Robotic vs Open Simple Enucleation for the Treatment of T1a-T1b Renal Cell Carcinoma: A Single Center Matched-pair Comparison

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OBJECTIVE To compare surgical, pathological, short-term functional data, and complications of endoscopic robotic-assisted simple enucleation (ERASE) and open simple enucleation (OSE).

METHODS We undertook matched-pair analysis (age, tumor size, and preoperative aspects and dimensions used for an anatomical [PADUA] score) of 392 patients treated with simple enucleation (SE) for T1a-T1b renal tumors in our department, including 160 patients in the OSE group and 80 in the ERASE group. Perioperative outcomes were compared with univariate analysis. Variables associated with warm ischemia time (WIT) >25 minutes, complications, and postoperative acute kidney dysfunction (AKD) were assessed with multivariate analysis.

RESULTS The groups were comparable in body mass index (BMI), comorbidity, and preoperative renal function. In the ERASE vs the OSE group, no significant differences resulted regarding WIT (18.5 vs 16.4 minutes, $P = .5$), complications, transfusion rate, reoperation rate for Clavien grade ≥ 3 complications, and positive surgical margin rate (2.9% vs 2.1%, $P = .63$). In elective patients, no significant difference resulted in variation of estimated glomerular filtration rate from baseline (8.5 vs 13.9 mL/min, $P = .17$) and AKD. In the ERASE group, the clamping of renal pedicle was used with a lower frequency ($P < .0001$), with lower estimated blood loss (EBL), longer operative time, and a 1-day shorter hospitalization ($P = .001$). On the multivariate analysis, the surgical approach was not independently associated with WIT >25 minutes, postoperative complications, and AKD.

CONCLUSION The ERASE is a feasible technique with a positive surgical margin rate comparable to OSE; it showed WIT and complication rates similar to the open approach, along with the advantages of mini-invasivity. UROLOGY 83: 331–338, 2014. © 2014 Published by Elsevier Inc.

Open partial nephrectomy (OPN) is the standard treatment for renal cell carcinoma (RCC) up to 7 cm of clinical size, if technically feasible.[1] The simple enucleation (SE) is a procedure of nephron-sparing surgery (NSS) that differs from the standard partial nephrectomy (PN), as it excides the tumor without any visible rim of healthy parenchyma around the tumor and developing, by blunt dissection, the natural cleavage plane between the tumor pseudocapsule and the healthy parenchyma. The oncological safety of SE, which has been previously debated, is supported by studies showing similar long-term oncological results to those of PN[2-7] (level of evidence 2b). The minimum depth of resection in healthy tissue brings to SE elements of attractiveness, as the maximal preservation of parenchyma, the fast execution, and a low incidence of postoperative complications.[8] Over the last several years, SE received a wider consensus, being adopted in several centers as an alternative to standard PN, particularly to treat corticomedullar RCC.[9] Laparoscopic partial nephrectomy and robotic partial nephrectomy (RPN) are the main mini-invasive alternatives to PN, aimed at reducing the added morbidity of open incision and potential rib resection. RPN resulted in a more reproducible technique,[10] and it is likely to become the new standard technique for minimally invasive PN. With the aim of a direct confrontation of the robotic approach with the standard surgical treatment, some comparative studies have evaluated the perioperative outcomes of RPN with those of OPN, reporting heterogeneous results that await further investigations.[11-13] However, the perioperative outcomes of the robotic SE have never been investigated.

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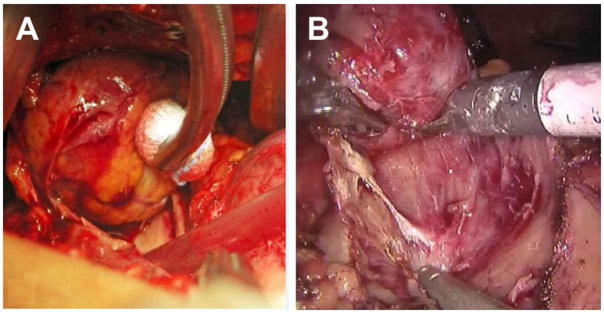

Figure 1. Smooth dissection of the natural cleavage plane between tumor pseudocapsule and healthy parenchyma. **A:** open simple enucleation (OSE). **B:** endoscopic robotic-assisted simple enucleation (ERASE). (Color version available online.)

The purpose of our study was to evaluate surgical, pathological, early functional results, and morbidity of endoscopic robotic-assisted simple enucleation (ERASE), and to compare them with those of open simple enucleation (OSE) in a single-center, prospectively maintained series matched for age, tumor size, and nephrometry.

MATERIAL AND METHODS

Patient Selection

Between July 2006 and December 2012, we prospectively gathered data from 392 consecutive patients treated with SE for clinically localized RCC in our department. Of these, 277 underwent OSE and 115 underwent ERASE. The preoperative data of the entire series of SE have been reported in Supplementary Table 1, online only. A matched-pair analysis was done regarding age, tumor size, and nephrometry (preoperative aspects and dimensions used for an anatomical [PADUA] score), including 160 patients after OSE and 80 after ERASE. All robotic procedures were done in a single institution by 3 surgeons who are experienced in OSE and robotic surgery. The approach selection was based on chronological criteria. Since January 2011, almost all patients underwent ERASE, with the exception of those with previous extensive transperitoneal surgery. This study was approved by the local ethics committee, and informed consent was collected for all patients.

Open Simple Enucleation

The OSE was done by a lateral retroperitoneal approach according to the technique reported previously.[3-5] The renal pedicle was usually controlled en bloc with vascular clamps. Renal hypothermia was never induced because our warm ischemia time (WIT) was usually under 25 minutes.[3-5] The tumor was enucleated without a visible rim of normal parenchyma by blunt dissection using the natural cleavage plane between the pseudocapsule and normal parenchyma (Fig. 1A). Any tears in the urinary tract, blood vessels, or parenchyma in the enucleation bed were repaired with running sutures. The parenchymal defect was usually closed with horizontal interrupted sutures after application of hemostatic agents.

Endoscopic Robotic-assisted Simple Enucleation

A transperitoneal approach was used in patients positioned in the flank position. Pneumoperitoneum was created using the Hasson open technique a few centimeters above the umbilicus for the camera. Two 8-mm ports for robotic instruments were used (one in midclavicular line 3 cm below the costal margin, and another one paraumbilically). An assistant 10-mm port was inserted between the Hasson and the paraumbelical 8-mm port. An additional subxiphoid port was used to retract the liver in case of right enucleations. The S da Vinci robot, (Intuitive Surgical, Sunnyvale, CA), was docked at the patient's back. The bowel was mobilized medially. Gerota's fascia was incised and the kidney was mobilized from fat to identify tumor limits and to exclude satellite lesions. The enucleation phase started without ischemia with a cold/diathermic incision of the capsule a few millimeters around the tumor, and the renal artery was clamped (with bulldog) if the bleeding was interfering with the safe removal of the tumor. The lesion was bluntly enucleated using monopolar scissors (closed) and forceps (Fig. 1B) by dissecting the natural cleavage plane between the tumor and normal parenchyma. Hemostasis in the resection bed was achieved with running sutures (Monocryl 3-0), according to the sliding clip technique.[14] Care was taken to repair all visible opened calices and bleeding sites. Usually the cortical defect was closed with interrupted sutures after apposition of hemostatic agents.

Data Collection

All conventional preoperative variables were collected. All the nephrometric variables considered in the PADUA score were prospectively gathered in our department since 2006, and included in previous analyses,[8] except for "renal sinus invasion," which was retrospectively assigned after review of preoperative imaging. After the validation of the PADUA score, since January 2011, this variable was recorded prospectively. The following surgical details were recorded: need for pedicle clamping, WIT, operative time, estimated blood loss (EBL), variation of blood hemoglobin (Hb) and serum creatinine on the third postoperative day from baseline, and length of stay. Estimated glomerular filtration rate (eGFR) was calculated with the modification of diet in renal disease equation.[15] Surgical specimens were processed in accordance with standard procedures by 2 uropathologists. Pathological tumor size, 2009 TNM stage,[16] Fuhrman nuclear grade,[17] positive surgical margin (PSM), and histological subtypes, according to World Health Organization classification,[18] were registered. All the perioperative (including intra- and postoperative) medical and surgical complications, occurring during surgery and within 30 days, were recorded and stratified with the Clavien system.[19] Postoperative blood loss with need of blood transfusions, superselective embolization, or

Table 1. Preoperative characteristics of patients and tumors stratified according to surgical procedure

Preoperative Variables	ERASE (n = 80)	OSE (n = 160)	*P* Value
Age (y) mean ± SD	62.1 ± 11.8	62.4 ± 115	.68
Gender, no. (%)			
Male	50 (62.5)	109 (68.1)	.32
Female	30 (37.5)	51 (31.9)	
BMI mean ± SD	24 ± 8	25 ± 3	.49
ASA score			
0-1 (%)	73 (91.3)	141 (88.1)	.23
2-4 (%)	7 (8.7)	19 (21.9)	
Charlson index median (IQR)	1 (0-2)	1 (0-2)	.49
Clinical diameter (cm) mean ± SD (range)	3.0 ± 1.5 (0.9-7.0)	3.1 ± 1.4 (1.0-8.2)	.71
Clinical stage, no. (%)			
cT1a	64 (80)	134 (83.7)	.63
cT1b	16 (20)	26 (16.3)	
PADUA score median (IQR)	7 (6-8)	7 (6-8)	.10
PADUA scores ≥10, no. (%)	4 (5)	10 (6.3)	.70
Preoperative Hb (g/dL) mean ± SD	14.1 ± 1.4	14.0 ± 1.8	.60
Preoperative serum creatinine (mg/dL) mean ± SD	0.89 ± 0.35	1.02 ± 1.01	.28
Preoperative eGFR (mL/min) mean ± SD	84.8 ± 21.0	83.7 ± 24.2	.75

ASA, American Society of Anesthesiology; BMI, body mass index; eGFR, estimated glomerular filtration rate; ERASE, endoscopic robotic-assisted simple enucleation; Hb, hemoglobin; IQR, interquartile range; OSE, open simple enucleation; PADUA, preoperative aspects and dimension used for an anatomical; SD, standard deviation.

reintervention was registered. Urinary fistula was recorded in case of persistent drainage leaks beyond the seventh postoperative day, and a fluid biochemical analysis consistent with urine (drainage fluid-to-serum creatinine ratio >2). Postoperative acute kidney dysfunction (AKD) in elective patients was defined, according to previous studies,[20] as an elevation in serum creatinine >2 mg/dL.

Statistical Analysis

Eighty patients who underwent the ERASE procedure and 160 who underwent OSE were matched 1:2 regarding age, tumor diameter, and PADUA score. Continuous parametric variables are presented as mean ± standard deviation (SD), nonparametric as median and interquartile range (IQR), and categorical with frequencies and proportions. Univariate analysis (Pearson's chi-square, unpaired *t* test, and Mann-Whitney *U* test) assessed the differences of pre- and postoperative variables between the ERASE and the OSE groups. A multivariate logistic regression model tested the ability of the surgical approach (robotic vs open), along with other relevant variables, to predict WIT >25 minutes, overall postoperative complications, and postoperative AKD, analyzed separately. All tests were 2-sided, with a statistical significance at *P* <.05 using the StatView version 5.0.1 program (SAS Institute, Cary, NC).

RESULTS

As summarized in Table 1, mean age at surgery was 62.1 ± 11.8 years in the ERASE group and 62.4 ± 11.5 years in the OSE group (*P* = .94). Mean clinical tumor diameter was 3.0 ± 1.5 in the ERASE group and 3.1 ± 1.4 in the OSE group (*P* = .71). Median (IQR) PADUA score resulted in 7 (range 6-8) in both series. The groups were also comparable regarding gender distribution, body mass index (BMI), American Society of Anesthesiology score, Charlson comorbidity index, preoperative blood Hb, serum creatinine, and eGFR.

Perioperative results stratified according to surgical procedure are summarized in Table 2. The clamping of the renal pedicle was used with a significantly lower frequency in the ERASE group than in the OSE group (60% vs 93.8%, *P* <.0001). When used, the mean WIT was 2 minutes longer in the ERASE group (18.5 vs 16.4 minutes), but this difference resulted to be not statistically significant (*P* = .50). With regard to the patients undergoing the ERASE procedure, 10.4% had WIT >25 minutes and 4.2% >30 minutes; of the patients undergoing the OSE procedure, the respective numbers were 4% and 1.3%, with no significant difference (*P* = .10 and *P* = .22, respectively). EBL was considerably lower in the ERASE group vs the OSE group (*P* <.0001). Intraoperative complications were comparable between the 2 groups (*P* = .54), and included 1 intraoperative bleeding complication that was treated with transfusions in both groups, 1 spleen damage that was treated with apposition of hemostatic agents, and 1 renal vein tearing that was repaired with sutures, all in the OSE series.

After ERASE, the mean Hb declined by 2.2 g/dL and the serum creatinine increased by 0.11 mg/dL from baseline. Similarly, after OSE, the respective changes were 2.4 g/dL and 0.16 mg/dL. In patients with elective indication (78/80 in the ERASE group and 132/160 in the OSE group), we found no significant differences in eGFR modifications (*P* = .17) and postoperative AKD (*P* = .10). The percentage of patients with postoperative overall complications was comparable in the ERASE and OSE groups: 10% and 15.6%, respectively (*P* = .17). Medical complications occurred with a similar rate (*P* = .54), whereas surgical complications were lower in the ERASE group, but with no statistical significance (8.8%

Table 2. Perioperative results stratified according to surgical procedure

Intraoperative Outcomes	ERASE (n = 80)	OSE (n = 160)	*P* Value
Clamping of renal pedicle/artery, no. (%)	48 (60)	150 (93.8)	<.0001
WIT (min) mean ± SD (range)	18.5 ± 6 (9-38)	16.4 ± 5.3 (7-35)	.50
WIT >25 min, no. (%)	5/48 (10.4)	6/150 (4)	.10
WIT >30 min, no. (%)	2/48 (4.2)	2/150 (1.3)	.22
EBL (cc) mean ± SD	109 ± 112	181 ± 136	<.0001
Operative time (min) mean ± SD	157 ± 50	108 ± 36	<.0001
Total intraoperative complications, no. (%)	1 (1.25)	4 (2.5)	.54
Transfusions	1 (1.25)	2 (1.25)	
Spleen lesion	-	1 (0.62)	
Renal vein lesion	-	1 (0.62)	
Postoperative outcomes			
LOS (d, including the day of surgery) median (IQR)	5 (5-6)	6 (5-7)	.001
Postoperative overall complications, no. (%)	8 (10)	25 (15.6)	.17
Postoperative medical complications, no. (%)	1 (1.2)	3 (1.8)	.54
Postoperative surgical complications, no. (%)	7 (8.8)	22 (13.8)	.37
Postoperative transfusions (Clavien 2)	5 (6.3)	15 (9.4)	
Selective embolization (Clavien 3a)	2 (2.5)	3 (1.9)	
Reoperation for bleeding (Clavien 3b)	-	1 (0.6)	
Urinary fistula without stenting (Clavien 1)	-	3 (1.9)	
Urinary fistula with stenting (Clavien 3a)	-	-	
Clavien 4	-	-	
Clavien 5	-	-	
Transfusion rate (intra- and postoperative), no. (%)	8 (10.0)	21(13.1)	.48
Clavien 3 complications, no. (%)	2 (2.5)	4 (2.5)	.99
AKD (elective indication only), no. (%)	1/78 (1.3)	8/132 (6.1)	.10
Delta Hb (3rd postoperative day − baseline) (g/dL) mean ± SD	2.2 ± 1.2	2.4 ± 1.2	.31
Delta Cr (3rd postoperative day − baseline) (mg/dL) mean ± SD	0.11 ± 0.18	0.16 ± 0.82	.34
Delta eGFR (elective indication only), mean ± SD	8.5 ± 10.4	13.9 ± 12.7	.17
Pathologic assessment			
Benign tumors, no. (%)	12 (15)	20 (12.5)	.52
Pathological T stage, no. (%)			.21
pT1a	51/68 (75.0)	113/140 (80.7)	
pT1b	11/68 (16.2)	18/140 (12.9)	
pT3a	6/68 (8.8)	9/140 (6.4)	
Fuhrman nuclear grade (%)			
Grade 1	11/68 (16.2)	27/140 (19.3)	
Grade 2	42/68 (61.8)	84/140 (60.0)	
Grade 3-4	15/68 (22.0)	29/140 (20.7)	
PSM (%)	2/68 (2.9)	3/140 (2.1)	.63

AKD, acute kidney dysfunction; Cr, creatinine; EBL, estimated blood loss; LOS, length of stay; PSM, positive surgical margin; WIT, warm ischemia time; other abbreviations as in Table 1.

vs 13.8%, *P* = .37). The frequency of Clavien 3 complications was comparable between approaches (2.5%, *P* = .99). No Clavien 4/5 complication occurred in this series. The transfusion rate (intra- and postoperatively) was 10.0% in the ERASE group and 13.1% in the OSE group (*P* = .48). Median hospitalization resulted in 1-day longer after OSE (*P* = .001). Benign tumors accounted for 15% of patients in the ERASE group and 12.5% in the OSE group (*P* = .52). Table 2 shows the stratification of all malignant tumors according to T stage and Fuhrman nuclear grade. The rate of PSM was similar in both groups (ERASE: 2.9%, OSE: 2.1%, *P* = .63).

Association Analysis

In the univariate analysis, clinical tumor size, clinical stage, and PADUA score were significantly associated with WIT >25 minutes (Table 3). In multivariate analysis, the PADUA score resulted to be independently associated with WIT >25 minutes. Each point increase in the PADUA score was related to a 1.59-fold increased risk of WIT >25 minutes. Clinical tumor size and PADUA score results were also associated with postoperative overall complications (Table 4), and the PADUA score was confirmed by the multivariate analysis (risk ratio [RR] = 1.47, *P* = .02). The surgical approach resulted to be not associated with either postoperative complications or with WIT >25 minutes. Patient age, preoperative eGFR, surgical indication and approach, and EBL >500 cc resulted to be significantly associated with postoperative AKD in the univariate analysis (Supplementary Table 2). The multivariate analysis confirmed the surgical indication and the EBL as independently associated to postoperative AKD.

COMMENT

To our knowledge, this is the first evaluation of perioperative results of robotic SE. We compared these results with those of the traditional OSE that has been used in

Table 3. Uni- and multivariate analysis to assess preoperative variables associated with warm ischemia time >25 minutes

	Correlation with WIT >25 min			
	Univariate Analysis	Multivariate Analysis		
Preoperative Variables	*P* Value	RR	*P* Value	95% CI
Age (y)	.24	-	-	-
Gender	.90	-	-	-
BMI	.72	-	-	-
Charlson comorbidity index	.33	-	-	-
Clinical tumor diameter	**.0368**	1.2	.37	0.795-1.859
Clinical stage	**.0357**	-	-	-
PADUA score	**.0043**	**1.59**	**.048**	**1.00-2.53**
Surgical approach (robot vs open)	.10	-	-	-
Preoperative Hb	.89	-	-	-
Indication (elective vs relative/imperative)	.88	-	-	-
Preoperative eGFR	.75	-	-	-

CI, confidence interval; RR, risk ratio; other abbreviations as in Tables 1 and 2.
The figures in boldface represent statistical significance.

our department for the last 25 years[4] as the standard technique of NSS. SE has proven to ensure excellent local control as, even in case of microscopic tumor capsule penetration, neoplastic cells are separated from the surgical margins by a thin layer of inflammatory tissue[6] that usually avoids a PSM. PSM after SE resulted as negligible in many studies,[2-6] and even lower than after PN in the SATURN study.[7] In case of intraoperative detection of macroscopic tumor infiltration beyond the pseudocapsule (undetected at imaging), in intrarenal veins, collecting system, or perirenal fat, NSS is usually switched to radical nephrectomy. This occurred in 9 patients in the OSE group (9/286 = 3.15%) and in 3 patients in the ERASE group (3/118 = 2.5%), which have been removed from our SE series. No patient was converted to a standard PN. In the present series, ERASE showed comparable perioperative outcomes to OSE, with the added benefits of lower rate of pedicle clamping and a 1-day shorter hospitalization, along with the clear advantages of the mini-invasivity. In the OSE technique, we usually clamp the renal pedicle before starting the procedure to obtain a maximally clear bloodless field, which is required to correctly develop the enucleation plane. Nevertheless, others have shown that OSE can be done without clamping the hilar vessels, exploiting the natural plane that is characteristically less bloody compared to the resection plane of PN.[2] In this series, which was matched for diameter and PADUA score, in the ERASE group, the ischemia was used with a significantly lower rate (P <.0001) and the EBL was maintained lower (P <.0001). The intraoperative bleeding was not low enough to affect the change of Hb after surgery, which was comparable between groups, but it allowed to

Table 4. Uni- and multivariate analysis to analyze preoperative variables associated with postoperative overall complications

	Correlation With Overall Postoperative Complications			
	Univariate Analysis	Multivariate Analysis		
Clinical Variables	*P* Value	RR	*P* Value	95% CI
Age	.82	-	-	-
Gender	.28	-	-	-
BMI	**.07**	1.1	.10	0.98-1.22
Charlson comorbidity index	.38	-	-	-
Clinical tumor diameter	**.05**	1.1	.56	0.82-1.45
Clinical stage	.06	-	-	-
PADUA score	**.0013**	**1.47**	**.02**	**1.06-2.02**
Preoperative Hb	.32	-	-	-
Indication (elective vs relative/imperative)	.50	-	-	-
Preoperative eGFR	**.06**	0.99	.15	0.97-1.00
Surgical approach (robot vs open)	.17	-	-	-
Pedicle clamping	.18	-	-	-
WIT	.90	-	-	-

Abbreviations as in Tables 1, 2, and 3.
The figures in boldface represent statistical significance.

effectively accomplish many clampless procedures. A possible explanation is that the robotic approach enhances the phase of enucleation, thereby reducing the bleeding coming from the surgical bed. Indeed, the vision magnification allows a more accurate identification of small vessels that can be readily coagulated during enucleation, whereas the pneumoperitoneum reduces the venous bleeding. An alternative explanation is that patients in the ERASE group were treated more recently, and, in recent years, surgeons have been motivated to avoid the ischemia in a greater number of NSSs, as a result of studies that have prioritized the concept of renal damage.[21] Others have reported lower EBL in RPN compared to OPN, as shown by Simhan et al[11] regarding moderate and highly complex RCC. In this study, the mean WIT of ERASE was similar to OSE, as well as the percentage of patients with WIT <25 minutes, and the surgical approach resulted to be not associated with longer WIT. However, looking at Table 2, the crude incidence of WIT >25 minutes and WIT >30 minutes was 2.6- and 3.2-fold higher in the ERASE group vs the OSE group. Nevertheless, the recourse to pedicle clamping is different (60% and 93.8%); given the similarity of the 2 groups according to the PADUA score, we might hypothesize that ischemia was avoided in the more simple robotic cases, exploiting the mentioned technical advantages, whereas the simple open cases have been done with a short ischemia, which has reduced the mean WIT and the rate of WIT >25 minutes and >30 minutes in this group. These findings suggest that the robotics may replicate the rapidity of open NSS in the more complex phase of SE, also leading to comparable early functional results. Several studies demonstrated a shorter WIT in RPN than laparoscopic partial nephrectomy[22-24]; but few previous comparison of robotic and open NSS are available. In one of these studies, Lee et al[12] reported a longer WIT in the RPN group ($P < .001$), and similarly Sprenkle et al[13] found a longer WIT in the mini-invasive PN group ($P = .006$). It is not easy to justify this heterogeneity of results. Surely, the increasing surgeons' experience in robotics may lead to a progressive reduction in WIT in the most recent series. Our WIT in the ERASE group was comparable to those reported in recent RPN series, such as 18 minutes for Ficarra et al[24] and 18.7 minutes for Khalifeh et al.[22] This suggests that ERASE might not be superior to RPN in terms of WIT, although conclusions can be drawn only after randomized comparative studies between these 2 techniques. After ERASE, we found a lower reduction of eGFR and a lower AKD rate compared to OSE. Repeating these analyses including only elective patients, the significances were lost. In the multivariate analysis, postoperative AKD was not associated with the surgical approach or the attitude on renal pedicle, but with EBL >500 cc and with surgical indication. However, further studies are needed to evaluate long-term functional results of ERASE. We identified no difference in intra- and postoperative complications between approaches, even stratifying them for type (medical or surgical), or severity (Clavien $\geq$3 vs others). The complication rate of SE resulted to be not associated with approach, but showed an independent association with nephrometry, according to what was reported previously.[25] In agreement with our findings on SE, Simhan et al[11] reported a similar morbidity after RPN and OPN. Our group has previously found a low rate of complications after OSE,[8] and with this evaluation we can state that ERASE is not inferior to OSE regarding morbidity. It is interesting that the robotic approach has not led to increased medical complications. Probably the effects of pneumoperitoneum and longer anesthesia time have been balanced by the beneficial consequences, also in cardiopulmonary apparatus, of avoiding the lumbotomical incision, reducing pain, and accelerating mobilization after surgery. Our major complications rate after ERASE (Clavien $\geq$3: 2.5%) is similar to those reported in literature after RPN, such as 8 of 269 (3.0%) for Khalifeh et al,[22] and 10 of 347 (2.9%) for Ficarra et al.[24] However, those series were not selected for tumor size and nephrometry. Only comparative studies between ERASE and RPN would clarify whether the actual perioperative morbidity differs. The oncologic outcomes of robotic surgery are usually presented using surrogate endpoints such as PSM rate, although a PSM in NSS has not been found to correlate with a higher rate of recurrences.[26] The PSM rate in the ERASE group was comparable to the OSE group, and both were within the range reported in the literature (0%-7%). In our experience, the loss of tactile sensation of robotics did not increase the difficulty of enucleation plane development, nor the PSM rate, contrary to what was suggested by others.[9] The primary limitation of this study was its retrospective nature, despite data being retrieved by a prospectively maintained institutional database. Moreover, the surgeons' experience was higher in OSE, but this is an intrinsic bias of studies comparing new techniques with the standard treatments. The present experience evaluated only the perioperative results because of an insufficient follow-up. Further studies are needed to verify the noninferiority of ERASE regarding long-term oncologic and functional outcomes.

CONCLUSION

ERASE is feasible and is associated with a PSM rate and perioperative outcomes, namely with WIT, complications, and early functional results, similar to those reported after OSE.

References

1. Campbell SC, Novick AC, Belldegrun A, et al. Guideline for management of the clinical T1 renal mass. *J Urol*. 2009;182:1271-1279.
2. Kutikov A, Vanarsdalen KN, Gershman B, et al. Enucleation of renal cell carcinoma with ablation of the tumour base. *BJU Int*. 2008;102:688-691.
3. Pertia A, Managadze L. Long-term results of simple enucleation for the treatment of small renal cell carcinoma. *Int Braz J Urol*. 2006;32:640-647.
4. Carini M, Minervini A, Masieri L, et al. Simple enucleation for the treatment of PT1a renal cell carcinoma: our 20-year experience. *Eur Urol*. 2006;50:1263-1268 [discussion: 1269-1271].
5. Carini M, Minervini A, Lapini A, et al. Simple enucleation for the treatment of renal cell carcinoma between 4 and 7 cm in greatest dimension: progression and long-term survival. *J Urol*. 2006;175:2022-2026 [discussion: 2026].
6. Minervini A, di Cristofano C, Lapini A, et al. Histopathologic analysis of peritumoral pseudocapsule and surgical margin status after tumor enucleation for renal cell carcinoma. *Eur Urol*. 2009;55:1410-1418.
7. Minervini A, Ficarra V, Rocco F, et al. Simple enucleation is equivalent to traditional partial nephrectomy for renal cell carcinoma: results of a nonrandomized, retrospective, comparative study. *J Urol*. 2011;185:1604-1610.
8. Minervini A, Vittori G, Lapini A, et al. Morbidity of tumour enucleation for renal cell carcinoma (RCC): results of a single-centre prospective study. *BJU Int*. 2012;109:372-377 [discussion: 378].
9. Laryngakis NA, Van Arsdalen KN, Guzzo TJ, Malkowicz SB. Tumor enucleation: a safe treatment alternative for renal cell carcinoma. *Expert Rev Anticancer Ther*. 2011;11:893-899.
10. Ficarra V, Benway BM, Bhayani SB, et al. Reply from authors re: Ricardo Brandina, Inderbir S. Gill. Robotic partial nephrectomy: new beginnings. *Eur Urol*. 2010;57:778-779; Eur Urol 2010;58:53-556.
11. Simhan J, Smaldone MC, Tsai KJ, et al. Perioperative outcomes of robotic and open partial nephrectomy for moderately and highly complex renal lesions. *J Urol*. 2012;187:2000-2004.
12. Lee S, Oh J, Hong SK, et al. Open versus robot-assisted partial nephrectomy: effect on clinical outcome. *J Endourol*. 2011;25:1181-1185.
13. Sprenkle PC, Power N, Ghoneim T, et al. Comparison of open and minimally invasive partial nephrectomy for renal tumors 4-7 centimeters. *Eur Urol*. 2012;61:593-599.

14. Benway BM, Wang AJ, Cabello JM, et al. Robotic partial nephrectomy with sliding-clip renorrhaphy: technique and outcomes. *Eur Urol*. 2009;55:592-599.
15. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150:604-612; Erratum in: *Ann Intern Med*. 2011;155:408.
16. Greene FL, Gospodarowicz M, Wittekend C, et al. *American Joint Committee on Cancer (AJCC) staging manual*. 7th ed. Philadelphia, PA: Springer; 2009.
17. Fuhrman SA, Lasky LC, Limas C. Prognostic significance of morphologic parameters in renal cell carcinoma. *Am J Surg Pathol*. 1982;6:655-663.
18. Eble JN, Sauter G, Epstein JI, et al. *Pathology and genetics of tumors of the urinary system and male genital organs*. *World Health Organization classification of tumors*. Lyon, France: IARC Press; 2004.
19. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205-213.
20. Nguyen MM, Gill IS. Halving ischemia time during laparoscopic partial nephrectomy. *J Urol*. 2008;179:627-632 [discussion: 632].
21. Thompson RH, Lane BR, Lohse CM, et al. Every minute counts when the renal hilum is clamped during partial nephrectomy. *Eur Urol*. 2010;58:340-345.
22. Khalifeh A, Autorino R, Hillyer SP, et al. Comparative outcomes and assessment of trifecta in 500 robotic and laparoscopic partial nephrectomy cases: a single surgeon experience. *J Urol*. 2013;189:1236-1242.
23. Benway BM, Bhayani SB, Rogers CG, et al. Robot assisted partial nephrectomy versus laparoscopic partial nephrectomy for renal tumors: a multi-institutional analysis of perioperative outcomes. *J Urol*. 2009;182:866-872.
24. Ficarra V, Bhayani S, Porter J, et al. Predictors of warm ischemia time and perioperative complications in a multicenter, international series of robot-assisted partial nephrectomy. *Eur Urol*. 2012;61:395-402.
25. Minervini A, Vittori G, Salvi M, et al. Analysis of surgical complications of renal tumor enucleation with standardized instruments and external validation of PADUA classification. *Ann Surg Oncol*. 2013;20:1729-1736.
26. Marszalek M, Carini M, Chlosta P, et al. Positive surgical margins after nephron-sparing surgery. *Eur Urol*. 2012;61:757-7763.

APPENDIX

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.urology.2013.08.080.

EDITORIAL COMMENT

The authors describe a well executed matched-pair comparison of robotic-assisted simple enucleation (ERASE) and open simple enucleation (OSE) for the treatment of renal cell carcinoma (RCC). The work joins a chorus of research that suggests nearly any open surgical procedure can be safely replicated using the robotic platform.

The primary advantage to ERASE seems to be the reduction in the necessity of pedicle clamping by 23% compared to OSE; however, it is not known if OSE requires pedicle clamping to the extent reported (93.8%). It is possible that OSE could be accomplished without pedicle clamping in fewer cases, and it can always be performed with renal cooling, mitigating the ischemic insult of pedicle clamping. A statistically significant reduction in blood loss was seen in the ERASE group, but the difference in volume of blood lost in the 2 groups was clinically insignificant (109 cc vs 181 cc). In nearly every other measure, ERASE is equivalent to OSE: hospitalization length, total, medical and surgical complication rates, and transfusion rate. ERASE was associated with prolonged warm ischemia times (WITs) compared to OSE, which can easily be attributed to the learning curve associated with ERASE; what is not known is if ERASE would add a second learning curve to a surgeon facile with standard robotic partial nephrectomy.

It is encouraging that the positive surgical margin rate was not different between the 2 arms, but this result must also be interpreted with caution. The authors represent a highly experienced surgical team with many years of experience with enucleation. Considering the loss of tactile feedback associated with robotic surgery and the lack of analogous robotic blunt dissecting tools (there is no robotic peanut dissector), it is predictable that incidental tumor incision/rupture will compromise the efficacy of the procedure in the hands of a less experienced surgeon compared to a wedge resection that includes a margin of normal parenchyma.

In an era of increasing scrutiny of health care expenditures, this work does not make a strong economical case for ERASE. Although costs were not included in this analysis, ERASE added nearly an hour of operative time along with the robotic instrumentation and the robot itself (estimated to add an average of $4000 US dollars per case compared to open partial nephrectomy[1]) for essentially equivalent results.

The authors' findings fortify the clear role for enucleation in the management of RCC. Emerging research suggests the quantity of residual normal renal mass is critical to preserving postoperative renal function,[2] and enucleation is certainly the best way to maximize existing renal parenchyma if partial nephrectomy is selected. Enucleation is a wise addition to the surgeon's armamentarium when approaching cortical RCC, particularly in those with pre-existing renal insufficiency, multiple renal masses, or a solitary kidney. However, ERASE requires further investigation (ideally a multi-institutional assessment of the oncological effectiveness of ERASE compared to standard robotic partial nephrectomy), before the feasibility of this new technique can be assured.

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References

1. Yu HY, Hevelone ND, Lipsitz SR, et al. Use, costs and comparative effectiveness of robotic assisted, laparoscopic and open urological surgery. *J Urol*. 2012;187:1392-1398.
2. Mir MC, Campbell RA, Sharma N, et al. Parenchymal volume preservation and ischemia during partial nephrectomy: functional and volumetric analysis. *Urology*. 2013;82:263-268.

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REPLY

This is the first study about the technical feasibility of endoscopic robotic-assisted simple enucleation (ERASE) of renal cell carcinoma. In our opinion, the primary advantage of ERASE is the combination of the benefits of the simple enucleation (SE), namely the maximum preservation of renal parenchyma, a proven oncologic safety and a low rate of calyceal tearing or vascular injuries that can minimize the risk of Clavien III complications,[1] with the advantages of mini-invasivity, such as reduced hospitalization length (in our analysis the median length of stay was 1-day shorter in ERASE vs open simple enucleation [OSE]), decreased pain, and faster recovery to an active life. Moreover, the 3D magnified vision, the extensive mobility of robotic arms, and their precision allows the surgeon to perform a more ergonomic and "intuitive" tumorectomy. Furthermore, the instruments used in robotic surgery are the ideal tools for conducting a safe SE. Indeed in right-handed surgeons, a Maryland bipolar forceps is used with the left hand to push the tumor upward, whereas the monopolar scissors, held with the right hand, can alternate the blunt dissection of the enucleation plane (done with a gentle pressure on the capsulated tumor tissue with the back of the instrument) with a prompt coagulation of small parenchymal vessels (done with the tip), which is easily identified with the visual magnification. These advantages, along with the well known effect of the pneumoperitoneum, allow the surgeon to avoid the clamping in selected cases. In our series, 40% of ERASE cases were treated without pedicle clamping, but this cannot be fully attributed to the above-mentioned advantages of robotic surgery, as the SE technique itself can minimize the risk of major bleeding from the surgical bed, regardless of the surgical approach, as previously reported by Kutikow et al.[2]

In our opinion, the ERASE procedure would not add a second learning curve to surgeons experienced with standard robotic partial nephrectomy, as we strongly believe that many surgeons are already adopting this technique in challenging cases, such as large, intraparenchymal or perihilar tumors. In such cases, in which the difficulty is the proximity of the tumor with major vascular and urinary structures, the adoption of the SE technique can be decisive, because the blunt dissection leads to their better identification and reduces the possibility of accidentally damaging them with a deeper excision. It is clear that to maintain the integrity of the tumor capsule during the enucleation plane development, the force exerted by the robotic instruments must always be under strict and continuous visual control, transmitting the pressure over a large surface of the tumor with the back of the monopolar scissors and bipolar Maryland forceps.

Finally, the postoperative surgical complications were lower in the ERASE group than in the OSE group (8.8% vs 13.8%). The lack of statistical significance may have been caused by the low number of events in the 2 matched groups. We cannot exclude that increasing the numbers would allow this difference to achieve the statistical significance.

In conclusion, this study represents the first analysis of SE done with the robotic system. ERASE will require further investigation, ideally multi-institutional, to assess the oncologic efficacy and the reproducibility of this technique, as recently has occurred for OSE.[3]

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References

1. Minervini A, Vittori G, Lapini A, et al. Morbidity of tumour enucleation for renal cell carcinoma (RCC): results of a single-centre prospective study. *BJU Int*. 2012;109:372-377 [discussion: 378].
2. Kutikov A, Vanarsdalen KN, Gershman B, et al. Enucleation of renal cell carcinoma with ablation of the tumour base. *BJU Int*. 2008;102: 688-691.
3. Minervini A, Ficarra V, Rocco F, , et alSATURN Project-LUNA Foundation. Simple enucleation is equivalent to traditional partial nephrectomy for renal cell carcinoma: results of a nonrandomized, retrospective, comparative study. *J Urol*. 2011;185:1604-1610.

http://dx.doi.org/10.1016/j.urology.2013.08.084