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Original article

Laparoscopic enucleation of renal masses

Enucleación laparoscópica de masas renales

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Abstract

Introduction: Tumor Enucleation (TE) of renal masses as an alternative of nephron-sparing surgery has increased in the past years.
Objectives: To describe the perioperative, oncological and functional outcomes of laparoscopic TE in a series of patients with renal masses.
Material and method: A descriptive and retrospective study of 71 patients who underwent laparoscopic TE surgery for renal mass in La Habana, Cuba at the Centro Nacional de Cirugía de Mínimo Acceso, between 2010 and 2019. Clinical-epidemiological and perioperative variables, complications, Clavien-Dindo grade and oncological variables were considered. The SPSS program, version 23.0 was utilized. Frequencies, mean percentages, standard deviation and Student´s t- test ($p<0.05$) were estimated. Survival was appraised by using the Kaplan Meier curve.
Results: Mean age was 58 years. Male patients prevailed (60.6%), with comorbidities (87.3%), incidental diagnosis (73.2%), low complexity tumors (64.8%). Mean tumor size and RENAL score was 33.6 mm and 6.1, respectively. Hand-assisted transperitoneal approach was performed (92.9%), mean bleeding was 335.9 ml and length of hospital stay 5.2 days. Postoperative renal function was preserved ($p=0.082$). Postoperative complications prevailed (14.1%), bleeding (8.4%) and grade II and IV (4.2%, respectively). Most masses were malignant (71.8%), ccRC prevailed (52.1%), pT1a (78.4%), overall survival and cancer specific survival was 100% and 96.0%, respectively. Mean follow-up time was 7.4 years.
Conclusions: Laparoscopic TE is a feasible alternative for treating select renal masses, with satisfactory perioperative, oncological and functional outcomes.

Keywords:
Kidney neoplasms, nephrectomy, laparoscopy, perioperative period

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Resumen

Introducción: La enucleación tumoral (ET) de las masas renales como alternativa de cirugía conservadora de nefronas se ha incrementado en los últimos años.
Objetivos: Describir los resultados perioperatorios, oncológicos y funcionales de la ET laparoscópica en una serie de pacientes con masas renales.
Material y método: Estudio descriptivo y retrospectivo en 71 pacientes operados de ET laparoscópica por masa renal, en el Centro Nacional de Cirugía de Mínimo Acceso, La Habana, 2010-2019. Se consideraron variables clínicas-epidemiológicas, perioperatorias, las complicaciones, grado Clavien-Dindo y variables oncológicas. Se empleó el programa SPSS versión 23.0. Se calcularon frecuencias, porcentajes medias, desviación estándar y el t student ($p<0.05$). Para la supervivencia se empleó curva de Kaplan Meier.
Resultados: la edad media fue 58 años. Predominaron los pacientes masculinos (60.6%), con comorbilidades (87.3%), el diagnóstico incidental (73.2%), los tumores de baja complejidad (64.8%). La media del tamaño tumoral y del RENAL score fue 33.6 mm y 6.1, respectivamente. Se empleó abordaje transperitoneal con mano-asistencia en (92.9%), el sangrado medio fue 335.9 ml y la estancia 5.2 días. La función renal postoperatoria se conservó ($p=0.082$). Predominaron las complicaciones postoperatorias (14.1%) y el sangrado (8.4%) y las grado II y IV (4.2%, respectivamente). La mayoría de las masas fueron malignas (71.8%), predominó el CRcc (52.1%), los pT1a (78.4%), la supervivencia global fue 100% y CE 96,0%. El tiempo medio de seguimiento de 7.4 años.
Conclusiones: La ET laparoscópica es una alternativa de tratamiento factible para el tratamiento de masas renales seleccionadas, con resultados perioperatorios, oncológicos y funcionales satisfactorios.

Palabras clave: Cáncer renal, nefrectomía, laparoscopia, período perioperatorio

Introduction

Renal carcinoma (RC) represents 2% of the diagnoses and deaths from malignant tumors in adults. This incidence has increased in the past years. Approximately 75% are diagnosed in patients over 60 years of age and are more frequent in males.[1,2]

The classic treatment for renal masses regardless their size, consisting of removing the complete organ, has progressively changed since 1980 when partial nephrectomy (PN) began to show excellent results as far as survival and recurrence, particularly in ≤4 cm tumors, but indicated even for ≥7 cm tumors.[3]

Compared to radical nephrectomy (RN), PN is associated with a marked reduction of the incidence of chronic kidney disease (CKD) and

the frequency of cardiovascular episodes related to renal damage. RN could accelerate the loss of kidney function, affect the quality of life and lead to death, particularly in the elderly, who could also suffer from other diseases that lead to CKD.[4,5]

These are the reasons why, nowadays, nephron-sparing surgery (NSS) is the standard treatment for stage cT1 renal tumors, provided that it is technically possible; the indications for NSS have been extended even to stage cT2.[4,6]

When NSS emerged, the prevailing criterion was that the resection of the tumor should be performed with a wide margin of normal renal parenchyma to minimize the risk of local recurrences. This criterion has changed because some investigations showed that the extension of the negative free margin did not correlate with the progression of the disease, therefore the consensus that a minimum amount of normal renal parenchyma as surgical margin is enough to ensure a good outcome, thus the increase of tumor enucleation (TE) as an NSS variant.[6]

Some studies have shown that short-term oncological outcomes for TE are similar to those for PN and RN but more evidence is required for long-term outcomes, as well as preoperative results; studies are still scarce particularly when analyzing the laparoscopic approach.[7]

Objective

To describe perioperative, oncological and functional outcomes of laparoscopic TE in a series of patients with renal masses.

Material and method

A descriptive and retrospective study of a series of 71 patients was carried out. They underwent TE for renal mass by laparoscopic approach; all the surgeries were performed by the same surgeon in Cuba at the *Centro Nacional de Cirugía de Mínimo Acceso*, (NCMIS) La Habana between 2010 and 2019.

The patients were assessed preoperatively with CBC, Creatinine, Total Protein, Albumin, Glycaemia, Liver Function Tests (Serum Glutamic-Oxalo-Acetic Transaminase-Serum Glutamic Pyruvic Transaminase-Alkaline Phosphatase), Coagulogram. Abdominal Ultrasound and Contrast CT scan of the abdomen and thorax were also ordered. MRI was exceptionally performed to define diagnosis.

Surgical Technique: tumoral enucleation was performed by Hand-assisted Transperitoneal Laparoscopic approach or by Laparoscopic Retroperitoneal approach.

Variables

Clinical-epidemiological variables were considered (age, gender, comorbidities, ASA, type of diagnosis, tumor size, RENAL score, preoperative creatinine, clinical stage of the tumor); perioperative (bleeding, surgical time, use of warm ischemia and warm ischemia time, conversion to open surgery, reintervention, complications, and their severity according to the Clavien-Dindo Classification), oncological (histology, pathological stage of the tumor, overall survival and cancer specific survival, follow-up time).

Statistical Analysis

The SPSS program, version 23.0 was utilized. Frequencies and percentages were estimated for qualitative variables; means and SD for quantitative variables. Student´s t-test was used to compare pre and postoperative creatinine ($p<0.05$), and the Kaplan Meier curve for survival.

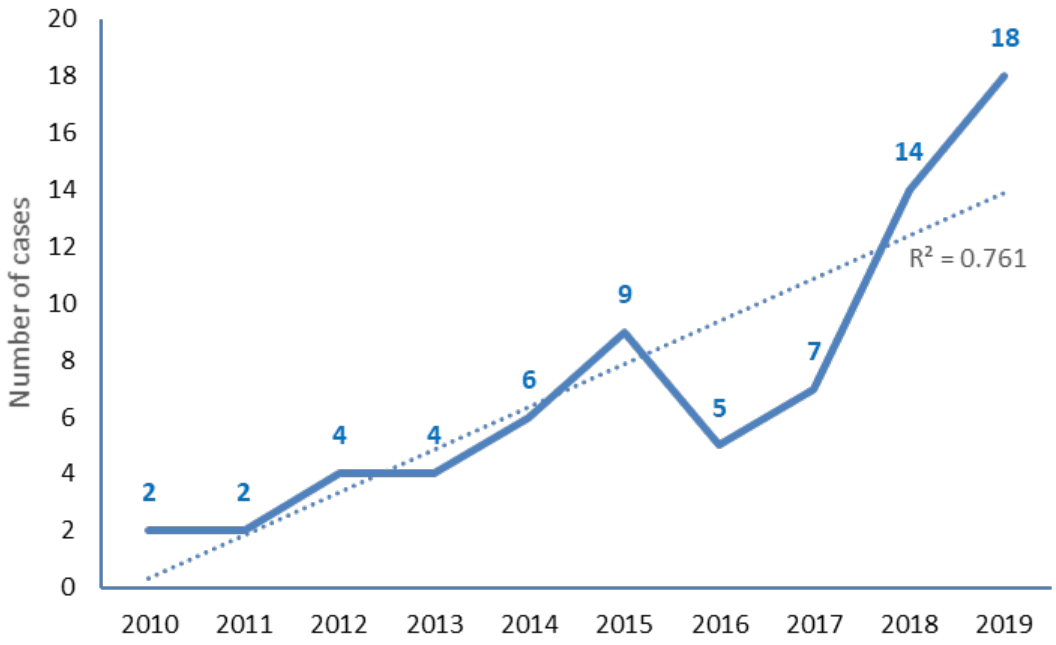
Ethical Considerations

This research is part of a Project approved by the NCMIS Institution Review Board and Ethical Review Board. The ethical principles of the Declaration of Helsinki for Medical Research with human beings were followed.[8]

Results

Laparoscopic TE has increased since it was introduced at the NCMIS, in 2010 (Figure 1).

Figure 1. Distribution of laparoscopic tumor enucleation per year



Mean age was 58.0 years (±11.1 years). Most were male patients (60.0%). 73.2% of renal masses were diagnosed incidentally. Physical status classification ASA II and ECOG 0 or I were the most frequent (69.0%, 54.9%, 42.3%, respectively). 87.3% of the patients had comorbidities; arterial

hypertension was the most frequent. Mean tumor size was 33.6 mm. cT1a clinical stage, in correspondence with renal masses ≤4 cm and most masses were of low surgical complexity (64.8%). Mean R.E.N.A.L score was 6.1 (Table 1).

Table 1. Characteristics of the patients in the series

Variables	Results	
	Mean	SD
Age (years)	58.0	±11.1
Tumor size (mm)	33.6	±12.07
R.E.N.A.L. score	6.1	±1.9
Preoperative Creatinine (mmol/L)	92.4	±20.8
	No.	%
Males	43	60.6
Comorbidities	62	87.3
ASA II	49	69.0
ECOG 0/I	39/30	54.9/42.3
Incidental Diagnosis	52	73.2
Surgical Complexity (low/moderate)	46/16	64.8/22.5
cT1a/cT1b N0 M0	46/23	64.8/32.4

Hand-assisted laparoscopic approach without warm ischemia (WI) was used in most patients (92.9%), one required conversion to open surgery and 5.6% needed surgical reintervention, which was performed by laparoscopic surgery. Other perioperative outcomes are presented in Table 2.

Table 2. Perioperative outcomes of laparoscopic tumor enucleation

Variables	Mean /Range	SD
Transoperative Bleeding (ml)	335.9/0-1200	±287.9
Operative Time (min)	163.3/90-320	±44.3
Warm Ischemia Time (min)	22.3/10-46	±9.2
Length of hospital stay (day)	5.2 /2-21	±3.6
Postoperative creatinine (mmol/L)	97.7	28.0
Variables	**No.**	**%**
Hand-Assisted transperitoneal approach	66	92.9
Lumboscopic approach	5	7.0
Warm ischemia	17	23.9
Conversion to open surgery	1	1.4
Reintervention	4	5.6

Six patients had renal function damage estimated by their preoperative level of creatinine and increased to seven postoperatively (measure at the end of the study). Mean postoperative creatinine was 97.6 mmol/l vs 92.4 mmol/l preoperatively, but this difference was not statistically significant (p=0.082) (Table 3).

Table 3. Pre and postoperative creatinine

Creatinine		Postoperative					
		Elevated		Normal		Total	
		No.	%	No.	%	No.	%
Preop	Elevated	3	50.0	3	50.0	**6**	100
	Normal	4	6.2	61	93.8	**65**	100
Total		**7**	**9.9**	**64**	**90.1**	**71**	100
Perioperative		**Mean**	**SD**	**Difference**		**t**	**p**
Preoperative		92.4	20.8	-5.2		-1.776	0.082
Postoperative		97.6	28.0				

16% of the patients presented complications, most postoperatively (14.0%). Bleeding prevailed (8.4%), resolved with medical measures in two patients (grade II); two others required laparoscopic exploration (one underwent RN, also by laparoscopy) and admittance in the intensive care unit (grade IV); and in two others that presented vascular lesions (a pseudoaneurysm and an arteriovenous fistula), the solution was selective arterial renal embolization (SRAE) (grade IIIb). One patient required laparoscopic exploration for prolonged paralytic ileus and was also admitted in the intensive care unit (grade IV). Reintervention was performed in an obese patient for eventration at the hand-assistance port (grade IIIb) (Table 4).

Table 4. Complications and severity of Laparoscopic Tumor Enucleation

Variables	No.	%
Complications		
• Transoperative	1	1.4
• Postoperative	10	14.1
Subtotal	11	16.0
Postoperative Complications /Treatment		
Bleeding	6	8.4
• Hemoperitoneum/ transfusion	2	2.8
• Hemoperitoneum/laparoscopic exploration	2	2.8
• PA or AVF/ SRAE	2	2.8
Paralytic Ileus	1	1.4
Related to the hand-assistance wound	3	4.2
Subtotal	10	14.0
Severity (Clavien-Dindo) of Postoperative Complications		
Grade I	1	1.4
Grade II	3	4.2
Grade IIIa	2	2.8
Grade IIIb	1	1.4
Grade IV	3	4.2

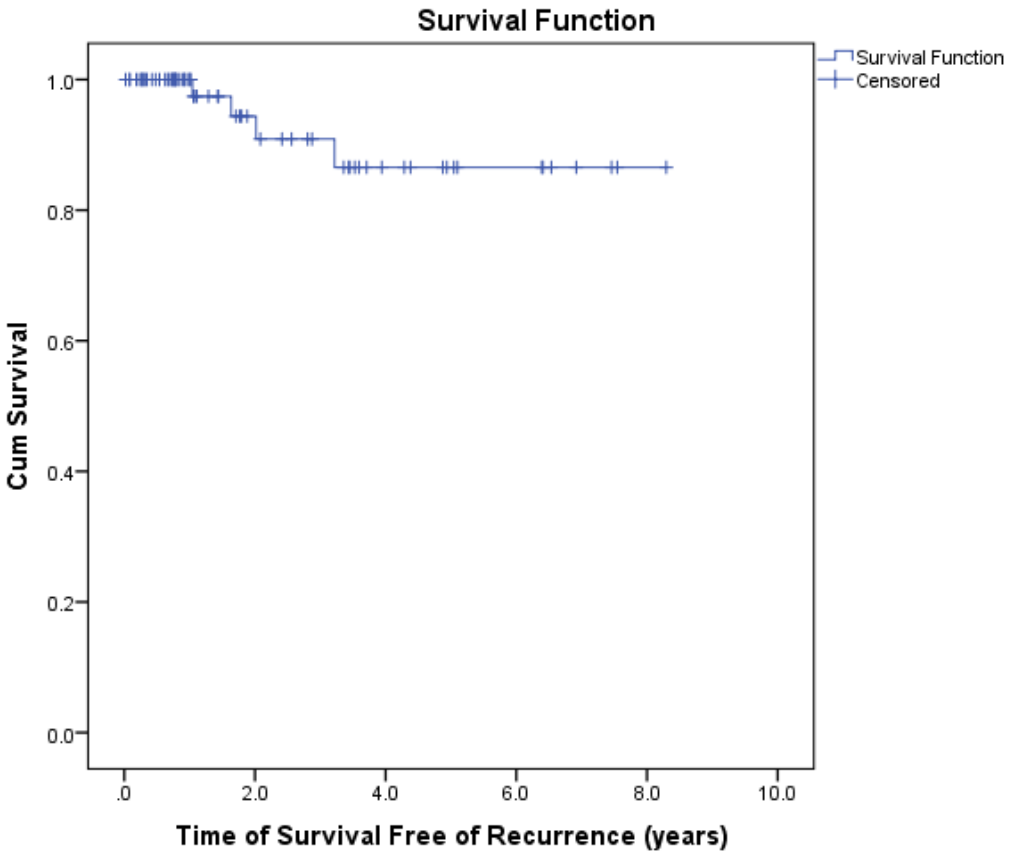
Malignant tumors were more frequent (71.8%) and 52.1% classified as clear-cell renal carcinoma (ccCR). Stage pT1a prevailed (74.8%); overall survival (OS) and cancer specific survival (CSS) at one year was 100%, respectively, and CSS decreased at five years because two patients recurred with malignant tumors in the same renal unit. They underwent RN by the laparoscopic approach. Mean time follow-up was 7.4 years (Table 5 and Figure 2).

Table 5. Oncological outcomes of laparoscopic tumor Enucleation

Variables	No.	%
Histology		
Benign Masses		
• Oncocytoma	10	14.2
• Angiomyolipoma	4	5.6
• Complex Cyst	4	5.6
• Others	2	2.8
Subtotal	**20**	**28.2**
Malignant Masses		
• Chromophobe Carcinoma	3	4.2
• Papillary Carcinoma	11	15.5
• Clear Cells Carcinoma	37	52.1
Subtotal	51	71.8
Tumor Stage*		
• pT1a/pT1b/pT2a	40/10/1	78.4/19.6/1.9
Overall Survival and Cancer Specific Survival*	51	100
Recurrence-free Survival 1/5 years*	51/49	100/96.07
Positive Surgical Margins	0	0
Mean time follow-up: 7.4 years (Standard Error 0.5)		

*Calculation was made considering 51 malignant masses.

Figure 2. Free-recurrence survival at 5 years. Laparoscopic tumor enucleation



Discussion

TE has gained acceptance due to its perioperative and oncological outcomes, as well as less potential risk of postoperative CKD, with the benefits this implies for the cardiovascular system and OS.[6,9]

As shown in Figure 1, TE by laparoscopic approach has increased at the National Reference Center for the development of laparoscopic surgery in Cuba, since it was introduced. Small renal tumoral lesions are currently approached differently: by open surgery, transperitoneal and retroperitoneal laparoscopy, hand-assisted or robot-assisted laparoscopy. Open surgery is the most utilized in Cuba for TE.[6]

Laparoscopic TE is a complex technique, even in experienced hands. It is a rather limited procedure and most urologists will not have enough cases to gain the required experience. The challenge of the laparoscopic approach is to excise the tumor within a limited ischemia time, followed by hemostatic renorrhaphy under restricted movements with laparoscopic instruments.[10]

The authors of this investigation have utilized hand-assistance with the intention of solving this difficulty and to guarantee hemosta-

sis at the expense of manual compression of the renal parenchyma, in those operated on by the transperitoneal approach without WI. Those who underwent the retroperitoneal approach, without hand-assistance, were strictly selected (when the tumor was posterior, located towards the lower pole, predominantly exophytic); however, the impossibility of controlling the bleeding quickly in a patient operated on by this approach, resulted in the conversion to open surgery reported in this series.

The transperitoneal approach is considered having the advantages of greater workspace, greater instrument maneuverability and better anatomical orientation, which is one of the disadvantages of the retroperitoneal approach. The advantages described in this approach are more direct access to the kidney and the renal hilum which avoids the need of mobilizing the intestine. As other authors, we choose the retroperitoneal approach for TE when the mass is posterior, postmedial or postlateral and also predominantly exophytic and small to achieve its enucleation successfully without utilizing WI. This approach is also recommended for patients with previous abdominal surgery, although no significant differences have been found in the percentage of complications and conversion to open surgery, when they are approached transperitoneally.[11]

Nevertheless, the study carried out by Porpiglia et al. reports not having found any differences between the transperitoneal and retroperitoneal approaches when PN is performed regardless tumor location and surgical complexity.[12]

There are two main aspects to keep in mind when assessing the surgical complexity of PN: the size of the tumor mass and the proportion of the endophytic component. In view of the growing need to measure the complexity of renal masses objectively, the R.E.N.A.L nephrometric system is one of the most widely used because it is an excellent tool to predict if the minimally invasive approach is safe as well as the kind of nephrectomy required.[13,14]

Studies on laparoscopic PN have reported a prevalence of low-complexity tumors, as in this series. In a study of small renal masses, Konstantinidis et al.[15] found a mean R.E.N.A.L score of 5.6±1.52. Dong et al.[7] reported a mean size of 3.4cm and a R.E.N.A.L score of 7 (moderate complexity) in their series of laparoscopic TE in 108 patients. Nevertheless, the experience of the team in this type of surgery also plays an important role in the surgical decision.

The indication for PN has moved from imperative, when in presence of a solitary functional or anatomical kidney, and relative, when the patient has a sick contralateral renal unit (lithiasis, chronic pyelonephritis or with diseases that affect renal function and hereditary tumors), to elective, which currently prevails and was the indication for the patients in this series. Today, PN is recognized as the gold standard according to the clinical guidelines for T1a-T1b exophytic renal masses with the aim to preserve more renal function.[6]

Most laparoscopic TE reports use WI, being the reason for reporting less bleeding than in this series, which was only utilized in 23.9% of the patients, as Tsivian et al.[16] who reported a blood loss of 125 ml while Rinott et al.[17] reported 100 ml.

Other researchers suggest that TE does not increase complications and is safe when dealing with small renal masses, despite absence of hilar control. The oncological outcome is similar to that of standard on-clamp PN and the outcome of renal function is better.[18,19]

Off-clamp simple enucleation of renal masses is feasible by laparoscopic approach and has produced comparable oncological outcomes with standard on-clamp partial nephrectomy, with an incremental advantage for the preservation of renal function.

In a meta-analysis that included 13 studies and 1 796 patients who underwent laparoscopic TE, when compared to PN showed significantly less operative time, length of hospital stay, blood loss, diminished eGFR and less complications in the TE group. There were no significant differences between TE and PN regarding ischemia time, positive margins, recurrence and survival.[20]

Postoperative renal function (RF) was assessed in the investigation by creatinine and the postoperative outcomes were satisfactory, as in other investigations, and there was no significant decrease of postoperative creatinine values. Blackwell et al.[21] did not observe statistically significant differences in a study where they compare RF between TE and PN, but it was better for TE. In one study, mean eGFR was preserved in 93% of the patients at one year, and in another which compared RN with PN mean postoperative eGFR was significantly higher for PN.[7,17]

Urological complications have been described in PN, which are, in general, persistent hematuria, hemorrhage, renal vascular damage, urinary loss, renal failure and infection (urinary infection, perirenal abscess and sepsis). It is considered that they occur in 23% of the patients and approximately 1/3 is Clavien grade I–II.[22]

Rinott et al.[17] reported 23% minor complications (Clavien-Dindo ≤III) and Zhao et al.[10] reported 1.4% major complications (grade IIIb) in 108 patients, whereas in another study there were five major complications, grade IIIa and only two related to the urinary tract. In this series, 6 (8.4%) patients presented major complications (≥grade III). Minervini et al.[23] confirmed similar results, as this investigation, with 8.9% complications.

The complications of laparoscopic PN are potentially serious, among them renal parenchyma bleeding, with an incidence between 1% and 2%, being more frequent postoperatively. Arterial pseudo aneurysm and fistulas of the arteriovenous system are, frequently, the cause of bleeding and their incidence is between 3% and 10%. The bleeding can spread to the retroperitoneal space or the collecting system, conditioning the appearance of a retroperitoneal hematoma and/or hematuria. They can be treated conservatively and require blood transfusions, but SRAE is the treatment of choice for hemodynamically stable patients, with good outcomes controlling the hemorrhage and preserving most of the renal parenchyma viable. In the study, three patients were treated conservatively and only required blood transfusion; two others needed SRAE due to the presence of an arteriovenous fistula and an arterial pseudo aneurysm, respectively. Occasionally, surgical reintervention for the suturing of the renal parenchyma or nephrectomy will be required, as occurred in one of the patients of the series.[24,25]

Less complications have been reported when comparing PN to TE which is why it is recommended for treating localized tumors even for complex renal masses.[26]

Other authors in TE studies have reported a similar behavior regarding the histological classification of the tumors: ccCR prevailed, followed by papillary and chromophobe carcinoma. They also found a prevalence of pT1a tumors (64.4%) and 31.5% pT1b, as well as

very low pT2 percentage, and unlike the results of the series, one pT3 was reported. They also coincide with tumor recurrence in two patients.[23]

The patients in the series developed recurrences after the first year, one at the first tumor bed and another patient developed multifocal tumors in the same renal unit, similar to what Minervi et al.[23] reported in two patients with recurrence. When robot-assisted and laparoscopic TE were compared, no differences were found regarding recurrence.[10]

Positive surgical margins (PSM) is one of the issues still discussed regarding TE because the PSM rate is significantly higher when compared to PN, although it has not been demonstrated that this phenomenon corresponds with a significant increase of recurrence.[26,27]

Nevertheless, a recent systematic review did not find significant differences between both techniques regarding occurrence of PSM.[28]

No positive margins were reported in this series unlike other authors. Minervi et al.[23] reported positive surgical margins in 3 (2.4%). The existence of a pseudocapsule in every patient of the present series contributed to these outcomes, as other researchers believe. TE has not shown an increase in recurrence nor mortality either, when compared with PN.[7,17,20]

The oncological outcomes obtained were satisfactory and similar to those published in medical literature. 95.7% CSS has been reported, 89.6% recurrence-free survival and 91.9% OS at 5 years. In another study CSS was 95.9% and OS 92.5%, in a 62-month mean-follow-up. Another investigation only reported one recurrence after a 44.5-month follow-up.[17,23]

A recent multi-center study which assessed the impact of tumoral resection techniques found that the laparoscopic approach VS the robotic approach and enucleoressection VS enucleation were predictors of complications higher than Clavien-Dindo grade II, ischemia time and trifecta (negative surgical margins, no perioperative grade II Clavien-Dindo, greater surgical complications and no postoperative acute kidney injury) were predictors of acute post-operative renal damage.[29]

TE is a safe and effective technique for treating T1 tumors and the short-term oncological outcomes are acceptable, although Dong W et.al. confirm these results after a follow-up of more than five years.[7]

Conclusions

Laparoscopic TE is a feasible surgical alternative for select renal masses, with satisfactory perioperative, oncological and functional outcomes. Most complications were postoperative, grade II or IIIb and related with bleeding. The patients with complications had a significantly higher ECOG and these were related with the increase of tumor diameter size, higher R.E.N.A.L. score, longer operative time and bleeding, but these differences were not significant. Malignant tumors and clear-cell renal carcinoma, pT1 masses prevailed, and an elevated overall and cancer-specific survival were confirmed.

Taxonomy CRediT

Tania González León, MD: conceptualization, data organization, formal analysis, investigation, methodology, supervision, validation, writing

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investigation, data organization, formal analysis
Anet López Chacón, MD: data organization, formal analysis, methodology
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Conflict of interest

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