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Association among the R.E.N.A.L. nephrometry score and clinical outcomes in patients with small renal masses treated with percutaneous contrast enhanced ultrasound radiofrequency ablation

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Introduction An association between the R.E.N.A.L. nephrometry score (RNS) and clinical outcomes in patients with a small renal mass (SRM) has been proposed. We analyzed clinical outcomes according to the RNS in patients with a SRM treated with percutaneous contrast enhanced ultrasound (CEUS) radiofrequency ablation (RFA).

Material and methods Patients with a SRM, who underwent RFA between January 2005 and March 2015, were retrospectively identified. The association between RNS and clinical outcomes was evaluated using parametric and non-parametric analysis.

Results We analyzed 163 SRMs in 149 consecutive patients. The mean age was 71.7 years. Mean follow-up time was 33.3 months ±20.6 (2–102). The mean RNS was 5.6 ±1.52 (4–11). A total of 121 (74.2%) cases were of low complexity and 42 (25.8%) were medium complexity. We identified 11 cases of tumor persistence (6.7%). The mean RNS was 5.58 in the cases with no persistence and 5.73 in the cases with persistence (p = 0.788). We identified 15 (9.2%) cases of recurrence. The mean RNS was 5.57 ±0.1 (4–11) in the cases without recurrence and 5.73 ±0.4 (4–9) in recurrence cases (p = 0.804). Of the 76 biopsy proven RCC cases, 8 (10.5%) cases of recurrence were observed, 5 in the low complexity group and 3 in the medium complexity group (p = 0.690). A total of 9 (5.5%) cases of complications were observed, with 5 (4.3%) in the low complexity group and 4 cases in the medium complexity group (p = 0.23). The mean length of stay was 1.5 days with a significant difference between low and medium complexity groups (1.3 vs. 2.1 days, p = 0.02). The mean difference between preoperative eGFR and estimated eGFRat 12 months was-3.08 mL / min ±13.3 (-49.4–34.1) and was significant (p = 0.008).However, this variation did not show significant differences between the low and medium complexity groups (p = 0.936). All-cause mortality was 11.7%, 14 cases (11.6%) in the low complexity group and 5 (11.9%) in the medium complexity group (p = 1.0). No cases of renal cell carcinoma (RCC) specific mortality were identified.

Conclusions The RNS was not associated with tumor persistence, recurrence, cancer specific mortality, complications or renal function 12 months after the first treatment, showing significant difference only in length of hospital stay between low and medium complexity groups.

Key Words: contrast enhanced ultrasound, R.E.N.A.L. nephrometry score ‹› radiofrequency ablation ‹› renal cell carcinoma ‹› small renal masses

INTRODUCTION

The incidence of renal cell carcinoma (RCC) has increased significantly in the last 50 years [1]. In Europe in 2008 there were 88 400 new cases and 39 300 kidney cancer-related deaths per year [2]. Nephron sparing approaches (NSA) using minimally invasive techniques are highly precise procedures specialized for small renal masses (SRM), which are defined as incidentally detected, contrast-enhancing renal tumors ≤4 cm in diameter [3]. While partial nephrectomy (PN) is the new gold standard of care for T1 RCC, there is a group of patients unfit for surgery given their short life expectancy, co-morbidities or denial. In response to the need for NSA in patients unfit for surgery, there has been an increasing interest in percutaneous ablation techniques such as radiofrequency ablation (RFA) and cryoablation (CA).
RFA for the treatment of kidney tumors was initially described by Zlotta et al. in 1997 [4] and consists of transferring alternating monopolar radiofrequency electrical currents through needle electrodes into the target tissue, which results in ionic agitation, heating, and eventual desiccation with sub-sequent coagulative necrosis [5].
During recent years, our knowledge has expanded regarding the influence of the tumor's anatomical complexity, rather than just the diameter, on clinical outcomes in terms of treatment for RCC by NSA [6, 7]. In order to measure and standardize that complexity, Kutikov and Uzzo developed the R.E.N.A.L. Nephrometry Score (RNS) in 2009 [8] which assigns points for size, location and depth of renal tumors, classifying complexity into low (4–6), medium (7–9) and high (10–12).
Contrast enhanced ultrasound (CEUS) is a real-time dynamic imaging technique that plays an important role in the management of patients treated with ablation for malignant tumors. Characterization of renal masses and cyst lesions is a well-established indication for CEUS [9]. In patients undergoing renal percutaneous tumor ablation, CEUS may be used as a pre-treatment evaluation to improve lesion visualization in difficult cases, to guide the placement of ablation devices and to detect residual tumors, either immediately or later after ablation [10, 11].
In the present study we analyzed the association between the RNS and clinical outcomes in patients with SRM treated with percutaneous RFA guided by CEUS.

MATERIAL AND METHODS

Patients who underwent percutaneous CEUS guided RFA performed in a single hospital in Barcelona, Spain between January 2005 and March 2015 were prospectively enrolled in this study. Institutional review board ethics approval was obtained. Patients were initially evaluated by a urologist to determine and counsel about the best treatment strategy. If ablation was decided upon, the patient was referred to an interventional radiologist for feasibility assessment using CEUS. Patients lacking digital images or other relevant data were excluded. Unless obtained beforehand, a simultaneous renal mass biopsy was incorporated into routine practice, particularly in later years. The biopsy was obtained during the RFA ablation, thus, the final pathology report was revealed afterwards. We used a 15 cm electrode-needle Cool-Tip TM RF ablation system under conscious sedation plus local anesthesia. When a biopsy was performed, an 18 G needle was used. If required, a bowel hydrodissection, transhepatic approach or a cold saline solution irrigation through an ureteral tube were performed. The technique used in our center was described in detail by Trilla et al. in 2017 [12]. Patients were evaluated in the urology clinic at 3, 6 and 12 months after treatment for the first year, then every 6 months for the following 4 years and yearly follow-ups thereafter, assessing clinical condition, renal function and imaging including a computed tomography (CT) scan and/or CEUS.

Outcomes and definitions

- Tumor persistence was defined as the presence of a contrast enhanced nodule or soft tissue in the treated area at the first 3 month control. The treatment was considered successful with the absence of these findings.
- Oncological outcomes
  - Recurrence, defined as a contrast enhanced nodule or soft tissue in the treated area after a negative first control.
  - Metastasis
  - Cancer specific mortality (CSM) and all-cause mortality (ACM).
- Complications, according to the Clavien–Dindo system and length of hospital stay.
- Functional results, using serum creatinine levels to calculate estimated glomerular filtration rate (eGFR) according to the Modification of Diet in Renal Disease formula. Levels at pre-treatment and at the 12 month follow-up were compared.

Statistical analysis

Clinicopathological data and outcomes were analyzed using descriptive statistics. Outcomes and R.E.N.A.L. nephrometry scores were compared us-

ing Fisher's test for categorical variables and Mann Whitney's and Wilcoxon's test for quantitative variables. Kaplan–Meier analyses was performed for overall, cancer-specific and local recurrence-free survival. Statistical significance was set at $p \leq 0.05$. SPSS software version 20.0 was used.

RESULTS

A total of 182 procedures were performed in a sample of 166 consecutive patients. We excluded 19 cases as we did not have the images necessary to calculate the RNS, which could be obtained in the 163 cases (89.5%) in the 149 (89.8%) patients who were included in the analysis. Cohort characteristics are summarized in Table 1. The mean age was 71.7 years and 69.1% were men. Mean follow-up time was 33.3 months ±20.6 (2–102). The mean RNS was 5.6 ±1.52 (4–11), 4.8 ±0.8 (4–6) in the low complexity group and 7.8 ±0.9 (7–11) in the medium complexity group ($p \leq 0.001$). Given that only one case was highly complex as determined by the RNS, this single case was included from the average complexity group. Thus, 121 cases were of low complexity and 42 of medium complexity.

Tumor persistence

We identified 11 cases of tumor persistence (6.7%). The mean size of the tumors in the non-persistent cases was 2.6 cm whereas in those with persistence it was 3.3 cm ($p = 0.01$). The mean RNS was 5.58 in the cases with no persistence and of 5.73 in the cases with persistence ($p = 0.788$). Of the 121 cases of low complexity, 8 (6.6%) had tumor persistence, whereas of the 42 cases of medium complexity, 3 (7.1%) had tumor persistence ($p = 0.57$) (Table 2). The 11 cases of persistence were submitted to a second treatment,

Table 1. *General characteristics of the whole cohort according to RNS*

Characteristc	Whole cohort	Low RNS	Medium RNS	p-value
Patients[1]	149 (100)	108 (72.5)	41 (27.5)	
Age (years)[2]	71.7 ±10.7 (36–92)	71.4 ±11.3 (36–92)	72.5 ±9.0 (50–86)	0.742
Male[1]	103 (69.1)	74 (68.5)	29 (70.7)	0.480
Female[1]	46 (30.9)	34 (31.5)	12 (29.3)	
Basal eGFR[2]	66.1 ±0.9 (3.7–159.8)	65.5 ±24.5 (16–160)	70.1 ±27 (15–114)	0.337
Right Kidney[1]	81 (49.7)	65 (53.7)	16 (38.1)	0.167
Left Kidney[1]	81 (49.7)	55(45.5)	26 (61.9)	
Renal graft[1]	1 (0.6)	1 (0.8)	0	
Procedures[1]	163 (100)	121 (74.2)	42 (25.8)	
Follow–up (months)[2]	33.3 ±20.6 (2–102)	33.3 ±19.5 (2–100)	33.4 ±23.7 (2–102)	0.678
Biopsy during procedure[1]	129 (79.1)	95 (73.6)	34 (26.4)	34 (26.4)
Tumor characteristics				
– Major diameter (cm)[2]	2.7 ±0.8 (1.2–4.9)	2.6 ±0.8 (1.2–4.9)	2.9 ±0.9 (1.5–4.9)	**0.015**
– Benign[1]	46 (35.7)	36 (37.9)	10 (29.4)	0.208
– RCC[1]	76 (58.9)	53 (55.8)	23 (69.7)	0.158
– Papillary[1]	20 (26,3)	16 (28,5)	4 (17,4)	0.256
– Clear cell[1]	39 (51,3)	26 (49,1)	13 (56,5)	
– Chromophobe[1]	11 (14.5)	6 (11.3)	5 (21.7)	
– Mucinous tubular[1]	1 (1.3)	0	1 (4.3)	
– Indeterminate[1]	5 (6.6)	5 (9.4)	0	
– Non–diagnostic biopsy[1]	7 (5.4)	6 (6.3)	1 (2.8)	

[1]: n (%); [2]: mean ±SD (min-max).
RNS – RENAL nephroemtry score; eGFR – estimated glomerular filtration rate; RCC – Renal cell carcinoma

Table 2. *Main outcomes of the whole cohort according to RNS*

Characteristc	Whole cohort	Low RNS	Medium RNS	p-value
Complications[1]	9 /163 (5.5)	5/121 (4.1)	4/42 (9.5)	0.230
Hospital stay (days)[2]	1.5 ±1.9 (1–23)	1.3 ±0.6 (1–5)	2.1 ±3.5 (1–23)	**0.020**
Basal eGFR[2]	66.6 ±25.2 (15.0–159.8)	64.3 ±2.6 (15.8–159.8)	72.1 ±4.4 (15.0–114.3)	0.298
12 months eGFR[2]	63.4 ±25.9 (8.6–138.8)	61.2 ±2.6 (8.6–138.8)	69.2 ±4.6 (8.6–119.8)	0.105
eGFR variation[2]	-3.08 ±13.3 (-49.4–34.1)	-3.1 ±1.3 (-47.8–29.1)	-2.9 ±2.6 (-49.4–34.1)	0.936
Persistence[1]	11/163 (6.7)	8/121 (6.6)	3/42 (7.1)	0.570
Recurrence[1]	15/163 (9.2)	10/121 (8.3)	5/42 (11.9)	0.530
Recurrence*[1]	8/76 (10.5)	5 /53 (9.4)	3/23 (13)	0.690
ACM	11.7 %	11.6 %	11.9 %	1.000

[1] n/total (%); [2] mean ±DS (min-max); [2] n (%); *only RCC biopsy proven
RNS – RENAL nephrometry score; eGFR – estimated glomerular filtration rate; ACM – all cause mortality

9 of them through a second RFA and 2 cases with PN. 3 cases presented a relapse after re-treatment. 2 of them were treated with a new RFA while in one case a radical nephrectomy (RN) was performed.

Tumor recurrence

We identified 15 (9.2%) cases of tumor recurrence, 8 biopsy proven RCCs (7 re-treated, with RFA), 3 initially reported as benign (2 Oncocytomas, both re-re-treated with RFA and one initially reported with no evidence, not re-treated) and 4 indeterminate (one re-treated with RN with final pathology diagnosis of RCC-clear cell, one re-treated with RFA and 2 not re-treated). No significant difference was observed in recurrence rates between these 3 groups (p = 0.344). Overall, 11 cases of recurrence were subjected to a second treatment, 10 RFA and 1 RN. In the remaining 4 cases, active surveillance was chosen considering the patients' general condition and life expectancy. The mean size of the tumors in cases without recurrence was 2.6 cm ±0.1 (1.2–4.9) whereas in those with relapse it was 3.2 cm ±0.2 (1.9–4.7) (p = 0.02). The mean RNS was 5.57 ±0.1

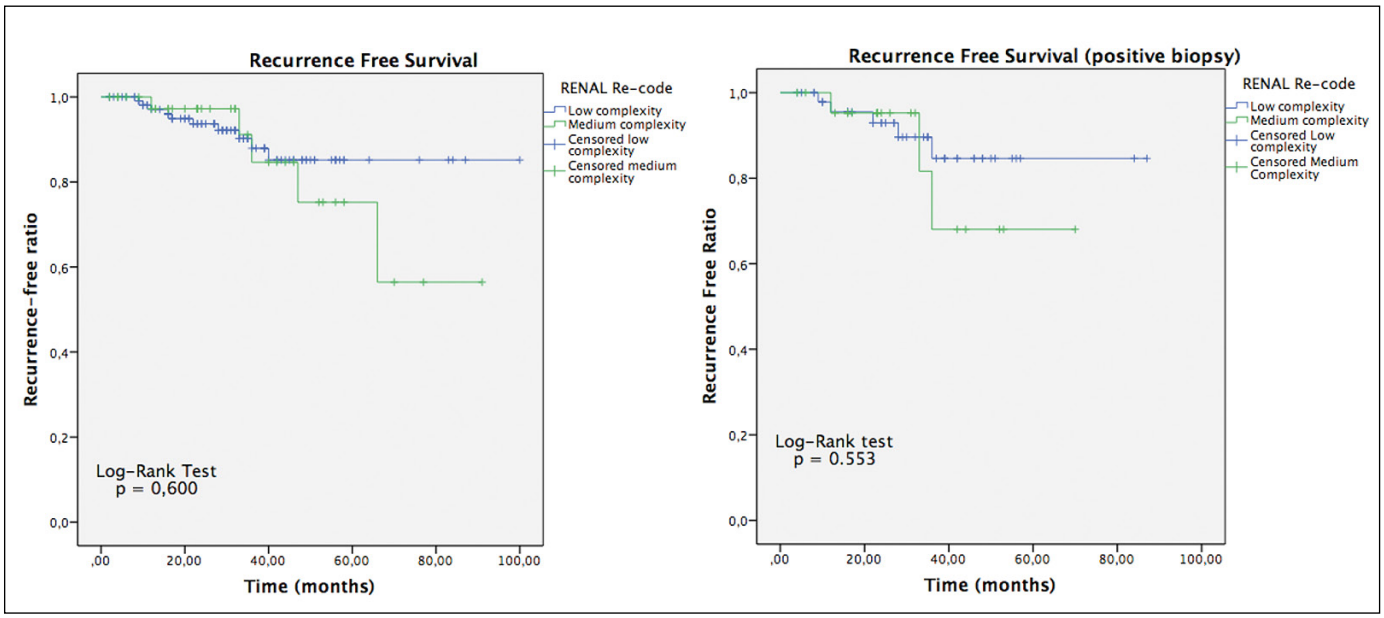

Figure 1. *Recurrence-free survival (Kaplan-Meier) according to R.E.N.A.L nephrometry score.*

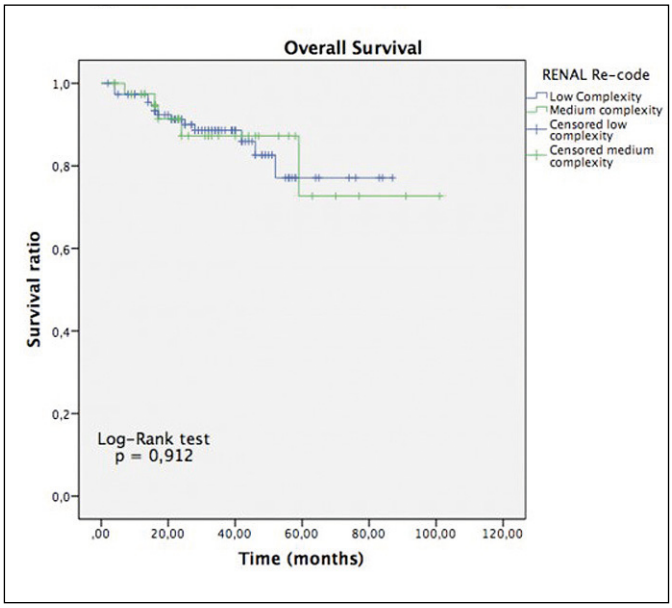

Figure 2. *Overal survival according RNS.*

(4–11) in the cases without recurrence and 5.73 ±0.4 (4–9) in cases with recurrence (p = 0.804). Of the 121 cases of low complexity, 10 (8.3%) had tumor recurrence, whereas, of the 42 cases of medium complexity, 5 (11.9%) had recurrence (p = 0.53). Of the 76 biopsy proven RCC cases, 8 (10.5%) cases of recurrence were observed, 5 in the low complexity group and 3 in the medium complexity group (p = 0.690). No significant differences of recurrence were observed among RCC subtypes (p = 0.927). Overall recurrence-free survival (RFS) and biopsy proven RCC group RFS according to RNS are presented in Figure 1.

Metastasis

One case (1.3% of biopsy-proven RCC group) of nodal metastasis was identified at 12 months after the initial treatment in a patient with tumor persistence that had been re-treated by PN. The initial tumor was 2 cm with a RNS of 4. Biopsy of the tumor showed a clear cell RCC Fuhrman grade 2.

Mortality

In total there were 19 deaths (11.7%), 14 (11.6%) in the low complexity group and 5 (11.9%) in the medium complexity group (p = 1.0). No significant difference was observed in mortality regarding the initial pathology report (7 RCC, 6 benign and 6 without biopsy, p = 0.353). No cases of RCC-specific mortality were identified. Overall survival according to RNS is presented in Figure 2.

Complications and length of stay

A total of 9 (5.5%) cases of complications were observed, 5 cases of 121 (4.3%) in the low complexity group and 4 of 42 (9.5%) cases in the medium complexity group (Table 2) (p = 0.23). In the uncomplicated group, the mean RNS was 5.5 ±0.12 (4–11), while in the group with complications the mean RNS was 6.33 ±0.5 (5–9) (p = 0.097). In the uncomplicated group the mean tumor diameter was 2.7 cm ±0.1 (1.2–4.9) whereas in the group with complications the mean tumor diameter was 3.3 cm ±0.5 (1.6–4.9) (p = 0.071). 5 complications were Clavien 1, 3 were Clavien 2 and 1 case was Clavien 3a (Table 3). The mean length of stay was 1.5 days for the whole group, with a significant difference between low and medium complexity groups (1.3 vs. 2.1 days, p = 0.02).

Renal function

There were 8 patients who were on hemodialysis prior to ablation, so they were excluded from the analysis of renal function. During follow-up 7 patients underwent renal replacement therapy (RRT), 6 of them in a hemodialysis program while 1 patient received a renal transplant. Only 1 patient required RRT during the first year of follow-up. The mean preoperative eGFR was 66.6 ±25.2 (15.0–159.8), in the low complexity group it was 64.3 ±2.6 (15.8–159.8) and in the medium complexity group, 72.1 +4.4 (15.0–114.3) (p = 0.298), while eGFR at 12 months post-ablation was 63.4 mL/min +25.9 (8.6–138.8), in the low complexity group, 61.2 mL/min +2.6 (8.6–138.8) and in the medium complexity group, 69.2 +4.6 (8.6–119.8) (p = 0.105). The mean difference between preoperative eGFR and estimated eGFR at 12 months was -3.08 mL/min +13.3 (-49.4–34.1) which was significant, (p = 0.008) however, this variation did not show significant differences between the low and medium complexity groups (p = 0.936) (Table 2).

Table 3. *Description of complications according to the RNS and Clavien-Dindo System*

	Clavien--Dindo	Low RNS	Medium RNS	Total
Subcapsular Haematoma	1	3	2	5
Subcapsular Haematoma	2	0	2	2
Abdominal collection	2	1	0	1
Skin burns	3a	1	0	1
Total		5	4	9

RNS – R.E.N.A.L. nephrometry score

DISCUSSION

Since the first publication of the RNS, there have been many articles showing a significant association with several clinical outcomes [13] such as surgical approach [14], surgical complications [15], renal functional outcome [16], ischemia time [17], histology [18] and hospital stay, [19] however there is still little evidence regarding percutaneous ablative techniques with contradictory results [20–23].

We observed a 6.7% tumor persistence rate, which is slightly higher than the 5.9% reported in the systematic review performed by Vollherbst et al. [24] but lower than the 13% reported by Ptsuka et al. [25]. We observed that tumor median size was significantly higher in patients with persistence. Using a CT guide, Ianuccilli et al. studied 203 biopsy-proven, percutaneous RFA findings that tumor size ≥3.5 cm confers a significantly increased risk for residual tumors [26]; whereas Wah et al. found, in a multivariate, logistic regression analysis of 200 percutaneous RFA, that two independent predictors of successful RFA in a single setting were tumor size (<3 cm) and exophytic location [27]. The RNS was higher in patients with tumor persistence but this difference was not significant. Concordantly, the local failure ratio reported by Bhindi et al. using CA (defined as failure of the ablation ice ball to extend beyond the tumor margin on monitoring CT imaging during the procedure) was also not associated to the RNS [23].

We found a recurrence rate of 9.2% (10.5% in biopsy proven cases) which is on the higher end of the interval observed in literature according to the Vollherbst et al. systematic review [24]. Tumor size was significantly higher in patients with recurrence. The RNS was higher in patients with recurrence but this difference was not significant. These findings are not concordant with the results of Camacho et al. who studied 101 biopsy proven SRMs treated with CA (54%) or RFA (46%) and reported a significant correlation between recurrence and a RNS >8 [28]. In another study performed by Schmit et al., 751 renal tumors were treated using a percutaneous approach with CA (57%) or RFA (43%) and retrospectively categorized regarding the RNS, finding that mean RNS was 7.6 versus 6.9 in patients with or without treatment failure respectively ($p = 0.001$). These differences may be explained by the lack of a high complexity group in our study whereas the Camacho et al. study had 61 low, 26 medium and 14 high patients regarding the RNS and the Schmit et al. study had 351, 330 and 70 low, medium and high complexity cases respectively. On the other hand, Maxwell et al. studied 217 biopsy-proven SRMs treated mainly with CT guided percutaneous RFA reporting that maximum tumor diameter was the strongest predictor of local recurrence with a Harrell C index = 0.81 while RNS was found to be significantly predictive but showing poor performance with a Harrell C index = 0.68, limiting its overall utility in the authors' opinion [29]. Neither pathology report nor subtype of RCC were associated with recurrence nor mortality, which is consistent with previous research, finding that 64–84% of SRM are indolent tumors. Contrarily, a significant proportion of patients with SRM who progress to metastatic cancer are not identified by current pathological techniques. New technology in imaging and molecular analysis are currently in development to address this issue [30].

We had only one case of metastatic progression, however, it was in a patient who had a small (2 cm), low RNS and low Fuhrman's grade tumor, which is concerning considering our current understanding that SRMs rarely provoke metastatic disease when sized <3 cm [25]. Minardi et al. studied 48 patients with a pT1a RCC treated with PN finding that distant metastatic disease occurred in 2.4% of patients with tumors <3 cm versus 8.4% of patients with tumors between 3.1 cm and 4 cm, which is concordant with our results [31].

We observed an ACM of 11.7% without statistical difference between low and medium RNS groups.

Our complication rate of 5.5% is within the range of the 5.1–37% reported by the Vollherbst et al. Systematic review [24]. RNS and tumor diameter were larger in the cases with complications, however no significant difference was found. Length of hospital stay was the only issue significantly associated with RNS. Tumor diameter or size has been considered a significant factor influencing the procedure's safety. In the Camacho et al. study, a diameter >2 cm and a RNS >8 were significantly correlated with the presence of complications while in the Schmit et al. study, the RNS was found to be significantly higher (8.1 vs. 6.8, $p = 0.001$) comparing patients with and without major complications. Again, the lack of a high complexity group in our study could explain these differences.

We observed a slight but significant decrease of eGFR one year after the first RFA which reflects the fragility of this population. No significant difference was observed between RNS groups. Lucas et al. studied renal function in patients with RCC, finding that patients treated with RN were 34.3 times more likely to develop stage 3 chronic renal disease than patients treated with PN or percutaneous RFA [32]. In our study, one patient was successfully treated by renal graft. Cool et al. studied outcomes and graft viability after percutaneous RFA of 12 biopsy-proven

RCC developing within renal transplant allografts. The authors reported 100% technical success and no recurrence nor progression after a mean follow-up of 54 months with no significant difference in eGFR previous to and 6 months after the procedure [33].
According to the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) guidelines, the use of CEUS can be useful in the management of RCC patients undergoing ablation procedures due to the improved visualization of ambiguous tumors, the assessment of therapeutic efficacy within 24 h after ablation, the detection of unablated tumors and local tumor progression, and the ability to guide re-ablation of recurrent viable tissue [10].
In our study, all cases had a first evaluation by the same radiologist who performed the procedure, assessing the reliability of the treatment. During the procedure, CEUS was used to guide the needle and to evaluate the ablation's success in difficult cases. In our follow-up protocol CT scan and CEUS were used, however, we did not evaluate the concordance between CT and CEUS to detect recurrence.
Our study has several limitations. First of all, we performed a retrospective analysis reflecting the experiences within the first ten years of a single hospital. Only in 79% of our treatments was a biopsy sample obtained as this was not part of our protocol in the beginning. Also, we had a lack of a high complexity group according to the RNS which could have influenced our results; having a very homogeneous sample of patients could have prevented us from finding more significant outcomes.

CONCLUSIONS

In conclusion, percutaneous CEUS-RFA is a feasible technique with excellent functional and oncological outcomes and low rate of complications. The RNS was not associated with tumor persistence, recurrence, cancer specific mortality, complications or renal function showing significant difference only in length of hospital stay between low and medium complexity groups.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

References

1. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. CA Cancer J Clin. 2008; 58: 71-96.
2. Ljungberg B, Bensalah K, Canfield S, et al. EAU guidelines on renal cell carcinoma: 2014 update. Eur Urol. 2015; 67: 913-924.
3. Finelli A, Ismaila N, Russo P. Management of Small Renal Masses: American Society of Clinical Oncology Clinical Practice Guideline Summary. J Oncol Pract. 2017; 13: 276-278.
4. Zlotta AR, Wildschutz T, Raviv G, et al. Radiofrequency interstitial tumor ablation (RITA) is a possible new modality for treatment of renal cancer: ex vivo and in vivo experience. J Endourol. 1997; 11: 251-258.
5. Carraway WA, Raman JD, Cadeddu JA. Current status of renal radiofrequency ablation. Curr Opin Urol. 2009; 19: 143-147.
6. Breen DJ, Rutherford EE, Stedman B, et al. Management of renal tumors by image-guided radiofrequency ablation: experience in 105 tumors. Cardiovasc Intervent Radiol. 2007; 30: 936-942.
7. Gervais DA, McGovern FJ, Arellano RS, McDougal WS, Mueller PR. Radiofrequency ablation of renal cell carcinoma: part 1, Indications, results, and role in patient management over a 6-year period and ablation of 100 tumors. AJR Am J Roentgenol. 2005; 185: 64-71.
8. Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. J Urol. 2009; 182: 844-853.
9. Wilson SR, Burns PN. Microbubble-enhanced US in body imaging: what role. Radiology. 2010; 257: 24-39.
10. Piscaglia F, Nolsøe C, Dietrich CF, et al. The EFSUMB Guidelines and Recommendations on the Clinical Practice of Contrast Enhanced Ultrasound (CEUS): update 2011 on non-hepatic applications. Ultraschall Med. 2012; 33: 33-59.
11. Meloni MF, Smolock A, Cantisani V, et al. Contrast enhanced ultrasound in the evaluation and percutaneous treatment of hepatic and renal tumors. Eur J Radiol. 2015; 84: 1666-1674.
12. Trilla E, Konstantinidis C, Serres X,et al. Ultrasound-guided percutaneous radiofrequency ablation for treating small renal masses. Actas Urol Esp. 2017; 41: 497-503.
13. Konstantinidis C, Trilla E, Lorente D, Morote J. Utility of the RENAL index -Radius; Exophytic/endophytic; Nearness to sinus; Anterior/posterior; Location relative to polar lines- in the management of renal masses. Actas Urol Esp. 2016; 40: 601-607.
14. Tobert CM, Kahnoski RJ, Thompson DE, Anema JG, Kuntzman RS, Lane BR. RENAL nephrometry score predicts surgery type independent of individual surgeon's use of nephron-sparing surgery. Urology. 2012; 80: 157-161.
15. Rosevear HM, Gellhaus PT, Lightfoot AJ, Kresowik TP, Joudi FN, Tracy CR. Utility of the RENAL nephrometry scoring system in the real world: predicting surgeon operative preference and complication risk. BJU Int. 2012; 109: 700-705.
16. Simmons MN, Hillyer SP, Lee BH, Fergany AF, Kaouk J, Campbell SC. Nephrometry score is associated with volume loss and functional recovery after partial nephrectomy. J Urol. 2012; 188: 39-44.
17. Zhang ZY, Tang Q, Li XS, et al. Clinical analysis of the application of R.E.N.A.L. nephrometry score for the nephron sparing surgery. Beijing Da XueXueBao. 2012; 44: 539-543.

18. Kutikov A, Smaldone MC, Egleston BL, et al. Anatomic features of enhancing renal masses predict malignant and high-grade pathology: a preoperative nomogram using the RENAL Nephrometry score. Eur Urol. 2011; 60: 241-248.

19. Ellison JS, Montgomery JS, Hafez KS, et al. Association of RENAL nephrometry score with outcomes of minimally invasive partial nephrectomy. Int J Urol. 2012; 20: 564-570.

20. McClure TD, Chow DS, Tan N, Sayre JA, Pantuck AJ, Raman SS. Intermediate outcomes and predictors of efficacy in the radiofrequency ablation of 100 pathologically proven renal cell carcinomas. J VascInterv Radiol. 2014; 25: 1682-1688.

21. Schmit GD, Thompson RH, Kurup AN, et al. Usefulness of R.E.N.A.L. nephrometry scoring system for predicting outcomes and complications of percutaneous ablation of 751 renal tumors. J Urol. 2013; 189: 30-35.

22. Seideman CA, Gahan J, Weaver M, et al. Renal tumournephrometry score does not correlate with the risk of radiofrequency ablation complications. BJU Int. 2013; 112: 1121-1124.

23. Bhindi B, Thompson RH, Mason RJ, et al. Comprehensive assessment of renal tumour complexity in a large percutaneous cryoablation cohort. BJU Int. 2017; 119: 905-912.

24. Vollherbst D, Bertheau R, Kauczor HU, Radeleff BA, Pereira PL, Sommer CM. Treatment Failure After Image-Guided Percutaneous Radiofrequency Ablation (RFA) of Renal Tumors- A Systematic Review with Description of Type, Frequency, Risk Factors and Management. Rofo. 2017; 189: 219-227.

25. Psutka SP, Feldman AS, McDougal WS, McGovern FJ, Mueller P, Gervais DA. Long-term oncologic outcomes after radiofrequency ablation for T1 renal cell carcinoma. Eur Urol. 2013; 63: 486-492.

26. Iannuccilli JD, Dupuy DE, Beland MD, Machan JT, Golijanin DJ, Mayo-Smith WW. Effectiveness and safety of computed tomography-guided radiofrequency ablation of renal cancer: a 14-year single institution experience in 203 patients. Eur Radiol. 2016; 26: 1656-1664.

27. Wah TM, Irving HC, Gregory W, Cartledge J, Joyce AD, Selby PJ. Radiofrequency ablation (RFA) of renal cell carcinoma (RCC): experience in 200 tumours. BJU Int. 2014; 113: 416-428.

28. Camacho JC, Kokabi N, Xing M, Master VA, Pattaras JG, Mittal PK et al. R.E.N.A.L. (Radius, exophytic/endophytic, nearness to collecting system or sinus, anterior/posterior, and location relative to polar lines) nephrometry score predicts early tumor recurrence and complications after percutaneous ablative therapies for renal cell carcinoma: a 5-year experience. J Vasc Interv Radiol. 2015; 26: 686-693.

29. Maxwell AWP, Baird GL, Iannuccilli JD, Mayo-Smith WW, Dupuy DE. Renal Cell Carcinoma: Comparison of RENAL Nephrometry and PADUA Scores with Maximum Tumor Diameter for Prediction of Local Recurrence after Thermal Ablation. Radiology. 2017; 283: 590-597.

30. Shapiro DD, Abel EJ. Predicting aggressive behavior in small renal tumors prior to treatment. Ann Transl Med. 2018; 6 (Suppl 2): S132.

31. Minardi D, Lucarini G, Mazzucchelli R,et al. Prognostic role of Fuhrman grade and vascular endothelial growth factor in pT1a clear cell carcinoma in partial nephrectomy specimens. J Urol. 2005; 174: 1208-1212.

32. Lucas SM, Stern JM, Adibi M, Zeltser IS, Cadeddu JA, Raj GV. Renal function outcomes in patients treated for renal masses smaller than 4 cm by ablative and extirpative techniques. J Urol. 2008; 179: 75-79.

33. Cool DW, Kachura JR. Radiofrequency Ablation of T1a Renal Cell Carcinomas within Renal Transplant Allografts: Oncologic Outcomes and Graft Viability. J VascInterv Radiol. 2017; 28: 1658-1663.