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Intraoperative ultrasound: technique and clinical experience in robotic-assisted renal partial nephrectomy for endophytic renal tumors

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Abstract

Objectives Surgical removal of completely endophytic renal tumors has presented great technical difficulties for surgeons. In this study, we aim to introduce the role and use of intraoperative ultrasound (IOUS) performed in robotic-assisted renal partial nephrectomy (RAPN) for endophytic renal tumors.

Methods We retrospectively assessed the demographics data and surgical outcomes of 58 consecutive endophytic renal tumor patients who were all attributed 3 points for the 'E' domain of the RENAL nephrometry score or 3 points for the exophytic rate of the PADUA score between October 2016 and September 2018. 38 patients who had undergone RAPN with IOUS were grouped. RAPN was carried out in another 20 patients without IOUS and these 20 patients were also grouped.

Results Patients in IOUS-guided group had significantly lower estimated blood loss ($P<0.001$), shorter warm ischemia time ($P=0.010$) and improved MIC (Margin, ischemia, and complications) rate ($P=0.026$) and Pentafecta achievement ($P=0.016$) compared to non IOUS-guided group. In multivariate logistic regression analysis, RAPN with IOUS was an independent predictor of MIC achievement (odds ratio 3.595; confidence interval 1.023–12.633; $P=0.046$). Surface-intermediate-base (SIB) margin score was lower for IOUS-guided group vs non IOUS-guided group ($P=0.029$).

Conclusion RAPN for completely endophytic renal tumors is a feasible procedure in terms of complication rates, oncologic and functional outcomes. A robotic ultrasound probe operated by console surgeon generates a favorable perioperative outcomes and surgical margin rates after RAPN.

Keywords Intraoperative ultrasound · Endophytic renal tumor · Robotic · Partial nephrectomy

Introduction

Since Da Vinci surgical system was approved by Food and Drug Administration (FDA) in 2000, it has been applied for radical prostatectomy, pyeloplasty, cystectomy and nephrectomy successfully [1–3]. With the advantages of three-dimensional stereoscopic optics, tremor elimination and 6° of motions, robotic-assisted laparoscopic surgery has been the contemporary trend for renal tumor surgeries for years.

Endophytic renal tumors as one of the complex renal tumors have always been a hot spot. Surgical removal of completely endophytic renal tumors presents great technical difficulties for localization and resection, and a higher likelihood of perioperative complications [4]. In this research, we describe our technique of intraoperative ultrasound in the setting of completely endophytic renal tumors, which means tumors are completely grew within renal parenchyma displayed in computed tomography (CT), ultrasound and

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magnetic resonance imaging (MRI). Surgeons do not have visual clues about tumor location when reaching the surface of the kidney. Traditionally, Laparoscopic partial nephrectomy (LPN) for endophytic renal tumors has problems in the high risk of complications. But now, robotic-assisted renal tumor enucleation for endophytic renal tumors is a feasible procedure in terms of complication rates, functional and oncologic outcomes [5]. Moreover, intraoperative ultrasound (IOUS) may play an important role in surgical management due to its localization of partially or completely endophytic renal tumors during robotic-assisted partial nephrectomy (RAPN) [6].

In this study, we examine the impact of intraoperative ultrasound for endophytic renal tumors on our large institutional experience in terms of intraoperative, early postoperative and pathological outcomes, and introduce the method of intraoperative ultrasound in localizing completely endophytic renal tumors during robotic-assisted renal partial nephrectomy.

Methods

Patient selection and outcome measurements

From 2016 to 2018, 58 consecutive patients with completely endophytic renal tumors who had undergone RAPN by a single surgeon at our center were retrospectively identified. Patients were all attributed 3 points for the 'E' domain of the RENAL nephrometry score or 3 points for the exophytic rate of the PADUA score [7, 8]. All patients received the same pre-operative diagnostic work-up, included contrast-enhanced CT, 3D CT and contrast-enhanced ultrasound. IOUS was applied for tumor localization in 38 of 58 cases, while preoperative contrast-enhanced CT and 3D CT were performed to localize the tumor in 20 of 58 cases as a result of the failure of tumor detection by preoperative ultrasound. We reviewed medical records to collect demographic data, preoperative surgical history, operative detail, postoperative outcomes and acquired follow-up data by telephone and outpatient follow-up. All specimens for histological analysis were assessed by two experienced pathologists. These two pathologists evaluated the positive surgical margin rate, the minimum distance between carcinoma tissue and margins and Surface-Intermediate-Base (SIB) margin score [9].

Surgical technique

IOUS-guided group

The ultrasonic machine is BK Medica FF880, as the probe is BK Medica 8826. We placed patients in a modified flank position with a 45° lateral tilt before the operation began. Initial steps of the procedure included renal vessels dissection and exposure of the kidney by dissecting the Gerota's fascia. A drop-in probe which was controlled by console surgeon attached the surface of the kidney to localize the tumor. We presented the step-by-step surgical technique in Fig. 1. There were four steps to localize the tumor: attach the probe to the renal surface perpendicularly and closely. Second, move the probe slowly to find the longest diameter of the tumor and make sure the tumor is in the center of the ultrasound image. Third, measure the longest diameter of the tumor and the minimum distance between tumor and renal surface. Fourth, based on the measurements, mark the resection range on the renal surface roughly with monopolar cautery. The renal artery was clamped and the pointcut was based on the previous marker margin. The renal parenchyma was incised by electrotome to find the tumor pseudocapsule. Along the pseudocapsule, the console surgeon resected the tumor by sharp and blunt dissection and maintained the tumor integrity. Hemostasis procedure included cautery, hemostatic agents, and renorrhaphy. Renorrhaphy is performed in one layer with a 1–0 Quill suture on an SH needle with a knot and Hem-o-Lok clip is applied to the free end. A hemostatic agent was also applied. When hemostasis was confirmed, the clamp was removed by the assistant. Finally, the tumor was placed in a retrieval bag and removed.

Non IOUS-guided group

Contrast-enhanced CT and 3D CT could sensitively demonstrate the size, shape, and the extent of endophytic renal tumors. We reconstructed kidney from the scanned images by helical CT and observed the size, location and depth of the tumor for the purpose of assessing the risk of renal failure and hemorrhage postoperatively and deciding the resection range. In addition, the procedure of tumor resection was similar to IOUS-guided group.

Statistical analysis

Demographic and perioperative data were analyzed using descriptive statistics. Counts of frequencies were expressed as percentages. In order to display advantages, we recorded operative time, estimated blood loss, hospital stay and warm ischemia time of each operation collected in the study group. Data were presented as the mean (SD) or frequency (%) respectively for continuous and categorical variables. Nonnormal data were presented as the median (IQR) for continuous variables. Comparisons were performed using Student's *T* test or Mann–Whitney *U* test for continuous data and chi-square or Fisher's exact for categorical data. For all statistical analyses, a two-sided P value < 0.05 was considered statistically significant. All analyses were performed using SPSS 25.0 statistical package.

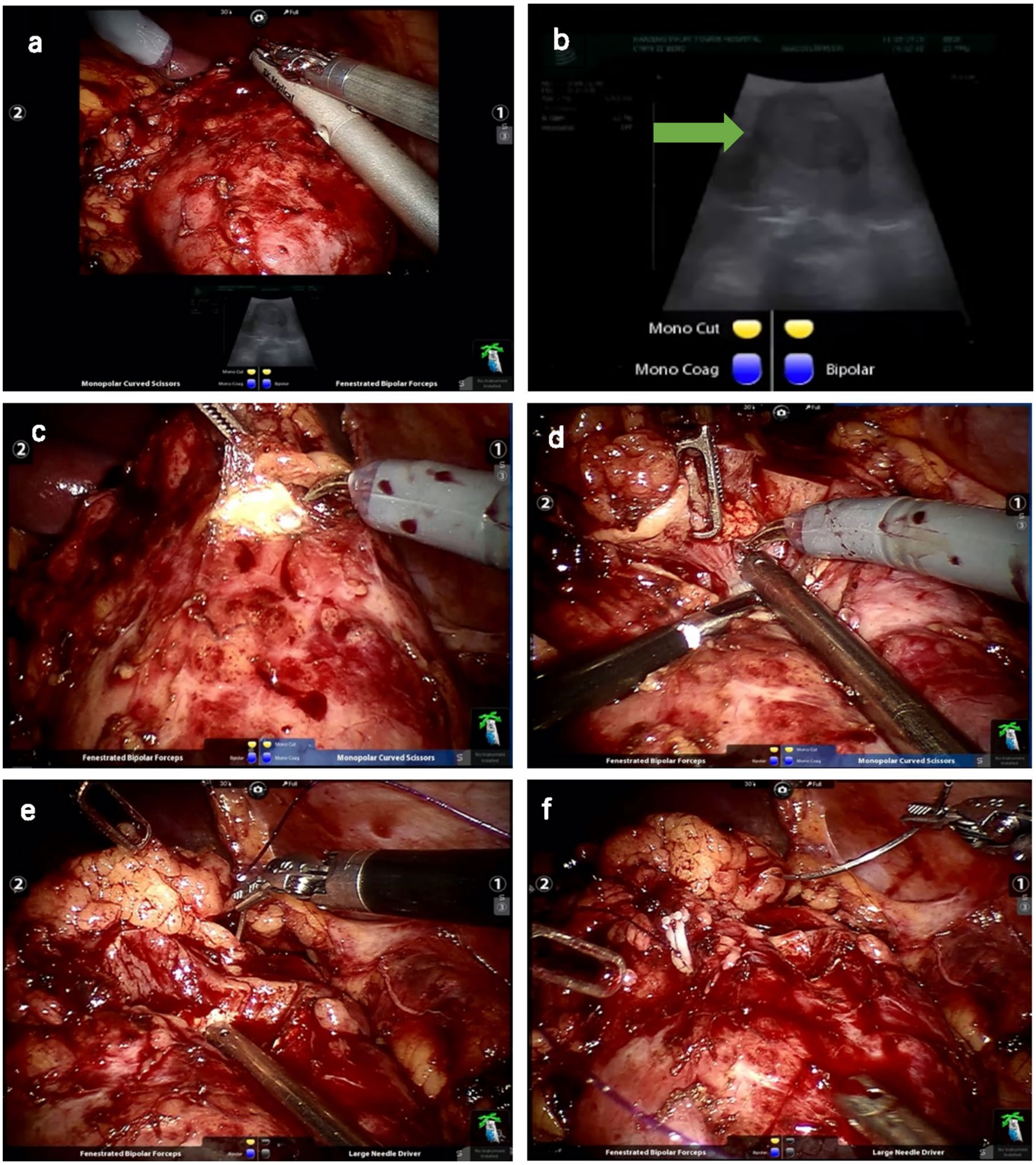

Fig. 1 Step-by-step surgical technique for completely endophytic renal tumor. **a** Intraoperative ultrasound locates the endophytic renal tumor. **b** An intraoperative ultrasound image showing a tumor margin (green arrow). **c** Resection ranges are marked on the renal surface roughly with monopolar cautery. **d** Along the pseudocapsule, surgeon enucleates the tumor by sharp and blunt dissection. **e** Renorrhaphy is performed in one layer with a 1–0 Quill suture on an SH needle with a knot. **f** Hem-o-Lok clip is applied to the free end

Results

Overall, 58 patients underwent successful operations for endophytic renal tumors and 38 patients underwent RAPN procedures requiring IOUS. Demographics and tumor characteristics were listed in Table 1.

We summarized the main surgical outcomes in Table 2. Estimated blood loss (EBL) (144.7 vs 257.5 ml; $P<0.001$) and warm ischemia time (WIT) (20.4 vs 25.6 min; $P=0.010$) were significantly lower in IOUS-guided group compared to non IOUS-guided group. There was no significant difference in operation time (OT) ($P=0.415$) and hospital stay (HS) ($P=0.411$). Perioperative complications occurred in 13 of 58 patients totally, of these, complications occurred in 6 cases in IOUS-guided group and 7 in non IOUS-guided group. In IOUS-guided group, surgical complications

Table 1 Demographics and tumor characteristics

Variable	IOUS-guided	Non IOUS-guided	*P*
No. of patients	38	20	
Female gender, *n* (%)	25 (38.3%)	10 (50.0%)	0.243
Solitary kidney, *n* (%)	2 (5.3%)	1 (5.0%)	1
Age, years, mean ± SD	50.7 ± 11.9	53.9 ± 13.6	0.364
Tumor size, cm, mean ± SD	2.9 ± 0.7	3.2 ± 0.8	0.137
Left side, *n* (%)	18 (47.4%)	11 (55.0%)	0.581
Clinical T stage, *n* (%)			1
1a	34 (89.5%)	18 (90.0%)	
1b	4 (10.5%)	2 (10.0%)	
2a	0	0	
3a	0	0	
Tumor polarity, n (%)			0.952
Superior/inferior	13 (34.2%)	7 (35.0%)	
Middle	25 (65.8%)	13 (65.0%)	
Tumor position, *n* (%)			0.995
Anterior	17 (44.7%)	9 (45.0%)	
Posterior	13 (34.2%)	7 (35.0%)	
Neither	8 (21.1%)	4 (20.0%)	
Urinary collecting system, *n* (%)			0.745
Not involved	25 (65.8%)	14 (70.0%)	
Involved	13 (34.2%)	6 (30.0%)	
Renal sinus, *n* (%)			0.739
Not involved	23 (60.5%)	13 (65.0%)	
Involved	15 (39.5%)	7 (35.0%)	
Renal rim, *n* (%)			0.521
Lateral	26 (68.4%)	12 (60.0%)	
Medial	12 (31.6%)	8 (40.0%)	
PADUA score, *n* (%)			0.902
Low (6–7)	0 (0)	0 (0)	
Moderate (8–9)	12 (31.6%)	6 (30.0%)	
High (10–13)	26 (68.4%)	14 (70.0%)	
RENAL score, *n* (%)			0.913
Low (4–6)	6 (15.8%)	4 (20.0%)	
Moderate (7–9)	27 (71.1%)	14 (70.0%)	
High (10–12)	5 (13.2%)	2 (10.0%)	

IOUS intraoperative ultrasound, *PADUA* preoperative aspects and dimensions used for an anatomical classification

Table 2 Comparison of operative outcomes

Variable	IOUS-guided	Non IOUS-guided	*P*
OT, min, mean ± SD	201.2 ± 56.3	189.8 ± 36.2	0.415
EBL, ml, mean ± SD	144.7 ± 88.3	257.5 ± 59.5	< 0.001
HS, days, mean ± SD	8.0 ± 2.4	7.5 ± 2.2	0.411
WIT, min, mean ± SD	20.4 ± 7.5	25.6 ± 6.0	0.010
Postoperative complications, *n* (%)	6 (15.8%)	7 (35.0%)	0.755
Clavien–Dindo grade I	3 (7.9%)	5 (25.0%)	
Clavien–Dindo grade II	2 (5.3%)	2 (10.0%)	
Clavien–Dindo grade III	1 (2.6%)	0	
Unclamped, *n* (%)	2 (5.3%)	0	0.540

OT operative time, *EBL* estimated blood loss, *HS* hospital stay, *WIT* warm ischemia time included postoperative fever in 2 (5.3%) patients, slightly gross hematuria in 1 (2.6%), blood loss treated with transfusions in 2 (5.3%) and a second invasive procedure in 1 (2.6%). In non IOUS-guided group, there were 2 (10.0%) patients with slightly urine leakage, 2 (10.0%) patient with postoperative fever, 1 (5.0%) patient with limited hematoma, and 2 (10.0%) patients with blood loss needing transfusions.

Tumor results and follow-up data were showed in Table 3. Pathologic results showed that 49 cases were malignant while 9 cases were benign. A margin, ischemia, and complications (MIC) binary system and Pentafecta, defined as combination of WIT < 25 min, negative surgical margins, no perioperative complications, eGFR > 90% of preop, and no chronic kidney disease upstaging, were to evaluate the cancer control, optimal functional outcomes, and safety [10, 11]. There was an improved rate of MIC ($P=0.026$) and Pentafecta ($P=0.016$) achievement in IOUS-guided group. The minimum distance between cancer tissue and margins of IOUS-guided group was significantly less than that of non IOUS-guided group ($P=0.017$). Statistical analysis indicated that IOUS-guided group had significant improvement in SIB scores compared to non IOUS-guided group ($P=0.029$). Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease formula before operation and six months after operation. The IOUS-guided group had similar outcomes to the non IOUS-guided group, including positive margins rate (7.9% vs 15.0%; $P=0.405$), eGFR preoperatively (95.1 vs 99.3 ml/min; $P=0.695$), and eGFR 6 months postoperatively (89.0 vs 88.3 ml/min; $P=0.954$). However, the percent of eGFR decline was significantly lower in the IOUS-guided (6.4% vs 9.9%; $P=0.007$). At a median follow-up of 30 months (range 17–40 months), no patients developed a local recurrence.

Table 4 showed logistic regression model predicting MIC achievement. In univariate logistic regression models, RAPN with IOUS was associated with a significantly improved achievement of MIC (odds ratio 4.125; confidence interval 1.243–13.690; $P=0.021$). The results were confirmed by multivariate logistic regression models. After adjustment for age, gender, clinical T stage and tumor side, RAPN with IOUS emerged as predictor of MIC achievement (odds ratio 3.595; confidence interval 1.023–12.633; $P=0.046$).

A 49-year-old patient was presented with an interpolar completely endophytic left renal tumor. A computed tomography scan demonstrated a 2.5-cm solid, enhancing lesion infiltrating the renal pelvis (Fig. 2). RAPN was performed without any perioperative complications, with a WIT of 17 min. Pathology showed renal cell carcinoma (RCC), clear cell type, Fuhrman nuclear grade 2, parenchymal and soft tissue margins of resection were negative for tumor. The SIB score is 1 (Fig. 3).

Table 3 Comparison of tumor results and follow-up data

Variable	IOUS-guided	Non IOUS-guided	*P*
Pathology size, cm, mean ± SD	2.7 ± 0.8	3.0 ± 0.8	0.183
eGFR preop, ml/min, median (IQR)	95.1 (79.7–105.6)	99.3 (80.0–109.6)	0.695
eGFR 6 months po, ml/min, median (IQR)	89.0 (74.8–98.5)	88.3 (73.3–100.8)	0.954
eGFR percent decline, median (IQR)	6.4 (4.0–9.4)	9.9 (6.3–13.7)	0.007
Malignant, *n* (%)	32 (84.2%)	17 (85.0%)	1.000
Minimum distance to margins, *n* (%)			0.017
< 1 mm	22 (57.9%)	4 (20.0%)	
1–3 mm	9 (23.7%)	10 (50.0%)	
> 3 mm	7 (18.4%)	6 (30.0%)	
SIB margin score, *n* (%)			0.029
0	8 (21.1%)	2 (10.0%)	
1	11 (28.9%)	3 (15.0%)	
2	11 (28.9%)	2 (10.0%)	
3	5 (13.2%)	5 (25.0%)	
4	2 (5.3%)	6 (30.0%)	
5	1 (2.6%)	2 (10.0%)	
Positive margins, *n* (%)	3 (7.9%)	3 (15.0%)	0.405
MIC achievement, *n* (%)	22 (57.9%)	5 (30.0%)	0.026
Pentafecta achievement, *n* (%)	24 (63.2%)	6 (30.0%)	0.016

MIC defined as combination of WIT < 20 min, negative surgical margins and no perioperative complications. Pentafecta defined as combination of WIT < 25 min, negative surgical margins, no perioperative complications, eGFR > 90% of preop, and no chronic kidney disease upstaging

eGFR estimated glomerular filtration rate, *preop* preoperatively, *po* postoperatively; *SIB* surface-intermediate-base, IQR interquartile range

Table 4 Logistic regression model predicting MIC achievement

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Age	0.980	0.939–1.022	0.349	0.970	0.923–1.020	0.236
Gender (male vs female)	0.449	0.152–1.330	0.148	0.387	0.108–1.381	0.143
Clinical T stage (T1a vs T1b)	0.540	0.091–3.210	0.498	0.328	0.041–2.607	0.292
Tumor side (left vs right)	0.659	0.233–1.859	0.431	0.554	0.166–1.843	0.335
With IOUS vs without IOUS	4.125	1.243–13.690	0.021	3.595	1.023–12.633	0.046

CI confidence interval, *OR* odds ratio, *IOUS* intraoperative ultrasound

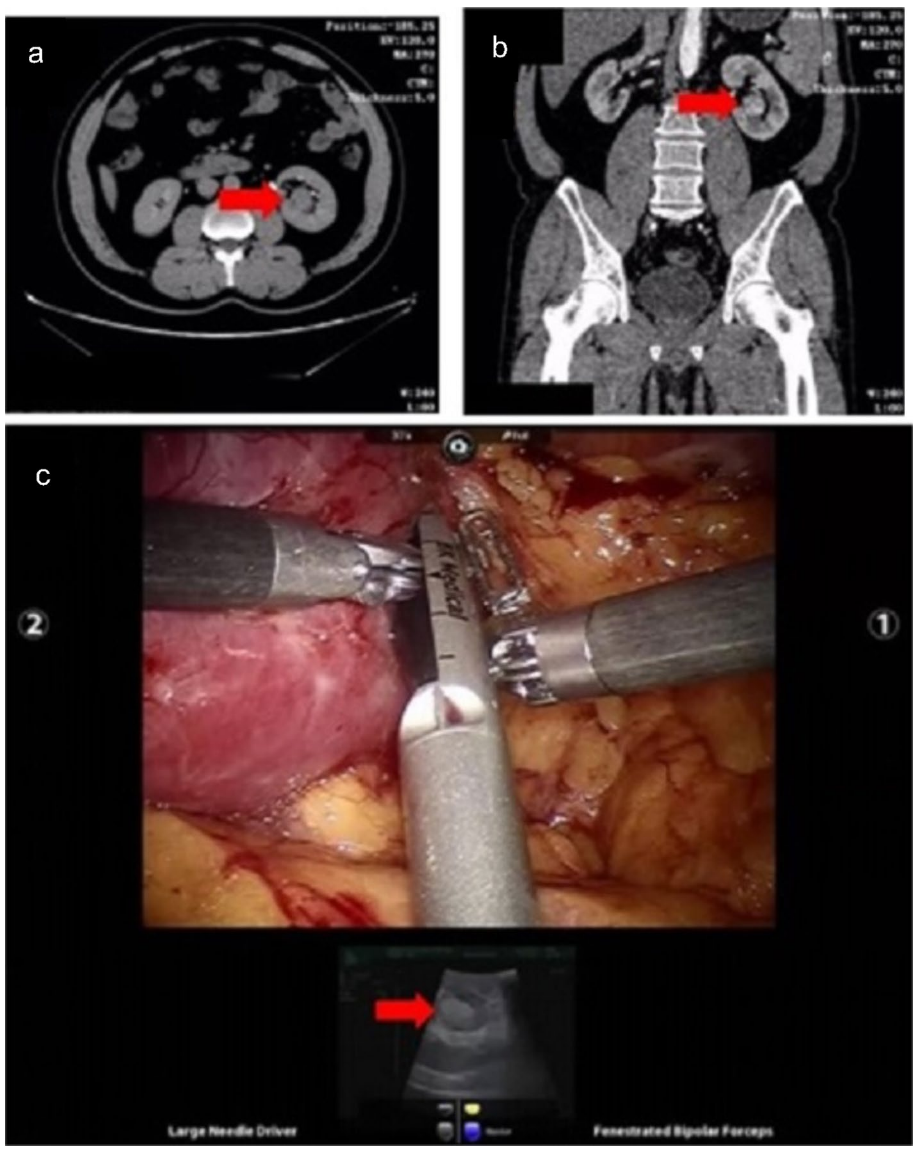

Fig. 2 A 49-year-old patient with 2.5-cm interpolar completely endophytic left renal tumor (red arrow). **a** Computed tomography (CT) transverse section. **b** CT coronal section. **c** Intraoperative US using Robotic Transducer (BK Medical 8826)

Discussion

The robotic advantages and increasing experience in minimally invasive nephron-sparing surgery allow experienced urological surgeons to perform robotic-assisted renal tumor enucleation in more challenging cases. Of these, completely endophytic tumors represent a unique case scenario. This research is to demonstrate that IOUS may play an important role in surgical management, especially for completely endophytic renal tumors. With robotic-assisted renal tumor enucleation, the tactile feedback inherent in

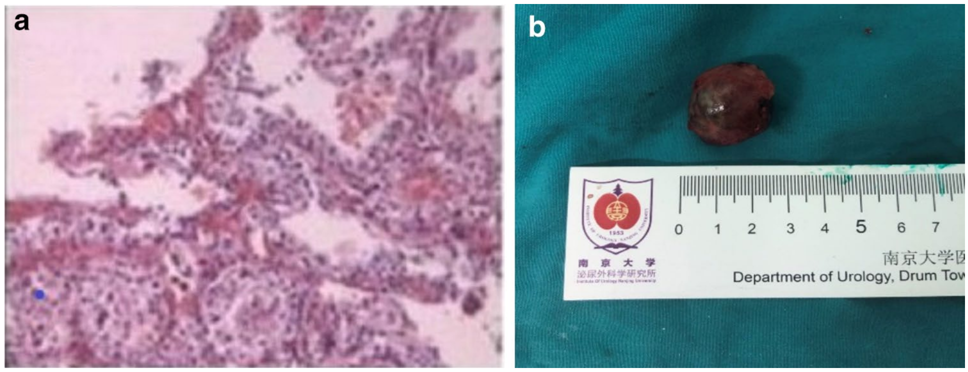

Fig. 3 **a** Pathology shows renal cell carcinoma, clear cell type, Fuhrman nuclear grade 2, and parenchymal and soft tissue margins of resection negative for tumor. **b** The size of resected tumor is 2.5 cm × 2.2 cm × 2.0 cm, SIB margin score is 1

open surgical procedures is reduced. IOUS provides more-detailed real-time guidance in the operating room for completely endophytic tumors.

Matin and Gill were the early supporter of IOUS who introduced using IOUS in renal cyst decortication, nephrolithotomy, and cryosurgery [12]. Gill et al. also reviewed the use of IOUS in their extensive laparoscopic partial nephrectomy series [13] and described laparoscopic ultrasonography as a step to decide on the final resection line when performing LPN [14]. Gilbert et al. reported two cases to introduce the use of intraoperative ultrasonography to localize tumors not palpable at operation [15]. Assimos et al. considered that IOUS for tumor identification is favorable for negative surgical margins [16]. In an analysis of 41 kidney surgeries, Marshall et al. found that IOUS helps to determine the extent of tumor, multicentricity, venous extension and associated cysts [17]. Polascik et al. evaluated 100 cases and reported that using IOUS is beneficial in defining preoperative indeterminate renal lesions and in evaluating extrarenal structures for tumor involvement [18]. Fazio et al. reviewed outcomes for intraoperative laparoscopic ultrasonography (ILUS) in 35 LPN procedures. Ultrasonography was considered essential to the success of LPN procedures and all the incised margins were negative [19]. Their center marked out a 1-cm perimeter of normal renal parenchyma on the basis of ILUS findings and reassessed margin adequacy by ILUS scanning along the marked line. Priya R. Bhosale et al. concluded that IOUS helps to characterize the primary tumor and the extent of renal involvement in real time, particularly central tumors that are not visible during open partial nephrectomy [20]. Moreover, Rogers et al. found color Doppler may be used to identify adjacent vessels and the renal capsule could be scored with monopolar cautery to delineate the boundaries of resection [21]. The robotic ultrasound probe appears to be more flexible because it can be moved by the surgeon, achieving appropriate angles while maintaining perpendicular contact of the transducer with the kidney surface [22]. The other benefit of intraoperative ultrasound is that it can reevaluate the resection margins based on acoustic shadowing which is created by trapped air between the probe and the parenchymal furrow after deeply marking the line of excision on the renal parenchyma [23].

Our study was not only designed to compare the two methods, but also to share our experience with IOUS and surgical techniques and describe our surgical outcomes with RAPN for patients with completely endophytic renal tumors. The technical feasibility and oncologic safety of RAPN for endophytic renal tumors depended on the presence of tumor pseudocapsule. The pseudocapsule could prevent the tumor from infiltrating the normal parenchyma. The IOUS was valuable for the accurate find of tumor pseudocapsule. We resected the tumor just along the pseudocapsule or a few millimeters away from the tumor margins and the single-layer suture technique was performed for renal reconstruction to prevent bleeding [24]. However, both groups had 3 positive margins respectively. The presence of positive margins as a risk factor for disease recurrence after partial nephrectomy was controversial. As indicated by Marszalek's report, most patients with positive margins after partial nephrectomy remained without disease recurrence [25]. In addition, the robotic probe could be performed to ensure surgical margins during RAPN. After tumor removal and before performing hemostasis, the surgeon placed the specimen into a retrieval bag filled with saline solution. The robotic probe was then placed into the retrieval bag and an ultrasonographic scan was performed to evaluate if the tumor's pseudocapsule was complete [26].

The loss of renal function after RAPN can be affected by several factors. Preoperative variables such as age, preoperative renal function, and intraoperative variables such as WIT and quantity of normal renal parenchyma removed may affect loss of renal function after RAPN. Choi et al. raised that resected volume of marginal healthy tissue, and WIT were independent predictors for functional reduction of the affected kidney [27]. Based on the present analysis, we discovered significantly shorter WIT, nearer distance from cancer to margins and lower SIB margin score in IOUS-guided group which implied more renal function in the affected kidney may be maintained. IOUS-guided group also had a more favorable MIC and Pentafecta achievement. This finding could be explained by the fact that better perioperative outcomes may be achieved when using ultrasound during RAPN. In 2 cases, the operations were completed without clamping the renal artery since there is little bleeding, the surgeon maintained a clear field of vision during the procedure. The unclamping of renal artery reduced the risk of renal necrosis by avoiding ischemia–reperfusion injury. IOUS-guided group seemed to offer similar perioperative complications and transfusion rate as non IOUS-guided group for completely endophytic renal tumors. The occurrence rate of perioperative complications and transfusion would be closely related to the experience and technique that the console surgeon had and correlated to the basic status of the patients. We followed up these patients for 6 months to evaluate renal functions by means of eGFR test. As a result, IOUS-guided group achieved more satisfactory results.

There are several limitations to this study. This is a retrospective study, a major limitation of the single-institute study is relatively small sample size due to the fact that endophytic renal tumors are rare and sometimes resected under open procedure or laparoscopic procedure. We also need more new techniques to compare, such as near-infrared fluorescence imaging which could differentiate normally perfused healthy parenchyma from non-perfused renal tumors, and more prospective researches to verify the present findings. Furthermore, the absent long-term follow-up failed to compare the prognosis between IOUS-guided group and non IOUS-guided group. A long-term complete follow-up is expected to begin in the near future.

Conclusion

RAPN for completely endophytic renal tumors is a feasible procedure in terms of complication rates, oncologic and functional outcomes. A robotic ultrasound probe operated by console surgeon generates a favorable perioperative outcomes and surgical margin rates after RAPN.

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Availability of data and materials The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflict of interest The authors declare there is no conflicts of interest regarding the publication of this paper.

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