



## Oncologic outcomes in patients treated with endoscopic robot assisted simple enucleation (ERASE) for renal cell carcinoma: Results from a tertiary referral center

Andrea Mari <sup>a,1</sup>, Fabrizio Di Maida <sup>a,1</sup>, Riccardo Tellini <sup>a</sup>, Riccardo Campi <sup>a</sup>, Simone Sforza <sup>a</sup>, Andrea Cocci <sup>a</sup>, Giampaolo Siena <sup>a</sup>, Gianni Vittori <sup>a</sup>, Agostino Tuccio <sup>a</sup>, Lorenzo Masieri <sup>a</sup>, Alberto Lapini <sup>a</sup>, Maria Rosaria Raspollini <sup>b</sup>, Marco Carini <sup>a</sup>, Andrea Minervini <sup>a,\*</sup>

<sup>a</sup> Department of Urology, University of Florence, Unit of Oncologic Minimally-Invasive Urology and Andrology, Careggi Hospital, Florence, Italy

<sup>b</sup> Histopathology and Molecular Diagnostics, University Hospital Careggi, Florence, Italy

### ARTICLE INFO

#### Article history:

Received 20 January 2019

Received in revised form

22 March 2019

Accepted 30 March 2019

Available online 4 April 2019

#### Keywords:

Partial nephrectomy

Simple enucleation

Renal cell carcinoma

Recurrence

Robotics

### ABSTRACT

**Introduction:** Open Simple Enucleation (OSE) has been demonstrated to be an oncologically safe alternative to standard partial nephrectomy. We assessed the mid-term oncologic outcomes and predictors of disease recurrence in patients treated with Endoscopic Robot-Assisted Simple Enucleation (ERASE) verified through a standardized reporting system at a single institution.

**Material and methods:** The clinical data of patients treated with ERASE for renal cell carcinoma at our Institution from January 2012 to September 2018 were retrospectively reviewed. Surface-Intermediate-Base (SIB) score was evaluated immediately after surgery. Patients with a  $\geq 2$  SIB score were excluded. The local and distant recurrence rates, the recurrence-free (RFS), cancer-specific (CSS) and overall (OS) survival were assessed. Kaplan-Meier and log-rank test were used to estimate survivals and to compare recurrence-free survival.

**Results:** Overall, 259 patients were considered eligible for the present study. The median PADUA score was 7 (interquartile range [IQR] 6–9). Positive surgical margins (PSM) were registered in 7 (2.7%) cases. Median (IQR) follow-up time was 36 (27–51) months. Overall, 4 (1.5%) patients experienced systemic recurrence (SR) and 5 (1.9%) patients experienced local recurrence alone (LR) of whom 3 (1.1%) were on tumor resection bed, and 2 (0.8%) experienced recurrence elsewhere in the ipsilateral kidney. The 5-year RFS, CSS and OS were 94.2%, 98.9% and 93.6%, respectively. Higher nucleolar grade and PSM were the two factors significantly associated with worse RFS.

**Conclusions:** ERASE is a safe procedure, achieving negative surgical margins in the vast majority of patients and providing excellent mid-term local control and oncologic outcomes.

© 2019 Elsevier Ltd, BASO ~ The Association for Cancer Surgery, and the European Society of Surgical Oncology. All rights reserved.

### Introduction

Partial nephrectomy (PN) is widely recognized as the standard treatment for the management of T1a and T1b renal cell carcinoma (RCC). In fact, PN demonstrated oncologic outcomes comparable to radical nephrectomy with the potential benefit of renal function

preservation [1,2].

Over the past years, simple enucleation (SE) has received a wider consensus as an alternative to standard PN. Particularly, SE has proven to be a feasible and safe procedure even for the treatment of highly-complex renal masses with excellent perioperative functional and oncologic outcomes [3]. Recently, two meta-analyses showed that SE seems to be at least non-inferior to standard PN in terms of positive surgical margins (PSM) and disease recurrence [4,5]. Nevertheless, available evidence on SE is mainly based on open series, making it difficult to directly translate such evidence to the robotic scenario. Due to the increasing use of robotic approach in PN, and to the differences of the technique itself

\* Corresponding author. Department of Urology, University of Florence, Careggi Hospital, Florence, Italy.

E-mail address: [andreamine@libero.it](mailto:andreamine@libero.it) (A. Minervini).

<sup>1</sup> Andrea Mari and Fabrizio di Maida equally contributed to this manuscript and fully share first authorship.

carried on with the open and the robotic approach, the assessment of the oncological outcomes of robotic SE is currently a research priority.

To this regard, we analyzed the prospectively collected data of consecutive patients treated with Endoscopic Robotic-Assisted Simple Enucleation (ERASE) verified through a standardized reporting system at a single tertiary high-volume center. The main endpoints of the study were 1) to evaluate the local and distant recurrence rates, the recurrence-free (RFS), cancer-specific (CSS) and overall (OS) survival at mid-term follow-up; and 2) to appraise any potential association between tumor-related characteristics and disease recurrence.

## Materials and methods

### Patients and dataset

After the obtainment of the institutional review board approval, we retrospectively reviewed the clinical data of 1078 consecutive patients treated with PN for localized RCC (cT1-2N0M0) from January 2012 to September 2018. All patients were examined with abdomen and chest contrast enhanced multiphase computed tomography (CT) or magnetic resonance imaging (MRI) for preoperative staging purposes, according to current guidelines [1]. All patients were scored according to the Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) classification of renal tumors [6]. Tumor stage was classified according to the 2010 TNM criteria [7] and nucleolar grading according to the most recent International Society of Urological Pathology (ISUP) grading recommendation by an expert uropathologist (M.R.R.) [8]. Histopathology was reviewed according to the WHO 2016 classification [9]. The presence of ink at the resected margins on gross assessment, confirmed by microscopic extension of malignant cells at the stained margins on final histopathological examination, was reported as a PSM.

### SIB score assignment

The type of surgical resection technique (RT) was prospectively assigned in the operating theatre on the pathologic specimen according to the Surface-Intermediate-Base (SIB) score [10,11] as part of an internal audit until 2014, when SIB score was firstly published by our team, and then as part of our standard research protocol.

For SIB score assignment, the intrarenal portion of the specimen was divided into 3 approximately equivalent circumferential macro areas (SIB score specific areas) (SSAs), defined as the macroscopically thinner zones of each macro area [10,11]. Then a visual analysis of each SSA was made by the surgeon to determine which of the 3 definitions of resection techniques proposed by the SIB model (enucleation, enucleoresection, resection) was the most appropriate to define the resection technique performed in that SSA. In detail, the term resection was used to designate removal of the tumor with a substantial margin in which the contour of the tumor could not be visualised through the resected parenchyma. Enucleoresection was assigned in case of a minimal margin ( $\geq 1$  mm) of normal parenchyma that allowed for clear visualization of the tumor contours. Enucleation was assigned to those cases in which only a tumoral pseudocapsule was visualised, without resection of surrounding tissue (margins less than approximately 1 mm).

Then the score was outlined by assigning 0, 1 or 2 points to each SSA depending on the RT appointed to that area. Finally, the overall RT was classified as pure enucleation (SIB score 0–1), hybrid enucleation (SIB score 2), pure enucleoresection (SIB score 3), hybrid enucleoresection (SIB score 4) or resection (SIB score 5) according to the SIB classification system [10].

### Exclusion criteria

Patients who had a SIB score  $\geq 2$  (not simple enucleation) at the visual examination ( $n = 257$ ), patients with a histologically-confirmed benign renal tumor ( $n = 189$ ), patients with clinically evident lymph nodal involvement (cN+) or metastases (cM+) ( $n = 7$ ), and with an oncologic follow-up lower than 24 months ( $n = 364$ ) were excluded for the final analyses.

### Surgical technique

The Da Vinci Si system was used in all the cases, (Intuitive Surgical, Sunnyvale, CA, USA), in a three-arm configuration with a 30° laparoscope. ERASE surgical technique has been previously described [12]. In brief, once the tumor template has been marked with monopolar cautery, the natural relatively avascular anatomic enucleation plane is developed by blunt dissection using circumferential, dynamic tractions with the two robotic arms that lift the tumor off the parenchymal bed; as such, the intent is to preserve as much vascularized renal tissue as possible by avoiding removal of macroscopic healthy renal tissue.

### Follow-up

Follow-up schedule included blood analysis, chest X-ray and ultrasonography of the abdomen followed by the alternating use of CT scan performed every 4 months from the first to the second postoperative year, every six months until the fifth postoperative year and then annually according to the risk profile, as postulated by the European Association of Urology (EAU) guidelines [1].

### Outcomes

Three outcomes were investigated in this study: the RFS, the CSS and the OS. Survivals were estimated using the Kaplan-Meier method, in which patients free from recurrence, dead of disease or dead from any cause, respectively, were censored at the date of their last follow-up. Disease recurrence was dichotomized in local (LR) and systemic (SR) recurrence. LR was exclusively defined as a recurrence localized in the tumor enucleation bed or a relapse in the same portion of the ipsilateral kidney. SR was defined as any other recurrence away from the ipsilateral kidney, including the ipsi- or contralateral retroperitoneal lymph nodes, the contralateral kidney or distant organs. Disease recurrence was reported in case of new lesions demonstrated by imaging and a definitive histopathological confirmation through a biopsy or the surgical removal of the recurrence according to the pattern of disease.

### Statistical analysis

For statistical purposes, independent variables included all patient- and tumor-related data available in our institutional RCC database. First, descriptive statistics were obtained reporting medians (and interquartile ranges, IQR) for continuous variables, and frequencies and proportions for categorical variables, as appropriate. The probability of survival was assessed by the Kaplan-Meier method, with the log-rank test (Mantel-Cox) used to estimate differences among levels of the analyzed variables. Statistical analyses were performed using SPSS v. 24 (IBM SPSS Statistics for Mac, Armonk, NY, IBM Corp). All tests were two-sided with a significance set at  $p < 0.05$ .

## Results

Overall, 259 patients were considered eligible for the present

**Table 1**

Preoperative features of 259 patients treated with Endoscopic Robot Assisted Simple Enucleation (ERASE) for localized renal cell carcinoma.

Preoperative features			
<b>Gender</b> , n. (%)	Male	159 (61.4%)	
	Female	100 (38.6%)	
<b>Age</b> , median (IQR)		62 (55–71)	
<b>BMI</b> , median (IQR)		26.1 (23.8–28.4)	
<b>ECOG</b> , n. (%)	0	199 (76.8%)	
	≥1	60 (23.2%)	
<b>ASA score</b> , n. (%)	0–2	229 (88.4%)	
	≥3	30 (11.6%)	
<b>Charlson Comorbidity Index</b> , n. (%)	0	130 (50.2%)	
	1	71 (27.4%)	
	2	34 (13.1%)	
	3	14 (5.4%)	
	>3	10 (3.9%)	
		1 (1–2)	
<b>Charlson Score</b> , median (IQR)			
	<b>Indication</b> , n. (%)	Elective	231 (89.2%)
		Relative	22 (8.5%)
<b>Tumor side</b> , n. (%)		Absolute	6 (2.3%)
		Right	146 (56.4%)
		Left	113 (43.6%)
<b>Clinical diameter</b> (cm), mean (SD)		2.72 (±1.9)	
<b>Clinical T</b> , n. (%)	cT1a	192 (74.1%)	
	cT1b	61 (23.6%)	
	cT2a	6 (2.3%)	
		7 (6–8)	
<b>PADUA score</b> , median (IQR)		7 (6–8)	
<b>PADUA score complexity</b> , n. (%) (PADUA score)	6–7 (low)	160 (61.8%)	
	8–9 (medium)	69 (26.6%)	
	≥10 (high)	30 (11.6%)	
<b>Preoperative haemoglobin</b> (mg/dL), mean (SD)		14.2 (±1.4)	
<b>Preoperative creatinine serum level</b> (mg/dL), mean (SD)		0.84 (±0.36)	
<b>Preoperative eGFR</b> (ml/min/1.73 m <sup>2</sup> ), mean (SD)		89.3 (±24.0)	

Legend: BMI: body mass index; ECOG: Eastern Cooperative Oncology Group; ASA: American Society of Anesthesiologists; PADUA: Preoperative Aspects and Dimensions Used for an Anatomical; eGFR: Estimated glomerular filtration rate.

study. Table 1 shows baseline clinical and demographic characteristics of the patients included in the study. Median age was 62 (IQR: 55–71) and 159 (61.4%) were males. Median PADUA score was 7 (IQR: 6–8) with elective indications accounting for 231 (89.2%) of cases. The surgical and pathological features are summarized in Table 2 and Table 3 respectively.

Tumor histotype was clear cell, papillary and chromophobe RCC in 184 (71.0%), 43 (16.6%), 29 (11.2%) cases, respectively. Mean ± SD pathological diameter was 3.2 ± 1.46 cm. Upstaging to pT3a was reported in 26 (10.0%) cases. In 7 (2.7%) specimens PSM was reported. Data on the histologic features of the specimens are reported in Table 3.

At a median follow-up of 36.0 (IQR: 27.0–51.0) months, 5 (1.9%) patients experienced LR, of whom 3 on the tumor resection bed and 2 on the ipsilateral kidney but distant from the enucleation site; 4

(1.5%) patients experienced SR (one bone, two lung and one pancreas and thyroid metastases); and 2 (0.8%) patients experienced both LR and SR (one had ipsilateral kidney LR and a peritoneal recurrence; another had ipsilateral kidney LR and pancreatic metastasis).

At survival analyses, patients had 5-year OS of 93.6% (standard error [SE] 2.7%) and a 5-year CSS of 98.9% (SE 1.1%); of note, one cancer-specific death was recorded at 46 months. The 5-year RFS was 94.2% (SE 1.8%). Patients with a G3 nucleolar grading RCC had a lower 5-year RFS compared to those with a lower nucleolar grading (84% vs 97%,  $p = 0.02$ ) (Fig. 1A). Similarly, patients with a PSM had a significantly lower 5-year estimated RFS compared to those with negative surgical margins (75% vs 94.9% respectively;  $p < 0.001$ ) (Fig. 1B).

**Table 2**

Intraoperative features of 259 patients treated with Endoscopic Robot Assisted Simple Enucleation (ERASE) for localized renal cell carcinoma.

Legend: EBL: estimated blood loss, IQR: interquartile range

Intraoperative features			
<b>Approach</b> , n. %	- Transperitoneal	252	97.3
	- Retroperitoneal	7	2.7
<b>Hilar Clamping</b> , n. %	- Performed	196	75.7
	- Not performed	63	24.3
<b>Warm Ischemia Time</b> (min), median IQR		14	6–18
<b>EBL</b> (cc), median IQR		100	60–150
<b>Operative Time</b> , median IQR		140	110–180
<b>Intraoperative Complications</b> , n. %	- Absent	254	98.1
	- Present	5	1.9
• Accidental incision of the ureter, n. %		1	20%
• Vascular lesion, n. %		2	40%
• Bleeding requiring emotrassfusion, n. %		1	20%
• Bowel laceration, n. %		1	20%

**Table 3**  
Postoperative and anatomicopathological features of 259 patients treated with Endoscopic Robot Assisted Simple Enucleation (ERASE) for localized renal cell carcinoma.

Postoperative features	
Postoperative complications, n. (%)	14 (5.6%)
-Surgical complications, n. (%)	11 (4.3%)
Bleeding requiring transfusions, n.	7
Bleeding requiring superselective embolization, n.	2
Bleeding requiring surgical reintervention, n.	1
Spleen injury requiring splenectomy	1
Clavien 2 surgical complications, n. (%)	7 (2.7%)
Clavien 3 surgical complications, n. (%)	4 (1.5%)
-Medical complications, n. (%)	3 (1.1%)
Cardiologic complication, n.	1
Acute Renal Failure, n.	1
Respiratory complication, n.	1
Length of stay (days), median (IQR)	5 (4–6)
Anatomicopathological features	
RCC Histotype	
Clear Cell (cc-RCC), n. (%)	184 (71.0%)
• G1, n. (%)	26 (14.1%)
• G2, n. (%)	109 (59.2%)
• G3, n. (%)	49 (26.7%)
Papillary (p-RCC), n. (%)	43 (16.6%)
• G1, n. (%)	14 (32.6%)
• G2, n. (%)	14 (32.6%)
• G3, n. (%)	15 (34.9%)
Chromofobe (ch-RCC), n. (%)	29 (11.2%)
Other RCC subtypes, n. (%)	3 (1.2%)
Surgical Margins Status	
• Positive Surgical Margins (PSM), n. (%)	7 (2.7%)
• Negative Surgical Margins, (NSM) n. (%)	252 (97.3%)
pT stage	
• pT1a, n. (%)	182 (70.3%)
• pT1b, n. (%)	49 (18.9%)
• pT2, n. (%)	2 (0.8%)
• pT3a, n. (%)	26 (10.0%)
Pathological diameter (cm), mean (SD)	3.2 (±1.46)
SIB Score, median (IQR)	1 (0–1)

Legend: cc-RCC: clear cell renal cell carcinoma, p-RCC: papillary renal cell carcinoma, ch-RCC: chromophobe renal cell carcinoma.

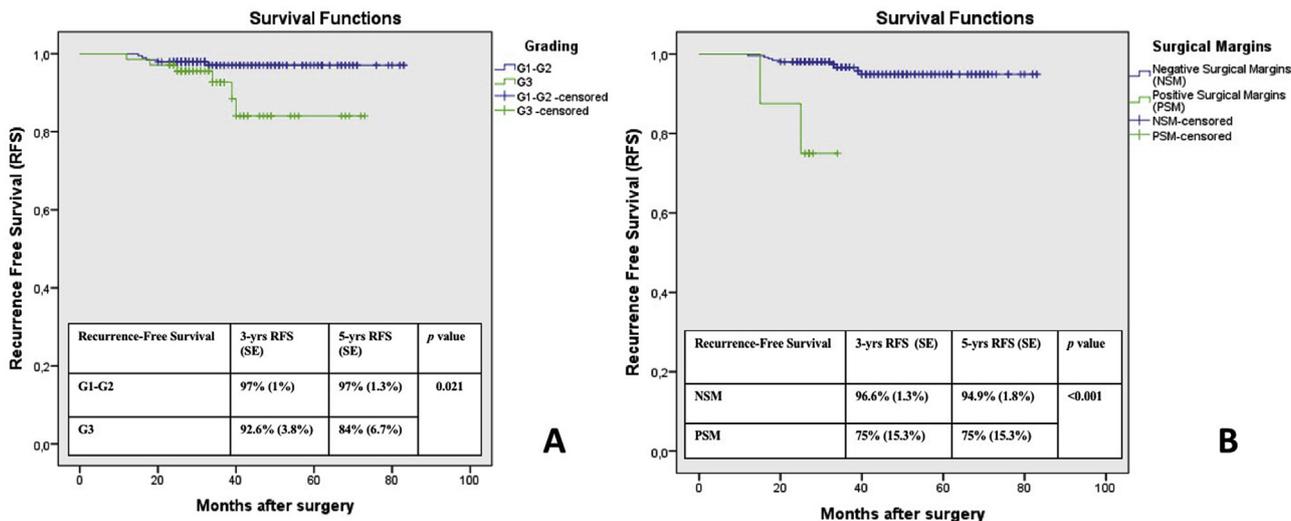
**Discussion**

The oncologic and functional advantages of partial over radical nephrectomy in the management of localized renal tumors is

nowadays widely recognized and documented [1,2]. On the other hand, the impact of SE on the incidence of PSM and disease recurrence rate compared to standard PN have been the object of great debate. A significant body of evidence advocated at least the non-inferiority of SE compared to standard PN with regards to PSM and risk of local recurrence [4,5,13,14]. However, the lack of use of a standardized reporting system led to include mixed resection techniques within the SE group undermining a meaningful comparison between SE and standard PN [10,11]. Furthermore, open SE was the technique performed in most of the studies, making it arduous to directly translate such evidence to the robotic scenario. ERASE actually represents the transposition of open SE to robotic surgery and, at our Institution, is already the standard of care for the surgical treatment of localized renal tumors [12]. Given the exponentially increased use of robotic approach in renal surgery, the assessment of oncologic outcomes after ERASE is currently a precise unmet need.

In this study, ERASE had a 2.7% PSM rate and disease recurrence occurred in 11 (4.2%) cases. Overall, the incidence of PSM after PN reported in the current literature varies from 0 to 7%, irrespective of the surgical approach [14–16]. An early report by Khalifeh et al. showed a PSM rate of 2.2% after robotic PN, which is consistent with our findings [17]. Furthermore, the PSM rate found in our cohort was in line with, if not better than the rate reported in previous open PN series [14,18]. Certainly, the lack of tactile feedback of the robotic system could have affected the risk of accidental capsulotomy of the tumor pseudocapsule during ERASE and, thus, increase the incidence of PSM at evaluation of pathologic specimen. However, the wide maneuverability of the robotic instruments and their design, together with the increased vision of the camera make robotic surgery very precise during the tumor excision phase. In particular, despite the lack of tactile feedback, the surgeon can perform ERASE achieving an accurate blunt dissection, following the natural cleavage plane between the healthy parenchyma and tumor pseudocapsule and, at the same time, keeping always in sight the tumor edges during enucleation in order to reduce the risk to violate its boundaries [19]. This might result in a lower theoretical prevalence of PSM.

In our study, patients treated with ERASE had a 5-year RFS of 94.2%. Similarly, in a wide multicenter collaboration of patients treated with robotic PN, Delto and coworkers reported a 12-month RFS of 99.6%, 100% and 91.7% for cT1a, cT1b and cT2 renal tumors,



**Fig. 1.** Kaplan-Meier curves depicting Recurrence-free Survival in 259 treated with Endoscopic Robot-Assisted Simple Enucleation (ERASE) according to nucleolar grading (A) and surgical margin status (B).

respectively [20]. In another multi-institutional study with a median follow-up of 5 years, local and distant recurrence rates were reported in 1.5% and 4.5% of patients, respectively [21]. Nevertheless, despite ERASE showed recurrence rates comparable to the available robotic PN series in literature, it is difficult to draw definitive conclusions due to the lack of extensive evidence on the long-term oncologic outcome after robotic SE and standard PN.

Several surgical and pathological factors have been advocated as potential predictors of disease recurrence after PN, such as PSM, histologic type, multifocality, nucleolar grading and pT stage [17,22,23]. The real clinical impact of surgical margin status on long-term oncologic outcome after PN still remains to be determined [24–26]. In this study, patients with PSM had a significantly lower 5-year RFS compared to patients with negative surgical margins (75% vs 94.9%;  $p < 0.001$ ). Kwon et al. in a large series of patients treated with open PN found that patients with PSM were at significantly higher risk of developing a disease recurrence. The Authors concluded that tumors with highly malignant potential and PSM might have a considerable risk of developing recurrence after treatment [27]. Similarly, Shah et al. corroborated these findings and highlighted that PSMs during PN might increase the risk of recurrence primarily in patients harboring tumors with adverse biology [28]. Interestingly, in our population the higher nucleolar grading was also found to be associated with an increased risk of disease recurrence. These findings may indicate that PSM is not an absolute predictor of disease recurrence, but rather a competing adverse feature of oncologic outcome with pathologic features. In particular, the inherent tumor characteristics of the primary lesion, such as multifocality, nucleolar grading and pT stage, may play an important role in patients with PSM. In this light, tumor biology and surgical margin status should be considered for a better risk stratification and for a tailored follow-up.

Especially, great concern has been raised about the oncologic safety of SE in G4 RCCs. To this regard, a previous multicenter, comparative study already highlighted that G4 RCCs were associated with a worse CSS if treated with open SE compared to those treated with standard PN [18]. Although these data must be confirmed in further larger perspective studies and with different NSS approaches, we must point out that in this study no G4 RCC was treated with an enucleative resection technique confirmed at the further visual inspection using the SIB score.

Finally, ERASE showed excellent results demonstrating to be a feasible and safe technique at mid-term follow up. In fact, the 5-year OS (93.6%) and CSS (98.9%) achieved in our series were comparable to previous reports for different surgical approaches confirming the oncological safety of this technique [29,30]. Indeed, in a multicenter prospective series of nearly 120 patients treated with robotic PN, at a 2-year follow-up, patients had an OS of 96.8% and a CSS of 99.2% [31]. Likewise, Andrade et al. reported an OS of 91.1% and a CSS of 97.8% after robotic PN in patients treated at a tertiary referral American institution at a median follow-up of five years [32]. These results are in line with the 5-year survival estimates of this study.

The present study was not devoid of limitations. First, this was a retrospective review of a prospectively collected database on ERASE for the treatment of RCC. The relatively small sample size together with the limited number of events might have undermined the survival analysis and the evaluation of potential predictors of recurrence in our series. Furthermore, SIB score assignment inherently shows a certain degree of interobserver subjectivity. Finally, all cases were performed by four surgeons with an extensive experience in open SE, but the learning curve of each surgeon was not considered in the present study. As such, our findings could not be applicable to all surgeon- or center-related scenarios. Acknowledged these limitations, our study represents the largest

series so far providing mid-term oncological results in patients treated with ERASE according to the SIB standardized reporting system. Larger studies with longer follow-up are needed to confirm the oncological safety of ERASE at a longer follow-up and to independently assess the relationship between positive SM, pathologic features and disease recurrence after ERASE.

## Conclusion

In our experience, ERASE is a safe treatment option for the conservative management of RCC with oncological optimal outcomes at medium term follow-up. PSM and higher nucleolar grade might predict an increased risk of disease recurrence. Further studies are needed to confirm our findings in larger series with longer follow-up.

## Conflict of interest statement

All authors disclose any financial and personal relationships with other people or organizations that could inappropriately influence their work.

No study sponsor has been involved.

## Acknowledgments

None.

## References

- [1] Lyunberg B, Albiges L, Bensalah K, Bex A, Giles RH, Hora M, et al. European Association of Urology guidelines on renal cell carcinoma. 2018. Version, <https://uroweb.org/guideline/renal-cell-carcinoma/>.
- [2] Lyunberg B, Albiges L, Bensalah K, Bex A, Giles RH, Hora M, et al. European Association of Urology guidelines on renal cell carcinoma. 2017. Version, <https://uroweb.org/guideline/renal-cell-carcinoma/>.
- [3] Serni S, Vittori G, Frizzi J, Mari A, Siena G, Lapini A, et al. Simple enucleation for the treatment of highly complex renal tumors: perioperative, functional and oncological results. *Eur J Surg Oncol* 2015 Jul;41(7):934–40.
- [4] Minervini A, Campi R, Sessa F, Derweesh I, Kaouk JH, Mari A, et al. Positive surgical margins and local recurrence after simple enucleation and standard partial nephrectomy for malignant renal tumors: systematic review of the literature and meta-analysis of prevalence. *Minerva Urol Nefrol* 2017 Dec;69(6):523–38.
- [5] Cao DH, Liu LR, Fang Y, Tang P, Li T, Bai Y, et al. Simple tumor enucleation may not decrease oncologic outcomes for T1 renal cell carcinoma: a systematic review and meta-analysis. *Urol Oncol* 2017 Nov;35(11):661.e15–661.e21.
- [6] Ficarra V, Novara G, Secco S, Macchi V, Porzionato A, De Caro R, et al. Preoperative aspects and dimensions used for an anatomical (PADUA) classification of renal tumours in patients who are candidates for nephron sparing surgery. *Eur Urol* 2009;56:786–93.
- [7] Edge SB, Byrd DR, Comptom CC, Fritz AG, Greene FL, Trotti A, et al. *AJCC staging manual*. seventh ed. Philadelphia: Springer; 2009.
- [8] Delahunt B, Chevile JC, Martignoni G, Humprey PA, Magi-Galluzzi C, et al. The International Society of Urological Pathology (ISUP) Grading System for renal cell carcinoma and other prognostic parameters. *Am J Surg Pathol* 2013;37:1490.
- [9] Srigley JR, Delahunt B, Eble JN, et al. The international society of urological Pathology (ISUP) Vancouver Classification of Renal Neoplasia. *Am J Surg Pathol* 2013;37:1469–89.
- [10] Minervini A, Carini M, Uzzo RG, Campi R, Smaldone MC, Kutikov A, et al. Standardized reporting of resection technique during nephron-sparing surgery: the surface-intermediate-base margin score. *Eur Urol* 2014 Nov;66(5):803–5.
- [11] Minervini A, Campi R, Kutikov A, Montagnani I, et al. Histopathological validation of the surface-intermediate-base margin score for standardized reporting of resection technique during nephron sparing surgery. *J Urol* 2015 Oct;194(4):916–22.
- [12] Minervini A, Tuccio A, Masieri L, Veneziano D, Vittori G, Siena G, et al. Endoscopic robot-assisted simple enucleation (ERASE) for clinical T1 renal masses: description of the technique and early postoperative results. *Surg Endosc* 2015;29(5):1241–9.
- [13] Longo N, Minervini A, Antonelli A, Bianchi G, Bocciardi AM, Cunico SC, et al. Simple enucleation versus standard partial nephrectomy for clinical T1 renal masses: perioperative outcomes based on a matched-pair comparison of 396 patients (RECORD project). *Eur J Surg Oncol* 2014 Jun;40(6):762–8.
- [14] Schiavina R, Serni S, Mari A, Antonelli A, Bertolo R, Bianchi G, et al. A

- prospective, multicenter evaluation of predictive factors for positive surgical margins after nephron-sparing surgery for renal cell carcinoma: the RECORD1 Italian Project. *Clin Genitourin Cancer* 2015 Apr;13(2):165–70.
- [15] Borghesi M, Brunocilla E, Schiavina R, Martorana G. Positive surgical margins after nephron-sparing surgery for renal cell carcinoma: incidence, clinical impact, and management. *Clin Genitourin Cancer* 2013;11(1):5–9.
- [16] Petros FG, Metcalfe MJ, Yu KJ, Keskin SK, Fellman BM, Chang CM, et al. Oncologic outcomes of patients with positive surgical margin after partial nephrectomy: a 25-year single institution experience. *World J Urol* 2018;36(7):1093–101.
- [17] Khalifeh A, Kaouk JH, Bhayani S. Positive surgical margins in robot-assisted partial nephrectomy: a multi-institutional analysis of oncologic outcomes (leave no tumor behind). *J Urol* 2013 Nov;190(5):1674–9.
- [18] Minervini A, Ficarra V, Rocco F, Antonelli A, Bertini R, Carmignani G, et al. Simple enucleation is equivalent to traditional partial nephrectomy for renal cell carcinoma: results of a nonrandomized, retrospective, comparative study. *J Urol* 2011;185:1604–10.
- [19] Minervini A, Campi R, Di Maida F, Mari A, Montagnani I, Tellini R, et al. Tumor-parenchyma interface and long-term oncologic outcomes after robotic tumor enucleation for sporadic renal cell carcinoma. *Urol Oncol* 2018 Dec;36(12):527.e1–527.e11.
- [20] Delto JC, Paulucci D, Helbig MW, Badani KK, Eun D, Porter J, et al. Robot-assisted partial nephrectomy for large renal masses: a multi-institutional series. *BJU Int* 2018 Jun;121(6):908–15.
- [21] Chang KD, Abdel Raheem A, Kim KH, Oh CK, Park SY, Kim YS, et al. Functional and oncological outcomes of open, laparoscopic and robot-assisted partial nephrectomy: a multicentre comparative matched-pair analyses with a median of 5 years' follow-up. *BJU Int* 2018;122:618–26.
- [22] Mouracade P, Kara O, Maurice MJ, Dagenais J, Malkoc E, Nelson RJ, et al. Patterns and predictors of recurrence after partial nephrectomy for kidney tumors. *J Urol* 2017 Jun;197(6):1403–9.
- [23] Volpe A, Garrou D, Amparore D, De Naeyer G, Porpiglia F, Ficarra V, et al. Perioperative and renal functional outcomes of elective robot-assisted partial nephrectomy (RAPN) for renal tumours with high surgical complexity. *BJU Int* 2014 Dec;114(6):903–9. <https://doi.org/10.1111/bju.12751>.
- [24] Bensalah K, Pantuck AJ, Rioux-Leclercq N, Thuret R, Montorsi F, Karakiewicz PI, et al. Positive surgical margin appears to have negligible impact on survival of renal cell carcinomas treated by nephron-sparing surgery. *Eur Urol* 2010;57:466.
- [25] Yossepowitch O, Thompson RH, Leibovich BC, Eggener SE, Pettus JA, Kwon ED, et al. Positive surgical margins at partial nephrectomy: predictors and oncological outcomes. *J Urol* 2008 Jun;179(6):2158–2163.
- [26] Tellini R, Antonelli A, Tardanico R, Fisogni S, Vecchia A, Furlan MC, et al. Positive surgical margins predict progression-free survival after nephron-sparing surgery for renal cell carcinoma: results from a single center cohort of 459 cases with a minimum follow-up of 5 years. *Clin Genitourin Cancer* 2019 Feb;17(1):e26–3.
- [27] Kwon EO, Carver BS, Snyder ME, Russo P. Impact of positive surgical margins in patients undergoing partial nephrectomy for renal cortical tumours. *BJU Int* 2007;99:286.
- [28] Shah PH, Moreira DM, Okhunov Z, Patel VR, Chopra S, Razmaria AA, et al. Positive surgical margins increase risk of recurrence after partial nephrectomy for high risk renal tumors. *J Urol* 2016 Aug;196(2):327–34.
- [29] Herr HW. Partial nephrectomy for unilateral renal carcinoma and a normal contralateral kidney: 10-year followup. *J Urol* 1999;161:33–4.
- [30] Lane BR, Gill IS. 5-year outcomes of laparoscopic partial nephrectomy. *J Urol* 2007;177:70–4.
- [31] Kylo RL, Tanagho YS, Kaouk JH, Stifelman M, Rogers CG, Hillyer SP, et al. Prospective multi-center study of oncologic outcomes of robot-assisted partial nephrectomy for pT1 renal cell carcinoma. *BMC Urol* 2012;12:11.
- [32] Andrade HS, Zargar H, Caputo PA, Akca O, Kara O, Ramirez D, et al. Five-year oncologic outcomes after transperitoneal robotic partial nephrectomy for renal cell carcinoma. *Eur Urol* 2016;69:1149–54.