European Radiology (2023) 33:7371–7379
https://doi.org/10.1007/s00330-023-09779-7

European Radiology
EUROPEAN SOCIETY OF RADIOLOGY

INTERVENTIONAL

Percutaneous radiofrequency ablation is an effective treatment option for small renal masses, comparable to partial nephrectomy

José Pablo Pedraza-Sánchez[1] · Reyes Chaves-Marcos[2] · Javier Mazuecos-Quirós[1] · Álvaro Luis Bisonó-Castillo[1] · Ignacio Osmán-García[2] · Carlos Miguel Gutiérrez-Marín[3] · Rafael Antonio Medina López[2] · Álvaro Juárez Soto[1]

Received: 30 June 2022 / Revised: 20 March 2023 / Accepted: 14 April 2023 / Published online: 6 June 2023

Abstract

Objectives The standard therapy for small renal masses (SRMs) remains partial nephrectomy (PN), which is associated with relatively high morbidity and complication rate. Therefore, percutaneous radiofrequency ablation (PRFA) emerges as an alternative therapy. This study aimed to compare the efficacy, safety, and oncological outcomes of PRFA versus PN.

Methods A multicenter non-inferiority study with retrospective analysis of 291 patients with SRMs (N0M0), who underwent PN or PRFA (2:1), recruited prospectively from two hospitals in the Andalusian Public Health System, Spain, between 2014 and 2021. Comparisons of treatment features were evaluated using the *t* test, Wilcoxon-Mann–Whitney *U* test, chi-square test, Fisher test, and Cochran-Armitage trend test. Kaplan–Meier curves depicted overall survival (OS), local recurrence-free survival (LRFS), and metastasis-free survival (MFS) rates in the overall study population.

Results A total of 291 consecutive patients were identified; 111 and 180 patients underwent PRFA and PN, respectively. Median follow-up time was 38 and 48 months, and mean hospitalization days were 1.04 and 3.57 days, respectively. The variables underpinned with high surgical risk were significantly increased in PRFA compared to those in PN (mean age was 64.56 and 57.47 years, the solitary kidney presence was 12.6% and 5.6%, ASA score ≥ 3 was 36% and 14.5%, respectively). The rest of oncological outcomes were comparable amongst PRFA and PN. Patients undergoing PRFA did not improve OS, LRFS, and MFS compared to those undergoing PN. Limitations comprise retrospective design and limited statistical power.

Conclusion PRFA for SMRs in high-risk patients is non-inferior in terms of oncological outcomes and safety compared to PN.

Clinical relevance statement Our study has a direct clinical application as it proves that radiofrequency ablation is an effective and uncomplicated therapeutic option for patients with small renal masses.

Key Points

- *There are non-inferiority results in overall survival, local recurrence-free survival, and metastasis-free survival between PRFA and PN.*
- *Our two-center study showed that PRFA is non-inferior to PN in oncological outcomes.*
- *Contrast-enhanced power ultrasound-guided PRFA provides an effective therapy for T1 renal tumors.*

Keywords Radiofrequency ablation · Nephrectomy · Interventional radiology · Minimally invasive surgery · Renal cancer

✉ José Pablo Pedraza-Sánchez
p.pedraza.sanchez@gmail.com

[1] Urology Clinical Unit, University Hospital of Jerez de La Frontera, Ctra. Trebujena, S/N, 11407 Jerez de La Frontera, Cádiz, Spain

[2] Department of Urology and Nephrology, Virgen del Rocío University Hospital, Biomedical Institute of Seville (Ibis), CSIC/University of Seville, Seville, Spain

[3] Department of Radiology, Virgen del Rocío University Hospital, Biomedical Institute of Seville (Ibis), CSIC/University of Seville, Seville, Spain

Abbreviations

CEPUS	Contrast-enhanced power ultrasound
Cr	Creatinine
CSS	Cancer-specific survival
CT	Computed tomography
eGFR	Estimated glomerular filtration rate
LRFS	Local recurrence-free survival
MFS	Metastasis-free survival
MRI	Magnetic resonance imaging
OS	Overall survival
PN	Partial nephrectomy
PRFA	Percutaneous radiofrequency ablation

RCC	Renal cell carcinoma
RN	Radical nephrectomy
SRMs	Small renal masses

Introduction

Small renal masses (SRMs) encompass a broad spectrum of renal tumors with metastatic potential, ranging from benign to more aggressive tumors [1, 2] including renal cell carcinomas (RCCs). Indeed, RCC is the most frequent form of renal cancer, accounting for nearly 85% of renal cancers and about 2% of cancer diagnoses and deaths worldwide, and its incidence is estimated to be spreading globally [3]. Recent technical advances have enabled the widespread use of imaging and cancer detection, leading to increased incidental findings of SRMs [4]. Partial nephrectomy (PN) remains the gold standard option for the therapy of T1 RCC as it allows better preservation of renal function than radical nephrectomy. However, PN exhibits a surgical complication rate of as high as 20% [5].

Patients with RCC of advanced age and/or with comorbidities may display surgical complications [6]. In addition, renal function progressively decreases in patients with hereditary RCC after undergoing several partial surgeries, with the complexity of the operative procedure increasing with each new surgery [7]. Therefore, other procedures, such as radiofrequency ablation (RFA), are starting to be an effective therapeutic option for patients with T1a RCC who cannot undergo surgery [8, 9]. RFA procedure can be carried out using open, laparoscopic, and percutaneous methods [10]. Specifically, percutaneous radiofrequency ablation (PRFA) is a minimally invasive method in which solid tumors are destroyed by high-frequency radio waves directed from an electrode inserted with a needle through the skin into the tumor and subsequent coagulative necrosis [11]. The electrode can be guided by computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound [10].

The validity of RFA treatment has been previously reported for RCC demonstrating outstanding oncological outcomes [7, 12]. Nevertheless, the superiority of RFA over PN as a treatment for RCC remains controversial [13], and more studies with more data comparing RFA with PN are lacking. Thus, we conducted a multicenter non-inferiority study to compare these two procedures' efficacy, safety, and oncological outcomes for handling patients with T1 renal tumors.

Methods

Study design

This is a retrospective analysis of a prospectively maintained registry from June 2014 to June 2021 at two hospitals belonging to the Andalusian Public Health System (SSPA) in Spain.

The Research and Ethics Committees of both hospitals approved this study. In addition, the study complied with the Declaration of Helsinki. All patients were informed about the procedures, and all of them signed a written informed consent form.

Inclusion and exclusion criteria

Patient, clinical, and follow-up data were recorded. All the patients were older than 18 years. Prior to participation, all patients gave written informed consent. Eligible patients had radiologic imaging diagnoses of small renal mass (SRMs) including benign lesions and had extension study (chest-abdomen CT) without evidence of distant metastasis disease. They were suitable to undergo radiofrequency or partial nephrectomy. In particular, patients who underwent radiofrequency had to be elderly (> 60 years) and have comorbidities, thus, with high surgical risk. Exclusion criteria were patients with radiological evidence of tumor extension beyond the kidney or vascular involvement, patients with metastatic disease at diagnosis, and patients who could not undergo any of these two surgical procedures. It should be noted that the patients with inconclusive biopsies in which the presence of a tumor was not confirmed on histology or they had a benign lesion was excluded from the TNM staging, the survival analysis, and analysis of histopathological results.

Study size

We calculated our sample size based on previous results from another similar study [14]. The calculation was based on Lachin and Foulkes [15] method implemented in the gsDesign package in R [16, 17] (v4.0). A non-inferiority margin of 7% was established based on clinical criteria and on previous results [14]. Due to recruitment capacity, an allocation ratio was established to 2 (PN 2:1 RFA). The Weibull distribution was assumed to calculate the median survival time of local recurrence. Hypothesized RFA/PN hazard ratio was 0.56 (95% CI 0.1–3.1). A total study length of 132 months and an average follow-up of 40 months were assumed. Therefore, 200 subjects are needed for the PN group and 100 for the RFA group to achieve non-inferiority, accepting an alpha risk of 0.05 and a beta risk of 0.3. The study is powered at 70% due to the reasonable sample size. A 5% dropout rate was anticipated for the total duration of the study.

Surgery: PN and percutaneous RFA

All patients were biopsied prior to surgery with a TruCore™ II automated needle (Argon Medical Devices) and

cool-tip system (STARmed Co., Ltd.). The surgeon decided on the surgical approach based on the patient's features and comorbidities and the location and size of the tumor. Thus, patients with high surgical risk, advanced age, or comorbidities were treated with RFA. Specifically, standardized procedures for performing percutaneous RFA under contrast-enhanced power ultrasound (CEPUS) guidance were established at both centers, similar to those previously described [18]. One surgeon for each center with more than 5 years of experience conducted PRFA. All tumors were ablated for at least one cycle of up to 7–12 min. PNs were performed through three approaches: robotic-assisted, laparoscopic, and open, similar to that described in [18]. Laparoscopic PN was used to treat posterior tumors. PN were performed by four surgeons from each center, with more than 5 years of experience. Meanwhile, anterior tumors placed close to the adnexal organs or bowel were usually surged on laparoscopically. All the surgeries were carried out under general anesthesia.

Contrast-enhanced ultrasonography and computed tomography

We used multiphase CT. The basal phase was acquired before injecting contrast, the corticomedullary phase at approximately 35 s after injection of intravenous Ultravist® contrast (300 mg I/mL, 300/370; Bayer AG,) and the nephrographic phase 80–100 s after contrast injection. The image displaying the best tumor was chosen for fusion imaging. CT images were reconstructed to a section thickness of 1.25 mm without gaps [19]. For CEPUS, harmonic microbubble-specific imaging with low acoustic ultrasonography pressure (2–4 MHz transducer; mechanical index < 0.2; 12–13 frame rate/s) was performed [20]. CEPUS was carried out right after the initial ablation. Additional ablation and CEPUS were performed, focusing on the highly suspicious area.

Patient follow-up

The standard method of patient follow-up for both groups was CT. However, patients who underwent RFA were examined with CEPUS to identify the ablated tumor's contrast or non-contrast uptake 1 month after RFA. Magnetic resonance imaging (MRI) was only requested if there were doubts about other imaging tests (CT or CEPUS). Hence, as appropriate, RFA patient follow-up was performed by alternating CT and CEPUS [21] every 6 months during the first 3 years and every 12 months for the following years. According to the risk classification and follow-up algorithm of the European Association of Urology guidelines on RCC, patients treated with PN were followed up by contrast-enhanced CT every 6 months for the first 3 years and every 12 months thereafter [22]. In addition, renal function was tested at that time by simultaneously collecting serum creatinine (Cr) and estimated glomerular filtration rate (eGFR) values. We used the CKD-EPI method to analyze eGFR [23]. The lack of detection of contrast enhancement in the first postoperative test was considered a complete tumor ablation.

Clinical features, variables, and data acquisition

Data were obtained from the patient's electronic medical record and peer-reviewed. We analyzed the following variables: clinic-pathological features, follow-up time of patients, follow-up tests (CT and CEPUS), renal function (Cr levels and eGFR), days of hospitalization, complications categorized according to the Clavien-Dindo classification, overall survival (OS), local recurrence-free survival (LRFS), and metastasis-free survival (MFS).

The clinic-pathological variables included sex, age at diagnosis, presence of solitary kidney, tumor size, exophytic growth, and histology. Exophytic tumors were categorized according to the degree to which the tumor protruded from the renal surface ($\geq 50\%$ or $< 50\%$). In addition, the tumors were classified according to using the TNM staging system, which describes the size and spread of the primary tumor. The ASA score was also applied, which is a valuable tool in preparation for surgery, as it is an independent system for predicting risk, complications, and mortality in selected patients.

Statistical methods

We used the R software to carry out the statistical analysis. The Anderson–Darling test analyzed the normality of the distribution of continuous variables. Continuous quantitative variables following a normal distribution were represented by the mean and standard deviation (SD), while categorical variables were displayed as the number N (%). Furthermore, a comparison analysis was carried out. We used the t test or Wilcoxon-Mann–Whitney U test to compare normally or non-normally distributed quantitative variables. Meanwhile, categorical variables were compared using Pearson's chi-square test or Fisher's exact test as appropriate. Finally, we used the Cochran-Armitage trend test for ordinal variables. OS, LRFS, and MFS were estimated using the Kaplan–Meier method, and comparison analysis was calculated using the log-rank test. A Cox proportional hazards model cannot be estimated since there are no recorded RFA deaths. In addition, a multivariate analysis was carried out to eliminate the effect of confounding variables that could modify the result such as malignant histology and tumor size. p value < 0.05 was considered significant (see Supplementary Material).

Results

The multicenter non-inferiority study comprised 308 recruited patients. Only 291 were analyzed retrospectively due to dropout to follow-up or exclusion criteria. All data from these 291 patients with renal tumors (mean tumor size 28.17 mm, median 25; range 4–80) undergoing PN (180) or PRFA (111) were collected.

Clinical data

The clinical features of all patients with renal tumors (RCC) included in this study are gathered in Table 1. A total of 291 patients with T1a, T1b, or T2 RCC met the inclusion criteria and were retrospectively analyzed, of whom 180 underwent PN and 111 underwent PRFA (PN 2:1 PRFA). Therefore, the final cohort of our study consisted of these 291 patients. Patients treated with PRFA were significantly elder (mean 62.5 years, range 33–84, $p < 0.001$) than patients who underwent PN (mean 57.47 years, range 25–79, $p < 0.001$). There were no significant differences in gender (60.6% male for PN vs. 72.1% male for PRFA, $p = 0.053$). Patients who underwent PRFA displayed a significantly greater preoperative risk (ASA ≥ 3) than patients in the PN group (36% vs. 14.5%, $p < 0.001$). Fourteen patients undergoing RFA (12.6%) had a solitary kidney, while in the case of PN, there were ten (5.6%).

Tumor features and clinical outcomes

The tumors were diagnosed radiologically and assessed by the multidisciplinary team of the urology departments of each hospital. Metastases to regional lymph node stages in

Table 1 Descriptive statistics of clinicopathological variables. Features of patients. Tumor histopathology and pathological stage of the patients studied

Variables		PRFA ($N = 111$; 38.1%)	PN ($N = 180$; 61.9%)	Total ($N = 291$; 100%)	Statistical test/p value
Sex, *N* (%)	Males	80 (72.1%)	109 (60.6%)	189 (64.9%)	Pearson's chi-squared test/$p = 0.053$)
	Females	31 (27.9%)	71 (39.4%)	102 (35.1%)	
Age, mean (SD), years		64.56 (11)	57.47 (11.9)	60.18 (12.04)	Two-sample *t* test ($p < 0.001$)
ASA score, *N* (%)	1	4 (3.6%)	12 (6.7%)	16 (5.5%)	The Cochran-Armitage trend test/$p < 0.001$
	2	67 (60.4%)	142 (78.9%)	209 (71.8)	
	3	40 (36%)	25 (13.9%)	65 (22.3%)	
	4	0	1 (0.6%)	1 (0.3%)	
Monorene, *N* (%)		14 (12.6%)	10 (5.6%)	24 (8.2%)	Pearson's chi-squared test/$p = 0.045$
Tumor size, mean (SD), mm		21.47 (8.48)	32.3 (14.39)	28.17 (13.52)	The Wilcoxon rank-sum test/$p < 0.001$
Tumor side, *N* (%)	Left	64 (57.7%)	95 (52.8%)	159 (54.6%)	Pearson's chi-squared test/$p = 0.453$
	Right	47 (42.3%)	85 (47.2%)	132 (45.4%)	
Exophytic location	No	51 (45.9%)	58 (32.2%)	109 (37.5%)	Pearson's chi-squared test/$p = 0.026$
	Yes	60 (54.1%)	122 (67.8%)	182 (62.5%)	
TNM staging, *N* (%)	T1a	109 (98.2%)	140 (81.2%)	249 (88.3%)	The Cochran-Armitage trend test/$p < 0.001$
	T1b	2 (1.8%)	29 (17%)	31 (11%)	
	T2	0	2 (1.2%)	2 (0.7%)	
Histology, *N* (%)	Clear cells	32 (29.1%)	105 (58.3%)	137 (47.2%)	Fisher's exact test/$p < 0.001$
	Papillary	20 (18.2%)	37 (20.6%)	57 (19.7%)	
	Chromophobe	9 (8.2%)	5 (2.8%)	14 (4.8%)	
	Oncocytoma	9 (8.2%)	5 (2.8%)	14 (4.8%)	
	Angiomyolipoma	2 (1.8%)	7 (3.9%)	9 (3.1%)	
	Eosinophilic cells	1 (0.9%)	2 (1.1%)	3 (1%)	
	Absence of neoplasia	17 (15.5%)	11 (6.1%)	28 (9.7%)	
	Inconclusive	15 (13.6%)	0	15 (5.1%)	

PN, partial nephrectomy; *PRFA*, percutaneous radiofrequency ablation; *ASA*, American Society of Anesthesiologists; *TNM*, T category describes the primary tumor site and size, N category describes the regional lymph node involvement, M category describes the presence or otherwise of distant metastatic spread. Monorene: single kidney

all the SRMs included in the study were N0 (no regional lymph node metastasis) and M0 (no distant metastasis). We found that the mean tumor size was significantly slighter in the RFA group than in the PN group (21.47, SD 8.48 vs. 32.3, SD 14.39, mm, $p < 0.001$; Table 1). Significant differences were detected in tumor location. Exophytic growth was found in fewer patients undergoing RFA than those undergoing PN (54.1% vs. 67.8%, $p = 0.026$). In addition, significant differences were found in tumor histology and tumor stage. Particularly, pathological stages were 98.2% T1a and 1.8% T1b for RFA and 81.2% T1a, 17% T1b, and 1.2% T2 for PN ($p < 0.001$; Table 1). Histopathological results exhibited clear cell RCC in 32 PRFA cases (29.1%) versus in 105 PN cases (58.3%), papillary RCC in 20 PRFA case (18.2%) versus in 37 PN cases (20.6%), chromophobe RCC in 9 PRFA cases (8.2%) versus in 5 PN cases (2.8%), oncocytoma RCC in 9 PRFA cases (8.2%) versus in 5 PN cases (2.8%), angiomyolipoma in 2 PRFA case (1.8%) versus in 7 PN cases (3.9%), eosinophilic cell RCC in 1 PRFA cases (0.9%) versus in 2 PN cases (1.1%), and absence of neoplasia in 17 PRFA cases (15.5%) versus in 11 PN cases (6.1%) (Table 1).

Renal function

The post-operative eGFR or Cr and change in eGFR or Cr peri-operatively of study patients undergoing RFA and PN are shown in Table 2. We found that renal function decreased in both procedures, although the decrease was more striking in patients who underwent PN than in those who underwent RFA. We found that the levels of creatinine/eGFR before and after surgery between the two groups were significantly different ($p < 0.005$, Table 2). However, there was no significant change in the renal function itself. In particular, we did not find any significant difference in the change in Cr pre- and postoperatively between treatments (mean RFA 0.064 vs. PN 0.079; $p = 0.956$). Likewise, the decrease in the change in eGFR pre- and postoperatively was not significantly different between treatments (mean RFA − 2.42 vs. PN − 3.8; $p = 0.533$).

Complications

In this study, we considered a Clavien grade I complication to be any postoperative deviation requiring analgesic

Table 2 Descriptive statistics on patient follow-up outcomes and time, renal function, and surgical complications and hospitalization days

Variables		PRFA ($N = 111$; 38.1%)	PN ($N = 180$; 61.9%)	Total ($N = 291$; 100%)	Statistical test/p value
Preoperative Cr, mean (SD), mg/dL		1.07 (0.61)	0.92 (0.37)	0.98 (0.48)	The Wilcoxon rank-sum test/$p < 0.001$
Postoperative Cr, mean (SD), mg/dL		1.13 (0.66)	0.98 (0.62)	1.05 (0.64)	The Wilcoxon rank-sum test/$p = 0.004$
Change in Cr pre- and postoperatively, mean (SD), mg/dL		0.064 (0.234)	0.079 (0.412)	0.072 (0.339)	The Mann–Whitney test/$p = 0.956$
Preoperative eGFR, mean (SD), mL/min/1.73 m^2		77.42 (22.99)	86.72 (19.42)	82.32 (21.64)	The Welch two-sample t test/$p = 0.001$
Postoperative eGFR, mean (SD), mL/min/1.73 m^2		74.97 (24.82)	82.92 (21.01)	79.25 (23.14)	The Welch two-sample t test/$p = 0.011$
Change in eGFR pre- and postoperatively, mean (SD), mL/min/1.73 m^2		− 2.42 (13.14)	− 3.79 (16.00)	− 3.133 (14.716)	The Mann–Whitney test/$p = 0.533$
Follow-up time, median (range), months		38 (range, 12–109)	48 (range, 12–78)	44 (range, 12–109)	The Wilcoxon rank-sum test/$p < 0.001$
ASA score, N (%)	1	4 (3.6%)	12 (6.7%)	16 (5.5%)	The Cochran-Armitage trend test/$p < 0.001$
	2	67 (60.4%)	142 (78.9%)	209 (71.8)	
	3	40 (36%)	25 (13.9%)	65 (22.3%)	
	4	0	1 (0.6%)	1 (0.3%)	
Clavien-Dindo complications, N (%)	1	107 (96.4%)	153 (85%)	260 (89.3%)	ns
	2	3 (2.7%)	15 (8.3%)	18 (6.2%)	The Cochran-Armitage trend test/$p = 0.004$
	3	1 (0.9%)	10 (5.6%)	11 (3.7%)	
	4	0	1 (0.6%)	1 (0.3%)	
	5	0	1 (0.6%)	1 (0.3%)	
Hospital stay, mean (SD), days		1.04 (0.2)	3.57 (3.06)	2.61 (2.70)	The Wilcoxon rank-sum test/$p < 0.001$

PN, partial nephrectomy; *PRFA*, percutaneous radiofrequency ablation; *eGFR*, estimated glomerular filtration rate; *Cr*, creatinine; *ns*, not significant

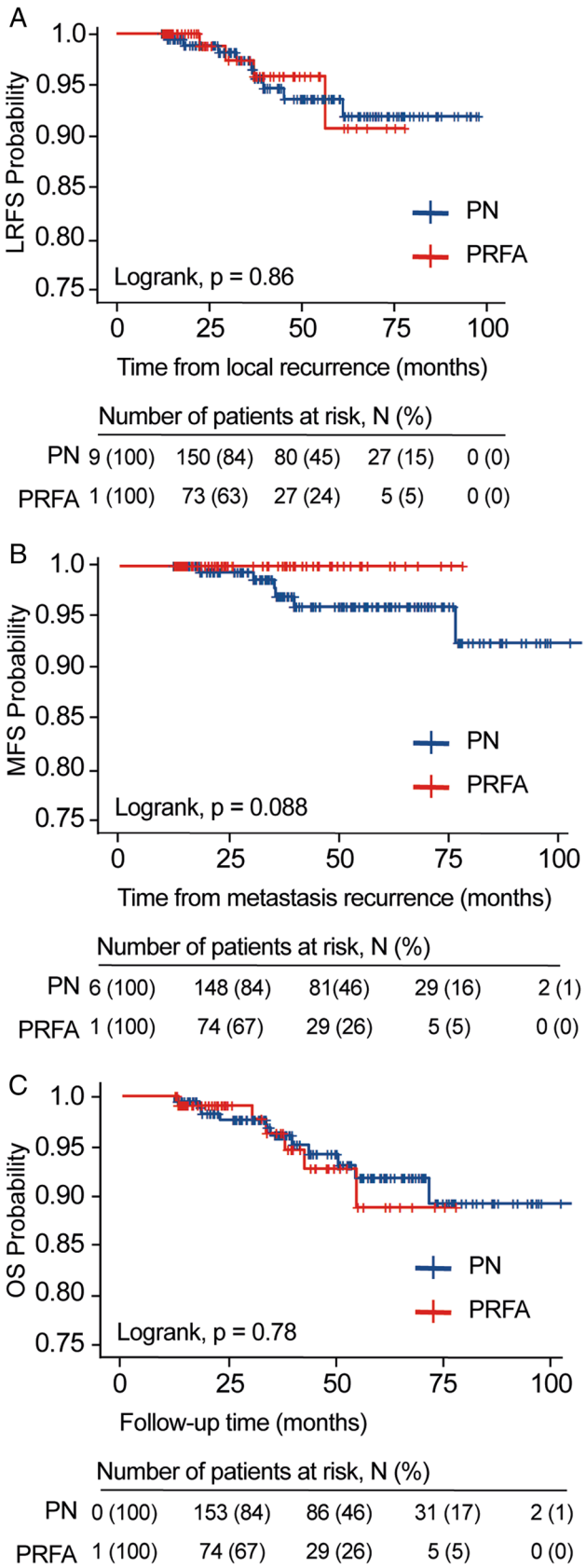

Fig. 1 Kaplan–Meier curves of patients who underwent RFA or PN for RCC treatment. **A** LRFS (local recurrence-free survival). **B** MFS (metastasis-free survival). **C** OS (overall survival). PN, partial nephrectomy; PRFA, percutaneous radiofrequency ablation. LRFS is defined as the percentage of patients without any tumor in the ablation site, incomplete PN, or residual operated kidney. MFS was the proportion of patients without tumors anywhere in the body other than the healed kidney. Cancer-specific survival (CSS) was the proportion of patients that did not die from RCC; OS was the ratio of patients that did not decrease for any reason

treatment. Therefore, we focused on Clavien 2 or 3, the most severe complications detected. Surgical complications according to Clavien-Dindo grade ≥ 2 were significantly lower in the RFA group compared to those in the PN group (Clavien-Dindo grade ≥ 2; 3.60% vs. 15.10%, $p = 0.004$; Table 2). The mean hospitalization time for RFA was 1.04 (SD 0.2) days shorter than for PN (mean 3.57, SD 3.06 days, $p < 0.001$; Table 2).

Follow-up outcomes

A successful surgical procedure was achieved on all 180 tumors (100%) for PN. Specifically, PNs were performed through three approaches: robot-assisted (5.0%), laparoscopic (64.4%), and open (30.6%). The number of PRFAs performed in a single surgical procedure was 104 (93.7%). Patients with an incomplete ablation who underwent a subsequent radical nephrectomy (RN) or a new PRFA were 1 (16.7%) and 5 (83.3%), respectively, being significantly different ($p = 0.021$). We found that the follow-up time for the patients undergoing PRFA was significantly lower (median 38, range, 12−109 months) than that in the PN group (median 48, range, 12−78 months, $p < 0.001$; Table 2).

Survival analysis

LRFS, MFS, and OS probabilities were calculated using Kaplan–Meier methods. Results were comparable between the two groups for all four endpoints (Fig. 1). Only one RCC-related deaths were observed (RFA: 0, PN: 1). A total of 17 deaths were observed (RFA: 6, PN: 11). Seven local recurrences were observed (RFA: 4, PN: 3). Six metastatic events were observed (RFA: 0, PN: 6). Proportional hazard was tested using the Therneau test. We estimated 95% confidence intervals (CIs) for each survival probability. No significant differences were detected between the two groups (PRFA vs. PN) in terms of LRFS (HR 0.9, 95% CI, 0.28–2.9, $p = 0.86$), MFS, and OS (HR 1.2, 95% CI, 0.42–3.1, $p = 0.78$). In addition, no significant differences were found in cancer-specific survival (CSS), but in this case, no deaths were recorded after RFA, and therefore, the Cox model and HR could not be estimated (Fig. 1A–C).

Discussion

Our early results support RFA as an alternative therapy in terms of OS, LRFS, and MFS with PRFA versus PN. Hence, we demonstrate that RFA is a feasible and safe treatment option for SMRs in high-risk patients with outcomes similar to PN. This is in line with what has been reported previously, where ablation was shown to be an effective therapy [24] and correlates with a generally low risk of complications [25-27] and specifically PRFA [8, 9]. Our statistical analyses displayed that age, ASA, presence of a single kidney, size, location, stage, histology of tumor, renal function (eGFR and Cr values), surgical complications, follow-up time, CT, CEPUS, and days of hospitalization were significantly different between the PRFA and PN groups (Tables 1 and 2 and Supplementary Table). However, no significant differences were found in OS, LRFS, and MFS.

Specifically, our study demonstrated a significant increase in age, ASA score, and presence of a single kidney in the PRFA group compared to those in PN, similar to what was previously reported in other studies [28]. This reflects that PRFA is suggested for aging patients and/or with underlying severe clinical comorbidities. In this regard, we also found significant differences in surgical complications according to the Clavien-Dindo classification with grades ≥ 2 between the RFA and PN groups (Table 2), being higher in PN patients. This concurs with previous studies, including metanalyses [11, 12, 26, 27]. It should be noted that the incidence of grade ≥ 4 or greater adverse events was very low and similar between the two groups. This lower number of complications after RFA would explain why these patients stayed fewer days in the hospital than patients undergoing PN (Table 2), as reported in other analyses [12, 13, 29].

Patients with RCC often show reduced renal function. It is especially true when these patients are older or have associated comorbidities, as their renal function is already impaired. Therefore, preservation of this kidney's function is critical in these cases to avoid the need for dialysis and maintain their life quality [12]. After surgery, renal function may be impaired, reflected in a rise in serum Cr and a decrease in eGFR. Previous studies have shown controversial evidence on these two variables after PN and thermal ablation [26, 30]. In this regard, our results showed that eGFR and serum Cr levels were reduced and increased in patients with PRFA compared to those who underwent PN (Table 2). This suggests better preservation of renal function after PRFA. Comparable results were found in a recent study that also compared RFA versus PN [9, 31]. One of the advantages of percutaneous procedures is that the main renal artery does not need to be clamped, thus eliminating the warm ischemia time required by other surgical methods [12].

In our study, we also found that the percentage of inconclusive biopsies or absence of neoplasia in the group of patients undergoing RFA was higher than in the PN group. Some studies would explain these results because the quality of biopsies obtained by percutaneous puncture would be lower than that of complete tumor analysis obtained in PN [32, 33]. Therefore, it is recommended that a biopsy of the renal mass is performed before the surgery [22].

The follow-up time for the patients undergoing PRFA was significantly lower than for the PN group. Radiological imaging is playing an increasingly important role in the diagnosis of RCC, as well as in surveillance after RCC treatment. In particular, it is recommended that patients undergoing ablation treatment be followed up with contrast-enhanced radiological imaging (MRI or CT) to evaluate the occurrence of residual diseases and postoperative difficulties. The success of this procedure is quantified when CT attenuation occurs, as this means a reduction of the tumor in the perfusion zone. In our study, we found a significant reduction in the percentage of CT scans performed between the PRFA and NP groups (Supplementary Table), as previously reported [4, 12, 34]. This makes sense since patients undergoing PRFA were also followed up with CEPUS, a new diagnostic ultrasound technology with contrast enhancers and specific analysis software to show tissue blood perfusion [21]. The main novelties of our study are that we compared the outcomes from CEPUS-guided PRFA [35, 36] under general anesthesia to the ones from PN, and we followed up with patients mainly with CEPUS in RFA and CT in PN at two different centers.

Regarding survival analysis in our study, no significant differences were detected in LRFS, MFS, and OS between PRFA and PN groups. Previously, it was already determined that the LRFS was similar for patients undergoing percutaneous ablation or PN [37]. LRFS and MFS were similar for both PN- and RFA-treated tumors in single-kidney patients [38] and in a comparative meta-analysis of RFA and PN [26, 27]. All these results indicate that in terms of survival, RFA is a feasible and safe treatment option for SRMs in high-risk patients with outcomes similar to PN. However, it is worth noting that the follow-up protocols were different between the two groups (PRFA and PN) which may lead to the comparison of LRFS and MFS being less reliable.

The main advantage of this study is that it is the first study with a reasonable number of patients and aims to compare patients undergoing CEPUS-guided PRFA and PN at two centers with experience in each procedure. Although the results are positive, this study had several limitations. Due to this retrospective study, selection bias in performing the procedures (PRFA or PN) could not be avoided, as well as other additional confounders, such as that the PN group may be favored due to the eligibility criteria. Therefore, to address this, a randomized controlled trial would be needed in the future. However, despite the

selection bias, the results remain positive. In addition, our sample size and statistical power of 70% are hardly enough to determine non-inferiority or superiority. This could be solved by increasing the sample size.

The main conclusion of our study is that PRFA for SMRs in high-risk patients is non-inferior in terms of oncological outcomes and safety compared to PN, meaning that PRFA proved to be equally effective and safe as PN. PRFA with the added benefit of being a minimally invasive procedure that may result in shorter hospital stays and fewer complications compared to PN. Hence, PRFA is an effective treatment option for SMRs. However, it is essential to note that the choice of treatment for each patient must be made on a case-by-case basis, considering factors such as tumor size, location, and patient preferences, as well as the experience and expertise of the treating physician.

Supplementary information The online version contains supplementary material available at https://doi.org/10.1007/s00330-023-09779-7.

Acknowledgements The authors are grateful for the commitment of the nurses and technicians involved in the appointments and assistance in surgery. In addition, they kindly acknowledge Patricia García-Sanz from BioMed Targets for her medical writing contributions and logistical support in preparing this manuscript.

Funding The authors state that this work has not received any funding.

Declarations

Guarantor The scientific guarantor of this publication is Dr. José Pablo Pedraza-Sánchez.

Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry Biostatech kindly provided statistical advice for this manuscript.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was not required because the study is not a randomized clinical trial.

Study subjects or cohorts overlap Not applicable.

Methodology
- prospective recruitment and retrospective analysis
- observational
- multicenter study

References

1. Sanchez A, Feldman AS, Ari Hakimi A (2018) Current management of small renal masses, including patient selection, renal tumor biopsy, active surveillance, and thermal ablation. J Clin Oncol 36:3591–3600
2. Liaw BC, Mehrazin R, Tsao CK (2019) Renal Cancer. In: Oh W, Chari A (eds) Mount Sinai Expert Guides . https://doi.org/10.1002/9781119189596.ch4
3. Padala SA, Barsouk AA, Thandra KC et al (2020) Epidemiology of renal cell carcinoma. World J Oncol 11:79–87. https://doi.org/10.14740/WJON1279
4. Krajewski KM, Pedrosa I (2018) Imaging advances in the management of kidney cancer. J Clin Oncol 36:3582–3590. https://doi.org/10.1200/JCO.2018.79.1236
5. Junker T,Duus L, Rasmussen BSB et al (2022) Quality of life and complications after nephron-sparing treatment of renal cell carcinoma stage T1-a systematic review. Syst Rev 11(1):4. https://doi.org/10.1186/s13643-021-01868-2
6. Wang J, Tang J, Chen T et al (2022) A web-based prediction model for overall survival of elderly patients with early renal cell carcinoma: a population-based study. J Transl Med 20:1–14. https://doi.org/10.1186/s12967-022-03287-w
7. Ito K, Soga S, Seguchi K et al (2017) Clinical outcomes of percutaneous radiofrequency ablation for small renal cancer. Oncol Lett 14:918–924. https://doi.org/10.3892/ol.2017.6262
8. Wai-Shun Chan V, Hanis Osman F, Cartledge J et al (2022) Long-term outcomes of image-guided ablation and laparoscopic partial nephrectomy for T1 renal cell carcinoma. Eur Radiol 32:5811–5820. https://doi.org/10.1007/s00330-022-08719-1
9. Chung DJ, Hwang H, Sohn DW (2022) Radiofrequency ablation using real-time ultrasonography–computed tomography fusion imaging improves treatment outcomes for T1a renal cell carcinoma: comparison with laparoscopic partial nephrectomy. Investig Clin Urol 63:159. https://doi.org/10.4111/icu.20210389
10. Young S, Golzarian J, Anderson JK (2019) Thermal ablation of T1a renal cell carcinoma: the clinical evidence. Semin Intervent Radiol 36:367–373. https://doi.org/10.1055/s-0039-1696650
11. Georgiades C, Rodriguez R (2013) Renal tumor ablation. Tech Vasc Interv Radiol 16:230–238. https://doi.org/10.1053/j.tvir.2013.08.006
12. Krokidis ME, Kitrou P, Spiliopoulos S et al (2018) Image-guided minimally invasive treatment for small renal cell carcinoma. Insights Imaging 9:385–390. https://doi.org/10.1007/s13244-018-0607-4
13. Pan XW, Cui XM, Huang H et al (2015) Radiofrequency ablation versus partial nephrectomy for treatment of renal masses: a systematic review and meta-analysis. Kaohsiung J Med Sci 31:649–658. https://doi.org/10.1016/j.kjms.2015.09.007
14. Andrews JR, Atwell T, Schmit G et al (2019) Oncologic outcomes following partial nephrectomy and percutaneous ablation for cT1 renal masses. Eur Urol 76:244–251. https://doi.org/10.1016/j.eururo.2019.04.026
15. Lachin JM, Foulkes MA (1986) Evaluation of sample size and power for analyses of survival with allowance for nonuniform patient entry, losses to follow-up, noncompliance, and stratification. Biometrics 42:507. https://doi.org/10.2307/2531201
16. R Core Team (2021) A language and environment for statistical computing. R. In: R Foundation for Statistical Computing, Vienna, Austria
17. Anderson K (2020) gsDesign: group sequential design. R package version 3.1.1. https://cran.r-project.org/package=gsDesign
18. Pantelidou M, Challacombe B, McGrath A et al (2016) Percutaneous radiofrequency ablation versus robotic-assisted partial nephrectomy for the treatment of small renal cell carcinoma. Cardiovasc Intervent Radiol 39:1595–1603. https://doi.org/10.1007/s00270-016-1417-z
19. Bazan F, Busto M (2014) Radiología del carcinoma renal. Radiologia 56:61–75. https://doi.org/10.1016/j.rx.2013.08.005
20. Xu L, Rong Y, Wang W et al (2016) Percutaneous radiofrequency ablation with contrast-enhanced ultrasonography for solitary and

sporadic renal cell carcinoma in patients with autosomal dominant polycystic kidney disease. World J Surg Oncol 14(1):193. https://doi.org/10.1186/s12957-016-0916-3
21. Pan KH, Jian L, Chen WJ et al (2020) Diagnostic performance of contrast-enhanced ultrasound in renal cancer: a meta-analysis. Front Oncol 10:1–9. https://doi.org/10.3389/fonc.2020.586949
22. Ljungberg B, Albiges L, Abu-Ghanem Y et al (2022) European Association of Urology guidelines on renal cell carcinoma: the 2022 update. Eur Urol. https://doi.org/10.1016/j.eururo.2022.03.006
23. Inker LA, Astor BC, Fox CH et al (2014) KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis 63:713–735. https://doi.org/10.1053/j.ajkd.2014.01.416
24. Chan VWS, Abul A, Osman FH et al (2022) Ablative therapies versus partial nephrectomy for small renal masses – a systematic review and meta-analysis. Int J Surg 97:106194. https://doi.org/10.1016/j.ijsu.2021.106194
25. Gobbo Garcia R, Katz M, Mina Falsarella P et al (2021) Percutaneous cryoablation versus robot-assisted partial nephrectomy of renal T1A tumors: a single-center retrospective cost-effectiveness analysis. Cardiovasc Intervent Radiol 44:892–900. https://doi.org/10.1007/s00270-020-02732-x
26. Katsanos K, Mailli L, Krokidis M et al (2014) Systematic review and meta-analysis of thermal ablation versus surgical nephrectomy for small renal tumours. Cardiovasc Intervent Radiol 37:427–437. https://doi.org/10.1007/s00270-014-0846-9
27. Uhlig J, Strauss A, Rücker G et al (2019) Partial nephrectomy versus ablative techniques for small renal masses: a systematic review and network meta-analysis. Eur Radiol 29(3):1293–1307. https://doi.org/10.1007/s00330-018-5660-3
28. Zhang F, Chang X, Liu T et al (2016) Prognostic factors for long-term survival in patients with renal-cell carcinoma after radiofrequency ablation. J Endourol 30:37–42. https://doi.org/10.1089/end.2015.0454
29. Bianchi L, Chessa F, Piazza P et al (2022) Percutaneous ablation or minimally invasive partial nephrectomy for cT1a renal masses? A propensity score-matched analysis. Int J Urol 29:222–228. https://doi.org/10.1111/iju.14758
30. Patel HD, Pierorazio PM, Johnson MH et al (2017) Renal functional outcomes after surgery, ablation, and active surveillance of localized renal tumors: a systematic review and meta-analysis. Clin J Am Soc Nephrol 12:1057–1069. https://doi.org/10.2215/CJN.11941116/-/DCSUPPLEMENTAL
31. Acosta Ruiz V, Båtelsson S, Onkamo E et al (2021) Split renal function after treatment of small renal masses: comparison between radiofrequency ablation and laparoscopic partial nephrectomy. Acta radiol 62:1248–1256. https://doi.org/10.1177/0284185120956281
32. Wells SA, Wong VK, Wittmann TA et al (2017) Renal mass biopsy and thermal ablation: should biopsy be performed before or during the ablation procedure? Abdom Radiol (NY) 42:1773–1780. https://doi.org/10.1007/s00261-016-1037-8
33. Cotta BH, Meagher MF, Bradshaw A et al (2019) Percutaneous renal mass biopsy: historical perspective, current status, and future considerations. Expert Rev Anticancer Ther 19:301–308. https://doi.org/10.1080/14737140.2019.1571915
34. Kassouf W, Monteiro LL, Drachenberg DE et al (2018) Canadian Urological Association guideline for followup of patients after treatment of non-metastatic renal cell carcinoma. Can Urol Assoc J 12:231–238. https://doi.org/10.5489/cuaj.5462
35. Iannuccilli JD, Dupuy DE, Beland MD et al (2016) Effectiveness and safety of computed tomography-guided radiofrequency ablation of renal cancer: a 14-year single institution experience in 203 patients. Eur Radiol 26(6):1656–64. https://doi.org/10.1007/s00330-015-4006-7
36. Balageas P, Cornelis F, le Bras Y et al (2013) Ten-year experience of percutaneous image-guided radiofrequency ablation of malignant renal tumours in high-risk patients. Eur Radiol 23(7):1925–32. https://doi.org/10.1007/s00330-013-2784-3
37. Thompson RH, Atwell T, Schmit G et al (2015) Comparison of partial nephrectomy and percutaneous ablation for cT1 renal masses. Eur Urol 67:252–259. https://doi.org/10.1016/j.eururo.2014.07.021
38. Xiaobing W, Wentao G, Guangxiang L et al (2017) Comparison of radiofrequency ablation and partial nephrectomy for tumor in a solitary kidney. BMC Urol 17:1–6. https://doi.org/10.1186/s12894-017-0269-4