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Research Article

Radiofrequency Ablation versus Partial Nephrectomy for Ct1 Small Renal Masses; a Comparison of Clinical and Oncological Outcomes

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Abstract

Introduction and objectives: Nephron-sparing treatment is the preferred option for management of clinical T1 (cT1) renal cell masses. Partial nephrectomy(PN) has lower recurrence rates in comparison to radiofrequency ablation (RFA). We aim to compare the safety profiles and oncological outcomes of PN and RFA for cT1 renal masses.

Methods and materials: We retrospectively analysed 83 patients with cT1 renal masses treated with PN or RFA at our regional centre between 2003 and 2016. Patients were analysed according to their demographics and RENAL nephrometry score. Follow-up protocol consisted of a tri-phasic renal CT scan at 3-6 months and yearly thereafter. Magnetic resonance imaging (MRI) was used for those with poor renal function.

Local recurrence (LR) for PN was defined as abnormally enhancing new lesion at the site of previous resection. For RFA, LR was defined as interval growth or new enhancement of a successfully treated lesion on subsequent imaging. Stats Direct was used for the statistical analysis. A *p*-value less than or equal to 0.05 was considered statistically significant.

Results: There was no significant difference in patients' demographics nor RENAL scoring system ($p=0.7$, 0.3 respectively). Peri-operative complication rate was significantly higher in the PN group ($p=0.047$). At 5-year follow-up, there were 6 failed RFA cases and one PN local and two distant recurrences ($p=<0.0001$). The 5-year cancer-specific survival was 98% and 100% for RFA and PN respectively ($p= 0.31$); 5-year overall survival for the RFA and PN was 89% and 92% ($p= 0.29$). Limitations include selection bias and the difference in patients' demographics in the two groups.

Conclusion: Peri-operative complications were predictably higher with the PN group. However, oncological outcome was better in this group, compared with RFA. Validation of these results with long-term follow up is important given the disparity in complication rate and severity.

INTRODUCTION

With an increasing diagnosis of small renal masses there is a parallel increase in offering nephron sparing procedures [1]. Partial nephrectomy has now become the gold standard for patients with cT1 renal tumours [2]. Radiofrequency ablative therapy (RFA) for small renal tumours have been traditionally offered to patients who are either high risk surgical candidates for nephron sparing operations, or are unwilling to proceed for such major operations. Therefore, it is challenging to draw viable conclusions due to unmatched cohort comparisons. There is increasing evidence in the literature about the safety, efficacy and oncological outcomes for these procedures [3].

Despite its wide use, RFA remains as an alternative to the gold standard partial nephrectomy (PN) for small renal masses, probably due to the lack of long term follow up. However, there is increasing evidence showing its oncologic safety being comparable to the PN [4,5]. We aim to overcome the cohorts mismatching by matching both groups were according to their demographics and RENAL nephrometry scoring system; (R) radius, (E) exophytic/ endophytic tumour, (N) nearness of the deepest portion of the tumor to the collecting system or renal sinus, (A) anterior (a)/posterior (p) descriptor, and the (L) location relative to the polar line [7].

We aim to present a comparative study between these modalities of treatment looking at the above parameters. We hope that this study will help assessing whether the current practice is optimal and to determine whether a less invasive approach should be pursued.

METHODS

We reviewed the data for 284 patients who underwent RFA and PN for patients with cT1 renal tumours, between July 2003 and October 2016at our hospital. Institutional Review Board was

obtained for quality improvement. Only cases with a minimum postoperative follow-up of 5-years cases were included in our study. All patients were discussed at the multidisciplinary team meeting and they are offered PN as the gold standard. Those who are high risk surgical candidates and/or those who decline PN are offered RFA as an alternative treatment. Patients with benign renal pathology were excluded from the study. Patients' demographics were compared and their comorbidities were evaluated using the ASA (American Society of Anaesthesiologists) scoring system [6]. Peri-operative renal function in both groups was assessed using the estimated glomerular filtration rate (eGFR), before, at 30 days post-procedure, and at 6-month follow up.

RFA technique

Percutaneous approach was used in the RFA cohort as described before [3]. Patients were admitted on the day of the procedure. Routine blood tests were performed on the day of admission, including full blood picture (FBP), urea and electrolytes (U&Es) and clotting profile. A pre RFA biopsy of the lesion is performed via a 17 gauge coaxial needle. RFA is delivered percutaneously under direct CT guidance. A 25 cm 7.3Fr ablation electrode is placed in the renal mass its position is confirmed on imaging. Ablation is performed at a power setting of 200W generating a core temperature of 105°C. Target temperature is maintained for 10 minutes. The number of cycles used is determined by tumour size with tumours greater than 3.5 cm in diameter treated with probe repositioning to create overlapping ablation sites.

A target ablation margin 0.5 cm to 1.0 cm beyond the CT measured maximum tumour diameter is obtained and CT is repeated to evaluate potential haematoma.

PN technique

Under general anaesthesia, endoscopic insertion of ureteric catheter is performed and secured to a urethral catheter, for a subsequent assessment of the pelvi-calyceal system (PCS) integrity. Patient is then placed in the lateral decubitus position. Four and five ports were placed in the lumbar region for left and right sided tumours respectively. For laparoscopic procedures, pneumoperitoneum with an initial pressure of 12 mmHg was achieved. Renal vessels were fully dissected to allow clamping if needed. The kidney was then fully mobilized and Gerota's fascia incised to expose the tumour completely.

Intraperitoneal pressure would then be increased prior to resection to 18 mmHg to minimise venous ooze from resection lines. Monopolar scissors were used to open the renal capsule 5-7mm away from the tumour and further cutting deep into the renal cortex slowly and carefully around the tumour aiming to achieve an enucleo-resection. Bipolar coagulation was applied when small arterial bleeding occurred. Arterial clamping was used with tumours of high RENAL nephrometry score, with an average warm ischaemia time of 22 minutes. After complete excision of the tumour. PCS breach was then assessed by methylene blue dye injection into the ureteric catheter. First layer renorrhaphy was performed using MedTronic V-Loc barbed suture. In cases where vascular clamping was used, the laparoscopic clamp would be removed at this stage to achieve an early unclamping hence minimal renal ischaemia. Evicel haemostatic agent (Ethicon) was used over the first renorrhaphy layer. Then, the second renorrhaphy layer is carried out to close the parenchymal defect using WeckHem-o-lok clips to tighten and secure the sutures at each exit point.

Surgical follow up

Initially, RFA patients were admitted overnight for observation. With increasing experience, RFA procedures were performed as Day Cases unless there is a clinical or social contra-indication. Patients are reviewed four weeks afterwards to discuss the biopsy results. Contrast-enhanced CT assessment was made at 1 month, 6 months, and then annually thereafter. Local recurrence (LR) was defined as interval growth or new enhancement of a successfully treated lesion on any subsequent imaging, as per the updated Image-Guided Tumour Ablation Standardization of Terminology and Reporting Criteria [8].

After being discharged from hospital, PN patients were reviewed four weeks later to discuss histology findings. First follow up CT is in 6 months, followed by annual CT.

Preoperative estimated glomerular filtration rate (eGFR) was compared with the eGFR at the last follow-up. eGFR was calculated using the modified Modification of Diet in Renal Disease equation [9].

Statistical analysis

Stats Direct was used for the statistical analysis. We used Exact Fisher test to compare both treatment groups according to their demographics, ASA and RENAL scoring system. Mann-Whitney test was used to compare the peri-operative outcomes and successful treatments. Disease-free overall survival (OS) were calculated using the Kaplan Meier technique and log rank test used for comparison. A *p*-value less than or equal to 0.05 was considered statistically significant.

RESULTS

Patients with benign renal pathology (*n*= 22) were excluded. Patients with less than 5-year follow up (*n*=179) were also excluded. A remaining 83 patients were included in this retrospective analysis as per the flow chart below, (Figure 1). Patients and tumours demographics are summarized in Table (1) and (Figure 2). Peri-operative data are summarized in Table (2).

We found a marginal, yet statistically significant difference in the age between the two groups. There is no significant difference in the other patients' demographics or the RENAL scoring system. There were more T1b cases in the partial nephrectomy group. However, this was not statistically significant.

Mean hospital stay was 1.3, 4.9 (p=0.04) for the RFA and PN groups, respectively. Peri-operative complications in both groups is shown in Table (2), with a significantly higher rate of complications with PN (2% in RFA and 16% in PN, p<0.0001).

Twelve (26%) RFA patients required second treatment, and 2(4%) needed a third treatment. Six RFA patients had a failed treatment, 3 were due to the large tumours (mean 3.6 cm); and the other 3 failed due to difficult tumour location close to

Table 1: patients' demographics and tumour charactaristics.

Demographics	RFA	PN	*P* value
Patient number (*n*)	46	37	0.95
Age (years)	65	53	0.02
Male/female	3:2	2:1	0.03
ASA(mean)	2.3	1.7	0.7
Single kidney	5	3	0.1
RENAL scoring (mean)	6.4	5.3	0.36
T1a tumours	42	33	0.9
T1b tumours	4	4	
PN (laparoscopic) (*n*)	--	22	
PN (open) (*n*)	--	15	
Pathology Clear Cell RCC G1 G2 G3 Papillary RCC	 30 7 1 8	 6 21 5 5	

Table 2: per-operative and long term outcomes in both groups:

Complications	RFA	PN	*P* value
LOS	1.8	5.2	<0.0001
Fever	1	2	<0.0001
Bleeding(managed conservatively)	0	3	<0.0001
Ileus	0	1	<0.0001
Change in eGFR	2.6	2	0.06
Failed treatment/local recurrence: Size	6 T1a:5 T1b:1	1 T1a:1	<0.0001

the PCS (*n*=2) or bowel despite attempted saline dissection (*n*=1) and pelvi-calyceal system (*n*=2). There was one local recurrence and two metastasis in the PN group (*p*=<0.0001). The local recurrence patient subsequently underwent radical nephrectomy (pathology at partial nephrectomy was G1T1a, 4mm positive surgical margins, same pathology at nephrectomy). Of the metastatic recurrences, one patient (imperative indication for PN) is still on systemic treatment (pathology at partial nephrectomy was G3T3a, 10mm positive margins), while the other patient (pathology was G2T1b, negative margins) died from metastatic disease.

The 5-year cancer-specific survival was 87% and 97% for RFA and PN respectively, (Figure 3); 5-year overall survival for the RFA and PN was 87% and 92% (*p*= 0.29), (Figure 4).

DISCUSSION

Partial nephrectomy is the gold standard for the management of patients with small renal masses [10]. It comes, however, with increasing peri-operative morbidity and may not be a safe option for high risk surgical candidates. There an increasing utilization of various minimally invasive procedures as an alternative to partial nephrectomy. However, until now, these procedures are mainly used for patients who are unfit or unwilling to go for a major operation [11].

There is increasing recent evidence with longer follow up of ablative techniques supporting their use as a competitor of the partial nephrectomy. Chang et al., showed a comparable 5-year outcome in RFA and PN groups, with adjusting the two cohort variables using propensity-score system [12].

A prior systematic review conducted by Pan et al., comparing RFA and partial nephrectomy, showed clearly the selection bias in the papers included, recruiting higher risk patients for the ablative techniques as opposed to PN. Nevertheless, they demonstrated shorter hospital stay and less complication, but a higher rate to local recurrence rate in the RFA group. There was no difference in metastasis in both groups [13].

Definition of treatment response remains a challenge with RFA. Contrast enhanced CT follows up is now accepted as the stand alone investigation to judge the efficacy of the therapy [8]. Post ablation biopsy is subject to significant interpretation error in RFA, as the cellular architecture may be preserved despite cell death, and its use is therefore contentious [14]. LR interpretation can therefore be difficult, and in such cases, a multi-disciplinary review with a consensus with the performing interventional radiologist present is considered as the gold standard.

One has to remember that both modalities, though being viewed as competitors, they could also be utilized simultaneously for complex tumours in a relatively high risk surgical patient, with close tumour proximity to other vital structures. Laparoscopy can be used to free the kidney from the surrounding structures and identify the tumour to be treated with RFA under direct vision, with an acceptable peri-operative risk [15].

Our study cohorts were compared according to their demographics and tumour complexity using RENAL scoring system. Despite the significant difference age between the two groups, there was no significant difference between the patients' co-morbidities, as manifested by the ASA scoring system. This may reflect the increase in offering partial nephrectomy to higher risk patients, and more acceptance of RFA procedures for patients who would otherwise be candidates for partial nephrectomy. This may also reflect the increase in surgical and procedural experience during the follow up period, which on the other hand, might be a confounding factor for bias. RENAL nephrometry scoring system was higher in the RFA group. However, this was not statistically significant. Similarly, there were higher numbers of patients with single kidney in the RFA groups as opposed to PN patients. This may reflect the selection bias towards a minimally invasive approach for patients with single kidney. However, the difference was not significant.

There were significant RFA cases that required multiple treatments (*n*=8). This may be explained by the conservative approach of the RFA aiming to minimize normal parenchymal injury, and the feasibility of repeating the procedure if needed, due to its relative safety and being performed as a Day Case [5].

More peri-operative complications occurred with the PN group. However, these were of Clavian-Dindo class II. There was no significant difference in the peri-operative change in the estimated glomerular filtration rate (eGFR) in both groups. On subsequent follow up, the incidence of recurrence with the PN group was significantly lower than the RFA group. A longer follow up is needed to provide stronger evidence (Table 2).

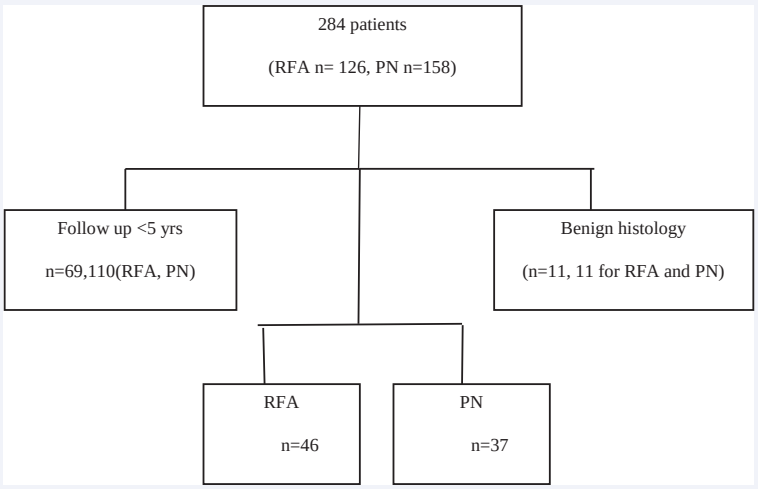

Figure 1 flow chart of the study patients:.

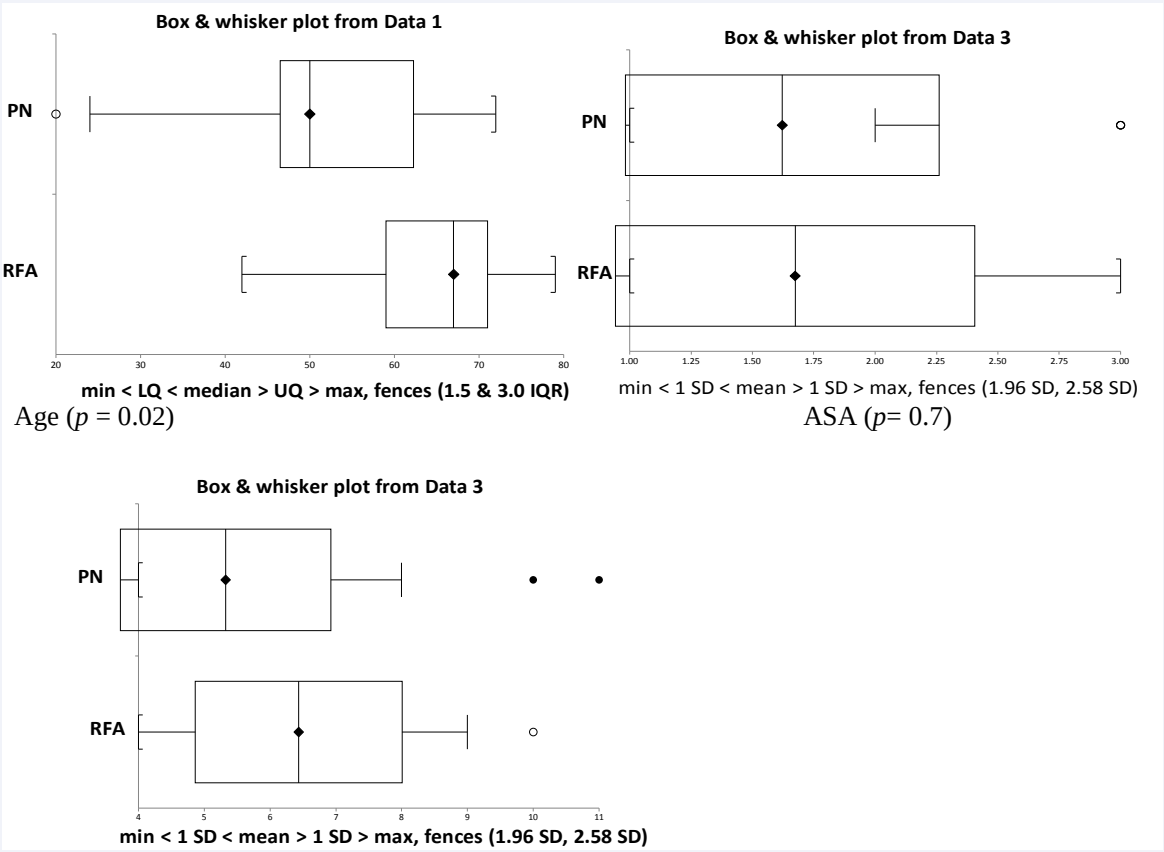

Figure 2 Box plot showing patients demographics in both groups:
RENAL scoring (p = 0.3)

Although the age is significantly higher in the RFA group, however, there is no significant difference in the ASA scoring in both groups. This may be a reflection of the extended provision of the PN for higher risk surgical patients, which parallels the increase of surgeons' experience and improvement in post-operative care.

The shortcomings in our study are its retrospective nature, which might be affected by selection bias. In addition, as we aimed to include people with long follow up. This resulted in excluding a significant number of patients leading to small groups.

On the other hand, our groups were compared and found matching in most peri-operative aspects, according to their

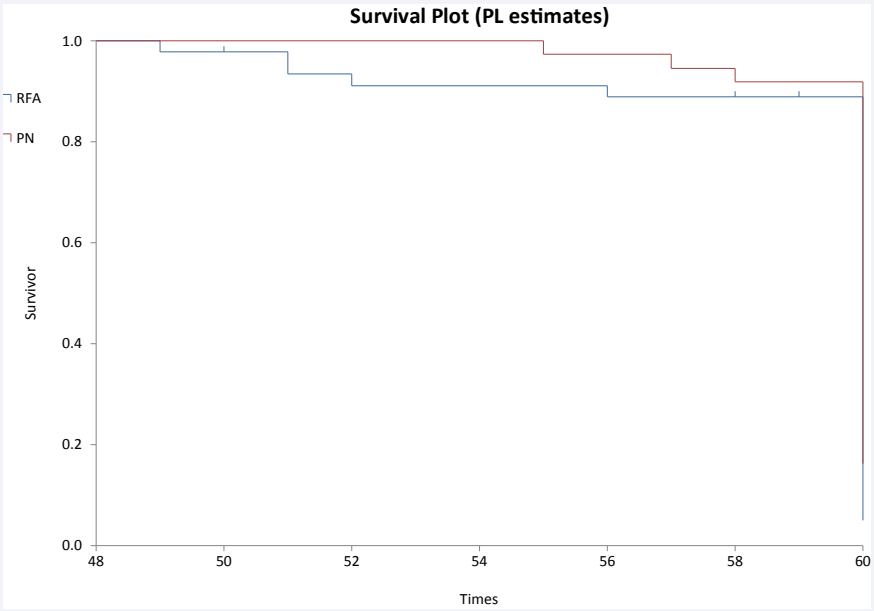

Figure 3 Kaplan-Meier CSS in both groups.

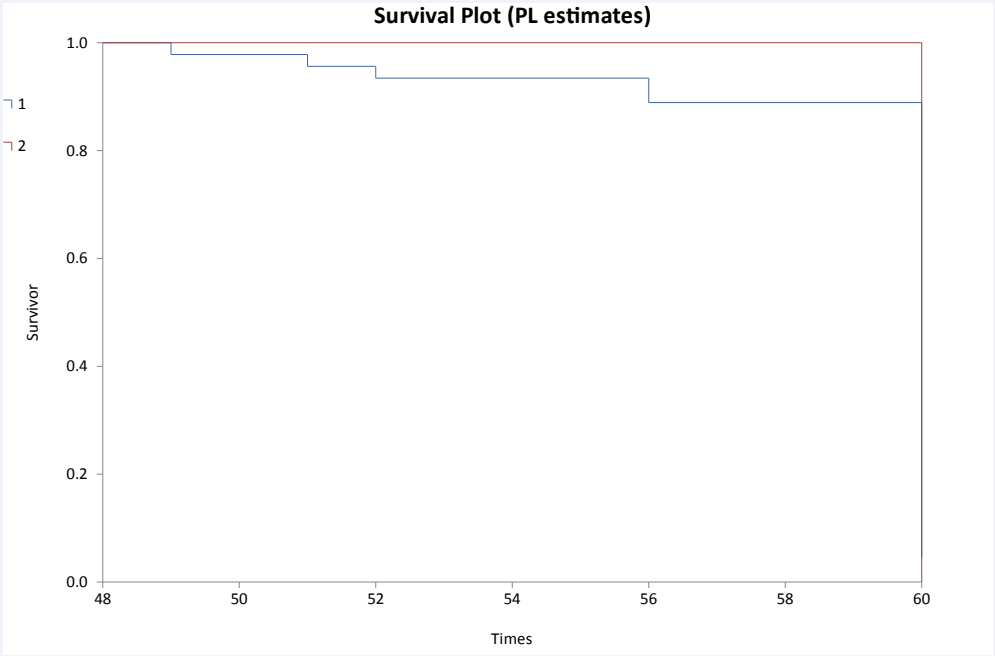

Figure 4 Kaplan-Meier overall survival in both groups.

demographics and RENAL scoring system, as shown in Table (1). Such points present limitations in similar studies.

CONCLUSION

PN and RFA provide viable treatment modalities for cT1 renal cancer. PN is associated with higher, though acceptable, peri-operative morbidity. RFA was associated with fewer peri-operative complications but a higher local recurrence rate. RFA could be offered alongside PN for selected cases. Prospective randomized trials will be useful to confirm the compatible use of these two methods of treatment of small renal tumours.

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