J Cancer Res Clin Oncol (2017) 143:905–912
DOI 10.1007/s00432-017-2342-5

ORIGINAL ARTICLE – CLINICAL ONCOLOGY

Comparing renal function preservation after laparoscopic radio frequency ablation assisted tumor enucleation and laparoscopic partial nephrectomy for clinical T1a renal tumor: using a 3D parenchyma measurement system

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Received: 26 October 2016 / Accepted: 3 January 2017 / Published online: 10 February 2017

Abstract
Purpose To compare the renal function preservation between laparoscopic radio frequency ablation assisted tumor enucleation and laparoscopic partial nephrectomy.
Methods Data were analyzed from 246 patients who underwent laparoscopic radio frequency ablation assisted tumor enucleation and laparoscopic partial nephrectomy for solitary cT1a renal cell carcinoma from January 2013 to July 2015. To reduce the intergroup difference, we used a 1:1 propensity matching analysis. The functional renal parenchyma volume preservation were measured preoperative and 12 months after surgery. The total renal function recovery and spilt GFR was compared. Multivariable logistic analysis was used for predictive factors for renal function decline.
Results After 1:1 propensity matching, each group including 100 patients. Patients in the laparoscopic radio frequency ablation assisted tumor enucleation had a smaller decrease in estimate glomerular filtration rate at 1 day (−7.88 vs −20.01%, $p<0.001$), 3 months (−2.31 vs −10.39%, $p<0.001$), 6 months (−2.16 vs −7.99%, $p=0.015$), 12 months (−3.26 vs −8.03%, $p=0.012$) and latest test (−3.24 vs −8.02%, $p=0.040$), also had better functional renal parenchyma volume preservation (89.19 vs 84.27%, $p<0.001$), lower decrease of the spilt glomerular filtration rate (−9.41 vs −17.13%, $p<0.001$) at 12 months. The functional renal parenchyma volume preservation, warm ischemia time and baseline renal function were the important independent factors in determining long-term functional recovery.
Conclusions The laparoscopic radio frequency ablation assisted tumor enucleation technology has unique advantage and potential in preserving renal parenchyma without ischemia damage compared to conventional laparoscopic partial nephrectomy, and had a better outcome, thus we recommend this technique in selected T1a patients.

Keywords Renal tumor · Functional renal parenchymal · Ablation techniques · Three-dimensional volume measurement

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Introduction

Renal cell carcinomas are diagnosed at Clinical T1a more frequently because of the wide use of abdominal imaging (Gill et al. 2010). And the minimally invasive laparoscopic partial nephrectomy (LPN) becomes the standard treatment of small renal masses (SRMs). PN provides equivalent oncological and superior renal function preservation compared to radical nephrectomy (Campbell et al. 2009), however, during the PN procedure, temporary hilar clamping may cause renal ischemia–reperfusion injury which can reduce the postoperative renal function. Therefore, some medical advances have provided some valid treatment options to avoid warm ischemia insult, including cryoablation, radiofrequency ablation and microwave ablation for the management of SRMs (Zargar et al. 2016; Venkatesan et al. 2011). However, those options probably increase the risk of local recurrence and also the patient psychological burden, and the follow-up examination was required more frequently. A randomized trial, which preformed in our center had demonstrated that laparoscopic radio frequency ablation assisted tumor enucleation (LRATE) without clamping the renal hilus, had several advantages and preserved more renal function (Huang et al. 2016). The study showed that LRATE had better renal function preserving after PN surgery due to the zero ischemia. While, the RCT study was limited with a small sample and some patients have lost their follow-up information. A more comprehensive study with a relatively large number of patients to compare the long-term renal function after LRATE and conventional LPN was limited. Moreover, some researches suggested that the preoperative glomerular filtration rate (GFR) and functional renal parenchyma volume preservation (FRVP) might play more important roles in protecting the postoperative renal function in a long-term period (Mir et al. 2013, 2014, 2015). So the aim of this work was also to evaluate the performance of LRATE in protecting renal function and FRVP compared to LPN, and using a novel three-dimensional renal volume system to predict long-term outcome.

Patients and methods

Patients and enter criterion

Through oncologic databases approved by our institution review board, we selected 119 patients who underwent LRATE and 127 underwent LPN for solitary cT1a RCC from January 2013 to July 2015. Only those with normal contralateral renal function, complete perioperative information and follow-up message more than 12 months, as well as the pathological confirmation of RCC were concerned in the study. The patients with hereditary RCC, bilateral tumors, synchronous multiple masses, metastatic disease, and past surgery history were excluded. To reduce the intergroup difference, we used a 1:1 propensity matching according to the patient baseline characteristic, such as age, sex, BMI, rate of hypertension, max tumor size, R.E.N.A.L score and preoperative serum creatinine (Scr), also the pathological data was attached.

Surgical methods

The LRATE technique has been described in detail previously (Huang et al. 2016). The renal artery was usually not isolated; radio frequency ablation (RFA) was performed after the tumor was determined under direct vision and laparoscopic ultrasonography, using 1–4 cycles for 2–8 min each depending on tumor size and depth. Laparoscopic enucleation without hilar clamping was then performed. The tumor was enucleated by blunt dissection and scissors on the natural transitional zone (between the pseudocapsule and normal parenchymal). Enucleation bed bleeding was controlled by unipolar or bipolar coagulation or ablation with a 1-cm electrode for a few minutes. The LPN procedure also has been described in detail before (Haber and Gill 2006). The renal hilum was clearly isolated and then the artery only was clamped during the entire tumor excision and renal repairement process in all cases.

Software and FRVP measurement

All contrast-enhanced computerized tomography (CT) examinations were performed using a 64-multidetector CT scanner (VCT LightSpeed, GE Healthcare). Patients were instructed to drink 1000 mL of water before the examination. Images in four phases were obtained in a craniocaudal direction. The unenhanced and arterial, portal, and nephrographic excretory phases spanned the area of the kidneys, area from the diaphragm to the lower pole of the kidneys, and the kidneys to the symphysis pubis, respectively. Contrast-enhanced images were obtained after intravenous administration of 150 mL of non-ionic contrast medium (Iopamiro, Bracco, Milan, Italy). The scanning parameters of each phase were 110–380 mA, 1.25-mm, and 1.375 of tube current using current modulation software, collimation, and pitch, respectively. The volume of tumor and functional renal parenchyma were measured in workstation (Healthcare, GE, USA) based on venous phase, and excluded the reanl sinus fat, collecting system, and especially the volume of tumor. FRPV were calculated (Fig. 1) according to the difference in the functional renal parenchymal volume between pre- and post-operation (12 months) (Mir et al. 2013; Liu et al. 2015; Simmons et al. 2011).

Outcome measures

First, tumor complexity of all the patients were accessed by preoperative images according to the R.E.N.A.L. nephrometry score (12). And the record information included patients' characteristic, tumor diameter, warm ischemia time (WIT) and the estimate blood loss (EBL). Total renal function was evaluated by Scr levels, and eGFR was assessed using the Modification of Diet in Renal Disease (MDRD) study equation (Matsuo et al. 2009), $\text{eGFR} = 194 \times (\text{serum creatinine})\ \text{mg/dL}^{-1.094} \times \text{age}^{-0.287} \times 0.739(\text{if female})$, and the spit GFR (sGFR) of each kidney was accessed by $^{99\text{m}}$Tc-DTPA renal scintigraphy preoperative and nearly 12 months after surgery.

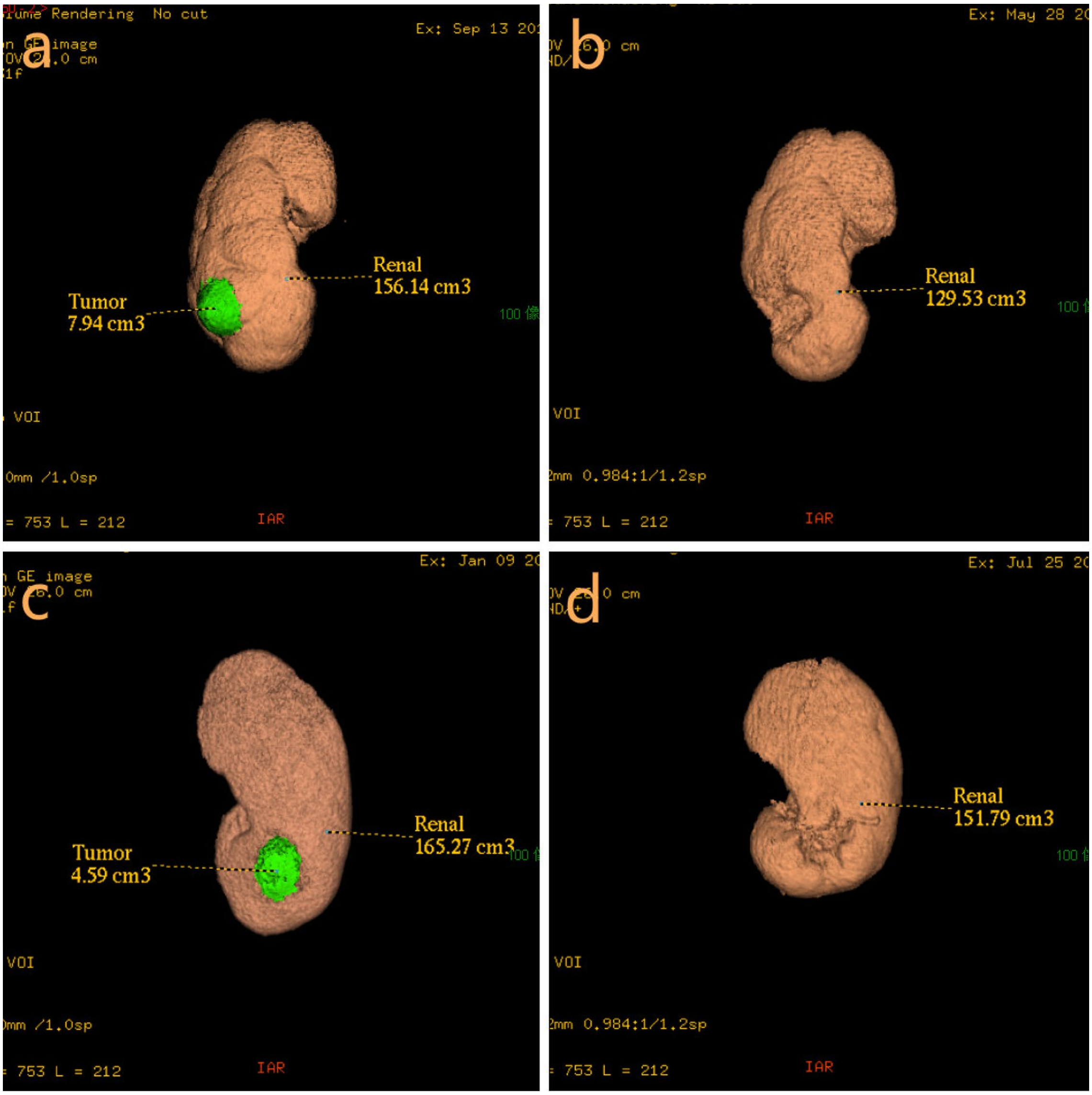

Fig. 1 3D renal parenchyma volume measurement system. Example of measurement of functional renal parenchyma volume preservation (FRVP) after LPN (**a, b**) and LRATE (**c, d**). **a, c** Preoperative normal renal parenchyma (*yellow*) and tumor (*green*) were reconstructed based on the 3D system, **b–d** FRVP at 12 months after surgery. **a, b** A patient with 3.1 max diameter underwent LPN and the postoperative FRVP rate was 129.53/156.14 × 100 = 82.96%, and **c, d**, patient with 2.1 max diameter underwent LRATE, the FRVP rate was 91.84%

Scr levels were evaluated preoperatively, and at 1 day, 3, 6, 12 months after PN surgery in every patient. Moreover, we also analyzed the last data as latest level. Follow-up examinations included blood chemistey studies, chest CT, and abdomen CT or magnetic resonance imaging (MRI) at 3 and 6 months postoperatively, and every 6 months with 3 years follow-up, then annual test. Importantly, patients must take contrast CT at nearly 12 months meanwhile. The FRVP measurements were using the images of preoperative and 12 months after surgery, respectively. The comparison of FRVP and renal functional recovery based on the eGFR was the primary outcome, and the change of the spilt renal function according to the renal sctintigraphy at 12 months was the second outcome. We also compared the postoperative status of CKD between two groups.

Statistical analysis

Continuous variables were compared using the Student's *t* test or Mann–Whitney test. Categorical variables were compared using the Pearson's Chi-square or Fisher's exact tests. Multivariable logistic regression analysis was used for predictive factors for the presence of renal function decrease over 10% evaluated by eGFR at latest time. All p values were two-tail and $p < 0.05$ was considered significant. Data were analyzed using IBM SPSS statistical version 19.0.

Results

Table 1 showed that the baseline characteristics of the two groups, 119 patients in the LRATE group and 127 underwent LPN. The R.E.N.A.L score was significant difference between LRATE and LPN ($p=0.013$), LPN patients had higher tumor complexity. And other basic information, such as sex, age, rate of hypertension, BMI, max tumor size, preoperative Scr were similar in two groups before matching. After 1:1 propensity matching, each group including 100 patients. The rate of hypertension was 37 and 32% in each group. And the R.E.N.A.L score ($p=0.274$), preoperative Scr ($p=0.174$), BMI ($p=0.072$), max tumor diameter ($p=0.174$) were not significant in two groups. The LPN surgery had more EBL than LRATE (125 vs 80, $p<0.001$) with a median WIT of 23 min. The pathological of all the patients was showed as well, and the most were clear renal cell carcinoma, the oncocytoma were smallest which was proved be conservatively managed with active surveillance (Liu et al. 2016).

Table 2 showed the comparison of parenchyma volume indicated that the LRATE had less normal parenchyma loss (−14.60 vs −21.26 cm^3, $p<0.001$), and better FRVP rate (89.19 vs 84.27%, $p<0.001$) in the tumor side kidney. The relative decrease of eGFR was presented in Fig. 2. LRATE had a smaller decrease in eGFR at 1 day (−7.88 vs -20.01%, $p<0.001$), 3 months (−2.31 vs −10.39%, $p<0.001$), 6 months (−2.16 vs −7.99%, $p=0.015$), 12 months (−3.26 vs −8.03%, $p=0.012$) and latest (−3.24 vs −8.02%, $p=0.040$).

Preoperative and postoperative spilt GFR (sGFR) evaluated by renal scan were analyzed in Table 3. The change sGFR of health side kidney had no significant difference between two groups (3.84 vs 5.90%, $p=0.412$). On the contrary, the tumor side, LRATE group has a lower decrease (−9.41 vs −17.13%, $p<0.001$). The factors may impact the long-term renal function were explored as well (Table 4). Multivariable analysis was presented, respectively, and on multivariable results, peroperative-eGFR (OR 1.102, $p<0.001$), FRVP% (OR 0.001, $p=0.001$),

Table 2 Parenchymal volume analysis between LRATE and LPN (Post-matching)

	LRATE	LPN	*p* value
Mean Pre-H V ± SD (cm^3)	147.11 ± 22.74	142.98 ± 26.75	0.241
Mean Post-H V ± SD (cm^3)	148.22 ± 22.86	144.22 ± 25.82	0.248
ΔH V ± SD (cm^3)	1.12 ± 5.47	1.24 ± 5.16	0.868
Mean Pre-T V ± SD (cm^3)	137.27 ± 22.51	138.07 ± 23.24	0.804
Mean Post-T V ± SD (cm^3)	122.67 ± 21.95	116.81 ± 22.57	0.064
ΔT V ± SD (cm^3)	−14.60 ± 4.66	−21.26 ± 6.10	<0.001
FRVP %	89.19 ± 3.52	84.27 ± 4.67	<0.001

T tumor side, *H* health side

Table 1 Baseline characteristics

	Pre-matching			Post-matching		
	LRATE (119)	LPN (127)	*p* value	LRATE (100)	LPN (100)	*p* value
N, male (%)	90 (75.6)	81 (63.8)	0.052	71 (71.0)	68 (68.0)	0.795
N, hypertension (%)	41 (34.5)	38 (29.9)	0.495	37 (37.0)	32 (32.0)	0.552
Median pt age (range)	56 (28–84)	54 (30–79)	0.253	56.5 (28–84)	54 (30–79)	0.176
Mdian BMI, kg/m^2 (range)	24.4 (16.0–34.9)	23.9 (17.8–30.7)	0.122	24.4 (16.0–33.8)	23.5 (17.8–30.7)	0.072
Median tumor size (range)	2.8 (0.8–4.0)	3.1 (1.2–4.0)	0.497	2.8 (1.0–4.0)	3.1 (1.2–4.0)	0.906
R.E.N.A.L score, *N*,%			0.013			0.274
Low (4–6)	97 (81.5)	85 (66.9)		78 (78.0)	85 (85.0)	
Moderate (7–9)	22 (18.5)	42 (33.1)		22 (22.0)	15 (15.0)	
Mean Preop-eGFR ± SD, mL/(min 1.73 m^2)	76.51 ± 19.75	78.83 ± 16.99	0.323	75.20 ± 18.59	77.73 ± 16.21	0.307
Median Preop-Scr mg/dL (range)	0.80 (0.43–5.59)	0.75 (0.42–1.41)	0.061	0.80 (0.43–1.89)	0.78 (0.44–1.41)	0.174
Median WIT min (range)	0	23 (12–36)	–	0	23 (12–36)	–
Median EBL mL (range)	80 (20–300)	120 (20–600)	<0.001	80 (30–300)	125 (20–600)	<0.001
Pathological, *N*, %			0.793			0.498
Clear	92 (77.3)	97 (76.4)		78 (78.0)	74 (74.0)	
Papillary	14 (11.8)	13 (10.2)		10 (10.0)	11 (11.0)	
Chromophobe	8 (6.7)	10 (7.8)		7 (7.0)	9 (9.0)	
Oncocytoma	5 (4.2)	7 (5.5)		5 (5.0)	6 (6.0)	

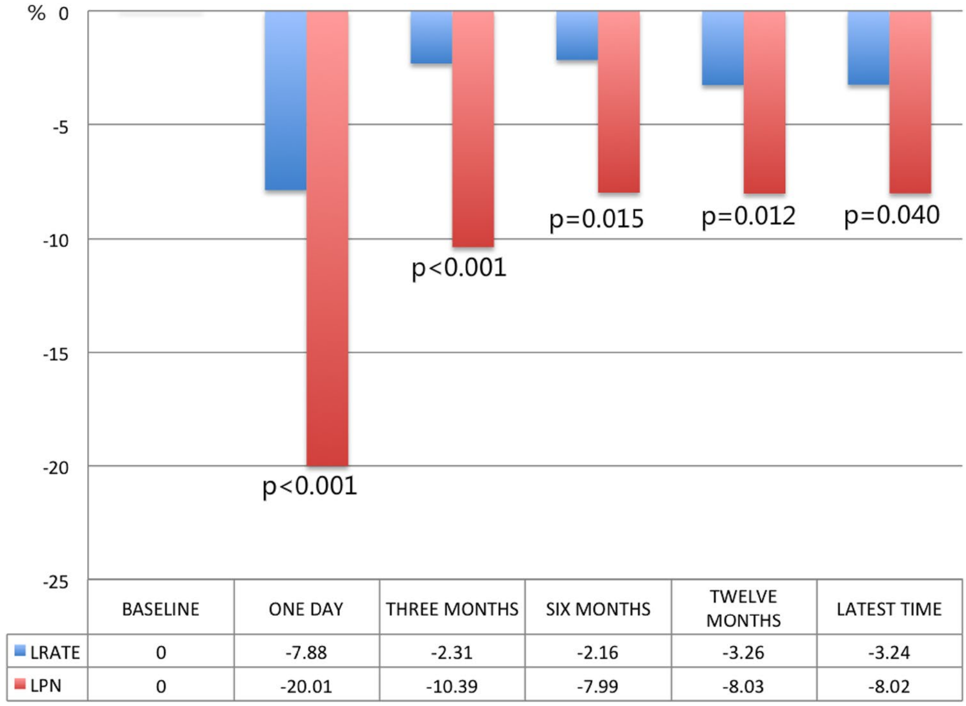

Fig. 2 Relative decrease of total renal function based on the eGFR

Table 3 The spilt GFR before and 1 year after surgery evaluated by renal scitigraphy

	LRATE	LPN	*p* value
Preop-TsGFR mL/(min 1.73 m^2)	36.30 ± 9.18	38.31 ± 8.29	0.107
Postop-TsGFR mL/(min 1.73 m^2)	32.41 ± 8.19	31.32 ± 7.04	0.314
ΔTsGFR %	−9.41 ± 13.82	−17.13 ± 15.19	<0.001
Preop-HsGFR mL/(min 1.73 m^2)	38.90 ± 9.52	39.42 ± 8.19	0.677
Postop-HsGFR mL/(min 1.73 m^2)	39.81 ± 9.85	40.94 ± 7.79	0.367
ΔHsGFR %	3.84 ± 15.98	5.90 ± 19.28	0.412

T tumor side, *H* health side

WIT (OR 1.125, $p=0.016$) were the independent factors with the presence of renal function decrease over 10% at latest follow-up in LPN patients. While age (OR 1.050, $p=0.045$), preoperative-eGFR (OR 1.052, $p=0.003$) and FRVP% (OR 0.001, $p=0.032$) were significant association in LRATE. We also compared the renal function at 3 months according to the CKD criteria which could show the surgical damage more accurate (Table 5). The falling range of latest eGFR (Fig. 3) compared either, and the results showed LRATE patients had better renal function, respectively. In addition, the incisal margin was negative both in LPN and LRATE surgery, and no patients had local recurrence and distant metastasis by the end of this work with a median follow-up of 23 months. The overall complications proportion in our study was very small, and two patients had urine leakage in LRATE group while none in LPN, and the delayed bleeding rate was 2% in LRATE compared 4% in LPN group.

Discussion

Since laparoscopic-assisted partial nephrectomy became the standard treatment of T1a renal tumor, the goal of PN is to get a trifecta outcome (Hung et al. 2013) (negative surgical margins, no urological complications and maximum renal function preservation). When it comes to the postoperative renal function, some research have been discussed that percent of normal parenchymal reduction and duration of ischemia both contribute to acute kidney injury, and the WIT damage may appears to get subsequent functional recovery (Zhang et al. 2016), however, the percent of functional renal parenchyma preservation seems to impact the long-term result. The aim of this study was to compare the renal function preservation between LRATE and LPN, and predict the long-term renal function recovery using a 3D volume parenchyma

Table 4 Multivariable analysis for the presence of renal function decrease over 10% evaluated by eGFR at latest follow-up, respectively

Factors	OR	95% CI	*p* value
LPN			
Sex	0.203	0.002–25.428	0.518
Age	1.045	0.981–1.113	0.174
Hypertension (yes, no)	0.890	0.251–3.154	0.857
BMI	1.043	0.832–1.306	0.718
Tumor size	0.706	0.294–1.691	0.434
R.E.N.A.L score	1.106	0.584–1.734	0.982
EBL	1.003	0.995–1.012	0.453
Preop-eGFR	1.105	1.052–1.160	<0.001
WIT	1.122	1.018–1.236	0.020
PRVP%	0.001	0.001–0.001	0.001
LRATE			
Sex	0.040	0.001–3.621	0.160
Age	1.052	1.002–1.104	0.041
Hypertension (yes, no)	1.652	0.478–5.705	0.451
BMI	0.924	0.752–1.135	0.419
Tumor size	1.075	0.415–2.784	0.881
R.E.N.A.L score	1.243	0.846–1.827	0.267
EBL	1.004	0.989–1.020	0.595
Preop-eGFR	1.054	1.019–1.092	0.003
PRVP%	0.001	0.001–0.348	0.038

measurement system. We also analyzed the independent factors affecting the postoperative renal function.

The LRATE technology was ulilized in several centers, including our department, and previous randomized clinical trial which performed in our center has demonstrated a significant renal functional outcome and similar perioperative complication of LRATE in treating cT1a renal tumors (Huang et al. 2016). LRATE procedure with renal hilar unclamping is expected to have no WIT damage and less EBL. Although, there were some other techniques have been used to minimize the renal ischemia–reperfusion injury, such as off-clamping (Kopp et al. 2012) and selective clamping (Shao et al. 2012), and even the zero ischemia PN (Gill et al. 2011). However, there are still some shortcomings or risk during the surgery. For example, though the superselective clamping skill is promising in protecting postoperative renal function, it is difficult to generalize because of the high requirement of operation skill, and it will take more time to finish the surgery. The renal hilar unclamping technology may also increase the risk of bleeding, and the operative field may become blurred, so that would increase the risk of positive surgical margin.

Just like previous study has showed (Huang et al. 2016; Zhao et al. 2012), during LRATE technique, the RFA electrode is inserted in the tumor, after ablation the tumor becomes solidified and firm, so the transitional zone between pseudocapsule and normal renal parenchyma is easy to distinguish. Hence, the tumor is enucleated from a relatively secure place without normal feeding arteries and avoiding damage of normal renal parenchyma, in this way will more ensure the negative margin, compared to those other techniques we think the additional cost of the RFA was worthy for getting a batter and safer surgical field. In our study, after matching, 100 patients included in each group, and LRATE group was associated with significantly lower EBL (80 vs 125, $p<0.001$). The functional renal parenchymal volume measured using a novel 3D volume measurement system, which showed more specific and reliable, was used in our study. Table 2 demonstrated the parenchyma volume analysis, the mean preoperative normal volume of tumor side was 137.27 cm^3 in the LRATE patients and 138.07 cm^3 in the LPN, $p=0.804$, whereas postoperative (12 months) volume was 122.67 cm^3 vs 116.81 cm^3, $p=0.064$. However, the FRVP rate was 89.19% in LRATE and 84.27% in LPN, $p<0.001$. The result showed that the LRATE tend to preserve more normal functional renal parenchyma than LPN because of the innovative procedure. Our study also compared the spilt GFR (sGFR) as well, and Table 3 showed that the LRATE was associated with a smaller decrease in sGFR of the affected kidney (−9.41 vs −17.13%, $p<0.001$) compared to LPN at nearly 12 months by renal scan. At the same time, the change of the health kidney had no statistical significance (3.84 vs 5.90%, $p=0.412$). The total renal

Table 5 Compare the preoperative renal function evaluated by eGFR according to CKD criteria

N,CKD criteria mL/(min 1.73 m^2)	Preoperative status			Postoperative status (3 months)		
	LRATE	LPN	*p* value	LRATE	LPN	*p* value
>90	15	22	0.185	15	9	0.054
60–90	69	65		67	62	
45–60	9	11		12	24	
30–45	7	2		6	5	
15–30	0	0		0	0	
<15	0	0		0	0	

The new-onset CKD status in each group, LRATE 16 vs 18, $p=0.851$, LPN, 13 vs 29, $p=0.009$

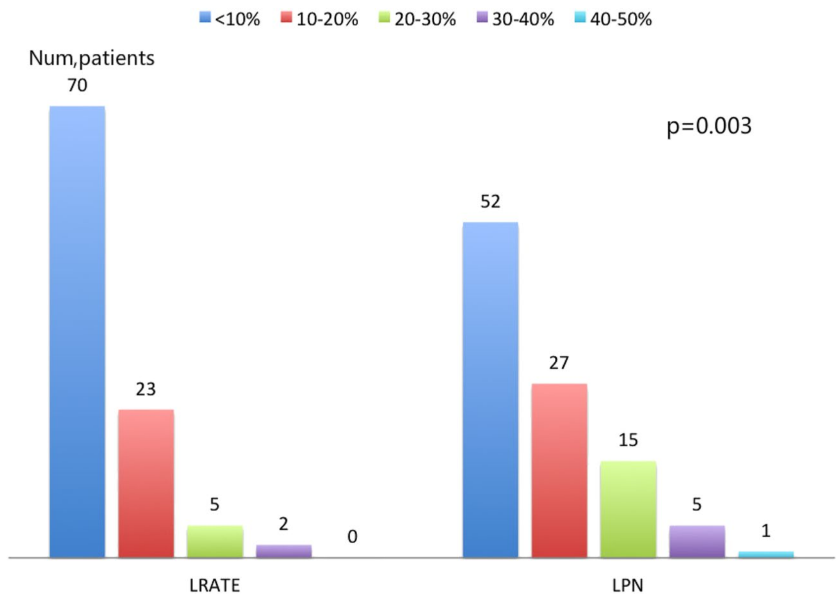

Fig. 3 Falling range of the latest eGFR

function evaluated by eGFR equation was compared too (Fig. 2). These data proved that the LRATE has advantage in terms of protecting renal function. Zhang et al. (2016) reported that percentage of parenchymal mass reduction and duration of ischemia both contributed to acute phase renal function decline and the acute data in our study also supported this viewpoint. The relative decrease of eGFR in LRATE patients was much lower than LPN at 1 day after surgery (−7.88 vs −20.01%, $p < 0.001$), because of the zero ischemia technique and better FRVP rate preservation.

The trifecta outcome for partial nephrectomy is widely accepted to evaluate the surgical satisfaction, and in our study we defined the falling range of eGFR less than 10% at latest follow-up as the satisfying result (Hung et al. 2013). On the multivariable analysis, respectively (Table 4), ischemia time, baseline renal function and FRVP rate were the factors significantly associated with the presence of eGFR decrease over 10%. The result showed that the FVRP rate and the WIT maybe the important independent factors in determining long-term functional recovery, and the maximum parenchymal should be a priority during PN. We put those patients whose renal function was stable or better or decrease less than 10% together at latest test (Fig. 3). The falling range of latest eGFR was significant between two surgery types, 93% of the patients in LRATE decrease less than 20%. However, only 79% of the patients decrease less than 20% in LPN. The postoperative renal function at 3 months was evaluated according to CKD criteria to compare the new-onset surgical CKD, because the recent data pointed the renal function appears to remain stable after 3 months from surgery (Porpiglia et al. 2012), and we think it was more accurate to show the surgical damage. The preoperative status between two groups was similar and the status at 3 months after surgery became different, despite the distribution trend of CKD was not statistically significant, more patients in the LPN group drop down a level to lower renal function, and new-onset CKD patients was 16 while only two patients in LRATE (the pre-post CKD status in each group, LPN 13 vs 29, $p = 0.009$, LARFE 16 vs 18, $p = 0.851$). LRATE surgery type had good ability to protect the renal function not only the perioperative period but also the long-term outcome. We think the better renal function preservation in LRATE patients due to the unique technique during the operation, there is no WIT insult because the renal artery was not clamped and the tumor was enucleated on the evident margin because of the ablation by the RFA electrode, thus ensure the least loss of renal parenchyma. However, there are few patients after LRATE lost more parenchyma than generous condition, we hypothesize that may the RFA electrode injure the normal arcuate artery or interlobular artery so that a part of renal parenchyma become atrophy. Therefore, intraoperative vascular Doppler ultrasound seems to be meaningful. More importantly, ultrasound may help preventing the collecting system damage during the LRATE procedure.

There were several limitations in this work. First, as a single center research, it still had not a relative big sample size with long follow-ups, which needs further study to prove the results. Besides, we performed the renal scan only preoperative and 12 months after surgery, the total renal function evaluated by eGFR equation at 1 day, 3, 6 months and latest time, may be not that accurate compared to the renal scintigraphy, but the changing rate based on the eGFR also can reflect the tendency of renal function recovery. And this technique seems more suitable for those had poorer baseline renal function, especially for patients who had bilateral tumors or single kidney.

Conclusions

In our prospective analysis, we compared the short-term and long-term renal function preservation between LRATE and LPN for clinical T1a renal tumor using a 1:1 propensity score matching. Our study showed LRATE technology has its advantage and potential in preserving renal parenchyma based on the 3D volume measurement system, and it predicted a better long period renal function compared to conventional LPN.

Compliance with ethical standards

Funding This study was funded by by National Natural Science Foundation of China (Nos. 81472378, 91129725), Shanghai Committee of Science and Technology (13ZR1425100), and Shanghai Health System Advanced Technology Popularization Project (2013SY024).

Conflict of interest No conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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