 18 patients treated with partial nephrectomy. Tumors had a low degree of complexity in 61% of the patients, according to the RENAL nephrometry score,[28] similar to our 64.6%.

Lucas et al. reported blood loss of 250 ml,[29] whereas in our study, mean blood loss was 449 ml. The results of different authors show that blood loss is lower in minimally invasive surgery than in the open procedure.[24,26,30] We also reported that LPN resulted in less blood loss than OPN (205 vs 490 ml). A review of 38,064 PNs described a transfusion rate of 10.6% in OPN, similar to the 11% reported in our study.[31]

Early complications have been reported at 15 to 30.5%,[15,31] and the most frequent are perioperative bleeding, transfusions, acute kidney injury, infection, and urine leaks. Similar early complications in our study were reported at 20%.

Mir et al. carried out a meta-analysis in which warm ischemia time on average was 25 to 30 min.[16] It was 19 min in our study. Numerous authors have shown the feasibility and trend of not utilizing ischemia.[18] That tendency has increased at our hospital center in the last 3 years

(more than 80% of the procedures have been performed with no ischemia since then).

Positive margins vary from 2.5 to 7%, in general.[9,32-33] In our study they were somewhat higher at 11%, and neither pathologic stage (p = 0.6), RENAL score degree of complexity (p = 0.5), or approach (p = 0.4) were factors for the presence of positive margins, most likely because an adequate enucleation technique was employed. Local recurrence factors are thought to be associated with multiple or central tumors, high nuclear grade, and positive margins.[34] Likewise, different authors conclude that intraoperative analysis has no therapeutic purpose and does not predict the margin status reported in the final histopathologic study.[9] The positive margins in our patients were not associated with recurrence (p = 0.2), but the type of nuclear grade was (Fuhrman IV) (p = 0.02). Therefore the recommendation for positive margins is surveillance.[9,11,33]

Weber et al. reported OS of 91 and 73%, CSS of 98%, RFS of 97 and 95%, and PFS of 98 and 96%, at 5 and 10 years, respectively.[19] In our study, OS was 92%, CSS was 100%, RFS was 89.3%, and PFS of 96.5% at 5 years. Simhan et al. reported distant recurrence of 2.1% and a mortality rate of 0.4% at 5 years.[30] In the EORTC study by Van Poppel et al., they showed disease progression of 4.1% at 10 years for PN.[6] In our study, five patients (6.3%) had distant recurrence or progression and three patients (3.8%) died from cancer, but at 10 years of follow-up, resulting in oncologic results similar to those at other experienced centers.

Finally, different studies and meta-analyses concur that PN offers better postoperative GFR preservation than RN.[19-20] Andrade et al. reported GFR preservation in 87.8% of 115 PNs.[8] In our study, the decrease in the mean GFR was minimal at 3 and 12 months, with a larger decrease in stage T1b tumors, probably due to greater loss of the renal parenchyma. Different authors have shown that not using ischemia or having an ischemia time under 20 min influences postoperative kidney function.[18,35] In our study, in the patients whose procedures included ischemia, the percentage of decrease in the GFR was higher than in the patients in whom ischemia was not carried out (15% vs 5% at one year, respectively).

The weaknesses of our study were the small number of patients analyzed and its retrospective design.

Conclusions

The results of the present study were comparable to those reported in the international literature. We observed that good perioperative management directly influenced adequate functional and oncologic control. The current trend at the *INCan*, and internationally, is to perform PN, preferably with no ischemia use and utilizing minimally invasive techniques, in all T1 tumors and some T2a lesions, when technically feasible, without compromising the oncologic result or increasing complications. Based on our study, we propose that future prospective analyses be conducted, to improve the management and results in patients that are candidates for PN.

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