Percutaneous Microwave Ablation is Comparable to Cryoablation for the Treatment of T1a Renal Masses: Results From a Cross-Sectional Study

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Abstract

Percutaneous microwave ablation (MWA) of renal tumors has been less investigated compared to cryoablation (CA). In this study we showed that perioperative, functional and oncological outcomes of patients with renal tumors treated with CA and MWA were similar. Operative time was shorter for MWA.

Introduction: Percutaneous microwave ablation (MWA) of renal masses (RM) is still considered experimental as opposed to established procedures such as cryoablation (CA). We aimed to compare perioperative, functional and oncological outcomes of patients with RM treated with CA and MWA. **Materials and Methods:** Data from 116 (69.9%) and 50 (30.1%) patients treated with CA and MWA for RM were analyzed. Patients' demographics and perioperative data were collected including nephrometry scores, complications, pre- and postprocedural renal function. Tumor persistence and recurrence were recorded. Descriptive statistics compared functional outcomes between groups. Cox regression analyses tested risk factors associated with recurrence. **Results:** Groups were similar in terms of RM diameter, nephrometry scores and histology distribution. Median follow-up was 26 (13-46) and 24 (14-36) months for CA and MWA, respectively. The rate of overall (36.2% for CA vs. 24% for MWA, $P = .1$) and major (Clavien $\geq$ 3a) complications (1.7% vs. 5.4%, $P = .1$) were similar among groups. The median decline of renal function after 6 months follow-up did not differ between CA and MWA ($P = .8$). Tumor persistence [4.3% vs. 12%] and recurrence [9.5% and 7.1%] rates were similar for CA and MWA. Three years recurrence free and overall survival were 91% versus 95% (log-rank $P = .77$) and 80 versus 88% (log-rank $P = .23$) in the CA and MWA groups, respectively. At Cox analysis no predictors were found associated with recurrence. **Conclusion:** Despite being considered still experimental, MWA showed comparable outcomes relative to CA in terms of safety, preservation of renal function and oncological efficacy.

Clinical Genitourinary Cancer, Vol. 20, No. 6, e506–e511
Keywords: Small renal mass, Microwave ablation, Cryoablation, Renal tumor, Oncologic outcomes

Introduction

Renal cell carcinoma (RCC) accounts for 3% to 5% of new cancer diagnosis and 90% of renal tumors.[1] In the past decades, extended use of abdominal imaging has led to a progressive increase in renal masses detection, particularly for early-stage tumors, which now represent more than half of new diagnosis.[2] Along with renal tumor stage migration, different nephron sparing approaches have been developed to optimize both functional and oncological outcomes. In this context, interest in nonsurgical management of small renal masses is continuously growing and thermal ablation (TA) has emerged as a valid alternative to surgery thanks to its limited surgical impact.[3] Different modalities have been employed, among which cryoablation (CA) and heat-based energies (radiofrequency (RFA) and microwave (MWA)) are the most used to date.[4] CA employs 2 freeze-thaw cycles to generate an "ice ball", in which osmotic and structural changes determine disruption of target cells as well as microvascular damage. On the other hand, heat-based techniques generate an area of coagulative necrosis. In MWA, the electromagnetic field generated by microwaves determines a high frequency movement of water molecules in the target tissue that augments their kinetic energy, which is in turn transformed into

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Submitted: Apr 24, 2022; Revised: Jun 29, 2022; Accepted: Jul 9, 2022; Epub: 16 July 2022

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Table 1 General Characteristics of the Study Cohort.

Variable	Frequency
Age (years), median (IQR)	74 (65-79)
Male gender, *n* (%)	96 (57.8)
BMI (kg/m^2), median (IQR)	26.3 (23.9-28.8)
CCI, median (IQR)	3 (2-5)
CCI > 2, *n* (%)	119 (72.6)
RM diameter (cm), median (IQR)	2.4 (1.8-3.0)
mR.E.N.A.L., median (IQR)	7 (5-8)
Preoperative CKD, *n* (%)	86 (52.5)
Single kidney, *n* (%)	15 (9.1)

Abbreviation: CCI = Charlson comorbidity index; CKD = chronic kidney disease; IQR = interquartile range; mR.E.N.A.L = modified radius, exophytic/endophytic, nearness, anterior/posterior, location; RM = renal mass.

thermal energy.[5] This specific modality of heat generation has been shown to reach higher temperatures, thus producing a larger and more uniform area of ablation compared to RFA, while significantly reducing the duration of the procedure.[6] Current European Association of Urology (EAU) Guidelines recommend partial nephrectomy as the first line option for small renal tumors, limiting thermal ablation to elderly or comorbid patients not eligible for surgery.[7,8] In this context, the use of CA is supported by a robust experience, whereas MWA has been studied less extensively and the technique is still regarded as “experimental” or “investigational.[7,8] Therefore, we aimed to assess and compare the perioperative, functional, and oncological outcomes of patients with renal masses treated with CA and MWA.

Materials and Methods

Separate cohorts of individuals harboring a renal mass (RM) treated at 2 academic centers by either CA (A. O. Universitaria Ospedali Riuniti di Trieste, Trieste, Italy) or MWA (Fondazione IRCCS Ca’ Granda, Ospedale Maggiore Policlinico, Milan, Italy) between 2013 and 2021 were retrospectively analyzed and compared. For each case, thermal ablation was deemed as the most appropriate treatment option by a multidisciplinary team of urologists and interventional radiologists.

Renal masses were diagnosed and characterized by contrast enhanced cross-sectional imaging (computed tomography and/ or magnetic resonance) which allowed for preprocedural planning and complexity definition.

Descriptive features of each patient and renal mass, as well as perioperative parameters and follow-up findings were recorded. Health significant comorbidities were scored according to the age adjusted Charlson comorbidity index (CCI)[9] and renal mass complexity was described through the modified radius, exophytic/endophytic, nearness, anterior/posterior, location (mR.E.N.A.L.) nephrometry system.

A preoperative evaluation consisting of blood examination (complete blood count, biochemistry, and coagulation profile) was performed within a month prior to the procedure and glomerular filtration rates estimated (eGFR) through the CKD-EPI formula. Antiplatelet and anticoagulant medications were managed according to each hospital protocol.

Each procedure was carried out under local anesthesia or deep sedation, and life parameters (EKG, heart rate, oxygen saturation, respiratory rate, and blood pressure) were continuously monitored throughout and briefly after the procedure. Ultrasound or computed tomography (either regular or cone beam) guidance was employed for probe positioning and perioperative monitoring. If deemed appropriate, a renal mass biopsy (RMB) was carried out either at the time of prior to the ablation through an 18G coaxial needle.[8]

Patients were then admitted to the urology department for postoperative monitoring, where a CBC was obtained after the procedure and on postoperative day 1; serum creatinine level was measured on postoperative day 1. Hospitalization time was tailored based on hospital preference and patients’ characteristics. Most of the patients underwent cross-sectional imaging on postoperative day 1 for detection of local complications (eg, hematomas); if no complications were found patients were discharged on postoperative day 1.

Ablation Techniques

Microwave ablation was performed percutaneously through the Emprint Ablation System (Covidien, Boulder, CO), composed by a 100 W generator and a straight probe with a pump for system refrigeration. Procedures were carried out under local anesthesia and sedation and either CT or US guided. In these latter cases, cone beam computed tomography (CBCT), or conventional CT was sometimes employed as complementary. Ablation time was decided based on the mass’ diameter according to the manufacturer’s guidelines.

Cryoablation procedures were mostly carried out under local anesthesia and occasionally under deep sedation. Every CA was performed trough a percutaneous access under CT guidance using the Galil Medical/BTG cryoablation system (Boston Scientific, MN) equipped with 17-gauge cryoprobes. The number of cryoprobes and their intertumoral placement was chosen by the interventional radiologist to obtain in a single session the radical treatment of the tumor with adequate safety margins of at least 5 mm. The ablation procedures consisted in 2 cycles of about 10 minutes of freezing followed by 8 to 10 minutes of thawing.

Follow-up was carried out after 1 month and every 6 months for the first 2 years, and yearly afterward up to 5 years, by means of contrast enhanced cross sectional imaging and GFR estimation. Tumor persistence was defined as the presence of focal enhancement of more than 15 Hounsfield Units (HU) at each scan at 1-month cross-sectional imaging. New focal enhancement on subsequent follow-up imaging was defined as local recurrence.[5] For long-term renal function, the last available creatinine level was employed (with at least 6 months of follow-up for all cases).

Data collection adhere to the principles of the Declaration of Helsinki. All patients signed an informed consent agreeing to share their own anonymous information for future studies. The study was approved by the IRCCS Foundation Ca’ Granda – Maggiore Policlinico Hospital Ethical Committee (Prot. 25508).

Table 2 **Baseline Characteristics of Each Cohort.**

Variable	Cryoablation	Microwave Ablation	*P* Value*
Age (years), median (IQR)	75 (67-80)	72 (59-78)	.034
BMI (kg/m^2), median (IQR)	26.2 (23.8-29.1)	26.3 (24.6-28.3)	.81
CCI (age-adjusted), median (IQR)	3 (2-4)	4 (3-6)	.023
CCI > 2, *n* (%)	79 (69.3)	40 (80.0)	.15
Follow-up (months), median (IQR)	26 (13-46)	24 (14-36)	.49
Previous renal tumor, *n* (%)			
- Radical nephrectomy			
- Partial nephrectomy	11 (9.4)		
10 (8.6)			
1 (0.8)	12 (22.6)		
6 (11.3)			
6 (11.3)	0.03		
0.34			
0.03			
RM diameter (cm), median (IQR)	2.4 (1.8-3)	2.5 (1.7-3.4)	.70
mR.E.N.A.L., median (IQR)	7 (6-8)	6 (5-8)	.06
Baseline eGFR (mL/min), median (IQR)	59 (42-71.5)	70.8 (54-90.5)	.03

Abbreviation: BMI = body mass index; CCI = Charlson comorbidity index; eGFR = estimated glomerular filtration rates; IQR = interquartile range; mR.E.N.A.L = modified radius, exophytic/endophytic, nearness, anterior/posterior, location; RM = renal mass.

* *P* value according to the Mann-Whitney test or the Fisher exact test, when indicated.

Statistical Analysis

Normality of data was tested with the Shapiro-Wilk test. Descriptive statistics of categorical variables focused on frequencies and proportions. Medians and interquartile ranges (IQR) were reported for continuously coded variables. The Mann-Whitney and Fisher exact tests were used to compare clinical and perioperative variables between the MWA and CA groups. Log-rank analyses were used to detect any possible difference in recurrence between the 2 groups. Kaplan-Meier analyses were used to create recurrence plots. Statistical tests were performed using SPSS v.26 (IBM Corp., Armonk, NY). All tests were 2 sided, with a significance level set at 0.05.

Results

Overall, 116 (69.9%) and 50 (30.1%) renal masses underwent percutaneous tumor ablation by means of CA and MWA, respectively. Descriptive features of the whole cohort are outlined in Table 1. Overall, median (IQR) age was 74 (65-79) years and 72.6% of participants had an age adjusted CCI > 2. Preoperative CKD was found in 87 (52.4%) patients. Median RM diameter was 2.4 (1.8-3.0) cm. Table 2 depicts descriptive statistics of the whole cohort as segregated according to the type of procedure. Patients in the CA group were older ($P = .03$) and had a worse baseline renal function ($P = .03$) than those in the MWA. Moreover, the age adjusted CCI score was lower ($P = .02$) and a history of previously treated renal tumors was less frequent ($P = .03$) in the CA group (Table 2). No differences between groups were noted in terms of maximum RM diameter and mR.E.N.A.L. score. Median follow-up was 24 (IQR 14-36) months and 26 (13-46) months in the MWA and CA group ($P = .4$), respectively.

A renal mass biopsy was performed in 134 (80.7%) cases, with an overall diagnostic yield of 78.1% (Table 3).

CA was associated with longer procedural time [84 (73-100) versus 45 (30-60) minutes, $P < .001$], but shorter hospital stays [1 (1-1) versus 2 (1-3) days, $P < .001$] than MWA (Table 4). Overall postoperative complication rates were 36.2% and 24% in the CA and MWA groups, respectively ($P = .1$). Bleeding was the most frequent postoperative adverse event and it appeared in 35 (30.2%) and 9 (18%) cases after CA and MWA ($P = .07$), respectively (Table 4). Major complications (Clavien ≥ 3a) were similar among groups ($P = .1$). In details, 2 patients in the MWA and CA groups underwent trans arterial embolization (TAE) for postoperative bleeding (Clavien 3a); after MWA there was one case of collecting system rupture for a completely endophytic mass, which was managed by percutaneous nephrostomy placement (Clavien 3a). Groups did not differ in terms of eGFR variation ($P = .8$).

Tumoral persistence was observed in 5 (4.3%) and 6 (12%) patients after CA and MWA, respectively. Local recurrence was found in 11 (9.5%) and 3 (7.1%) cases after CA and MWA, respectively (all $P > .05$) (Table 5). Similarly, tumor progression and cancer-specific mortality were comparable among groups (Table 5). A secondary intervention for either a persistence or a recurrence was necessary in 13 (10.1%) and 4 (7.7%) cases after CA and MWA, respectively ($P = .4$). Three years recurrence free and overall survival were 91% versus 95% (log-rank $P = .77$) and 80 versus 88% (log-rank $P = .23$) in the CA and MWA groups, respectively. At Cox analysis no predictors were found associated with recurrence (Table 6).

Discussion

Percutaneous thermal ablation is among the available treatment options for small renal tumors, particularly in frail patients. Current American Urological Association (AUA) and EAU guide-

Table 3 Histologic Characterization of Renal Masses for Each Procedure.

Histology, *n* (%)	Cryoablation (Total = 108)	Microwave Ablation (Total = 34)
Clear cell carcinoma	35 (32.4)	8 (23.6)
Papillary carcinoma	19 (17.6)	2 (5.9)
Chromophobe carcinoma	3 (2.8)	0 (0)
Oncocytoma	27 (25.0)	6 (17.6)
Angiomyolipoma	2 (1.9)	4 (11.7)
Other malignant	5 (4.6)	0 (0)
Inadequate material	7 (6.4)	8 (23.6)
No evidence of neoplasm	10 (9.3)	6 (17.6)

Table 4 Perioperative and Functional Outcomes.

	Cryoablation	Microwave Ablation	*P* Value*
Procedural time, median (IQR)	84 (73-100)	45 (30-60)	<.001
Hospital stay, median (IQR)	1 (1-1)	2 (1-3)	<.001
Overall complications *n* (%)	42 (36.2)	12 (24)	.12
- Postoperative bleeding *n* (%)	35 (30.2)	9 (18)	.1
- Pneumothorax	3 (2.5)	1 (1.8)	1
- Pneumonia	1 (0.8)	1 (1.8)	1
- Hematuria or UT disruption	1 (0.8)	2 (3.6)	.2
- Monosymptomatic fever	1 (0.8)	1 (1.8)	.51
- Transitory nerve damage	0 (0)	2 (3.6)	.1
- Major (Clavien ≥ 3a) complications *n* (%)	2 (1.7)	3 (5.4)	.15
- Bleeding *n* (%) (3a)	2 (1.7)	2 (3.6)	.30
- Collecting system rupture (3a) *n* (%)	0 (0)	1 (1.8)	.30
eGFR drop %, median (IQR)			
– Whole cohort	4.7 (−1.5 to 18.3)	5.4 (−6.4 to 19.0)	.83
- Single kidney	11 (−11.5 to 57.7)	9.2 (0.0-17.0)	.54

Abbreviation: eGFR = estimated glomerular filtration rates. * *P* value according to the Mann-Whitney test or the Fisher exact test, when indicated.

Table 5 Oncological and Survival Outcomes.

	Cryoablation	Microwave Ablation	*P* Value
Tumor persistence, *n* (%)	5 (4.3)	6 (12)	.07
Local recurrence, *n* (%)	11 (9.5)	3 (7.1)	.46
Secondary interventions, *n* (%)	13 (10.1)	4 (7.7)	.41
Cancer-related mortality, *n* (%)	3 (2.6)*	0 (0)	.33
Overall mortality, *n* (%)	18 (15.5)	4 (8)	.14

*Among the 3 patients in the CA group that were classified as dead due to tumor progression, 2 patients had previously undergone radical nephrectomy for pT3a cN0M0 clear cell renal cell cancer and subsequently developed a small renal tumor in the remaining kidney, which was treated by CA. One patient developed recurrences along the cryoprobe tract and subsequently a metastatic disease that induced deaths.

lines consider RFA and CA as established procedures, while microwave ablation is still deemed as experimental due to its more recent employment and a less robust body of evidence.[7,8] Our study shows that MWA lead to similar perioperative, functional, and oncologic outcomes as compared to CA, thus representing a valid option for percutaneous thermal ablation of selected renal tumors.

We revealed that procedural time for CA was almost doubled compared to MWA, which is due to the latter's intrinsic high efficiency in tissue heating and energy diffusion.[6] Bleeding was the most frequently observed complication for both groups in our series, with slightly higher incidence after cryoablation (30.2% vs. 18%). To this regard, MWA is thought to achieve better hemostatic effect thanks to the high temperatures produced.[10] In a large retrospective series focusing on complications, Atwell et al. observed a 5% incidence of perioperative bleeding after CA.[11] Of notice, authors reported only major events, frequently requiring trans arterial embolization (Clavien-Dindo 3a). This is in line with our results since we observed that TAE was performed in 3.6% and 1.7% of MWA and CA patients, without difference among groups. Furthermore, one patient in the MWA group experienced collecting system rupture requiring urinary drainage. In this matter, some authors raise the concern over the poor control of ablation margins

Table 6 Univariate Cox Regression Analysis Testing the Association Between Predictors and Disease Recurrence (HR; *P* Value [95% CI]) in the Whole Cohort.

Predictor	HR; *P* Value (95% CI)
Age	1.03; .61 (0.96-1.06)
CCI	0.98; .92 (0.72-1.34)
Previous kidney cancer	2.23; .17 (0.69-7.39)
Tumor diameter	1.12; .71 (0.62-2.03)
mR.E.N.A.L.	1.01; .51 (0.82-1.48)
CA procedure	1.25; .73 (0.34-4.57)

Abbreviation: CA = cryoablation; CCI = Charlson comorbidity index; mR.E.N.A.L = modified radius, exophytic/endophytic, nearness, anterior/posterior, location.

during MWA,[12] differently from CA where it is possible to monitor the procedure controlling the inclusion of the whole tumoral mass in the ice-ball, avoiding potential damage to nearby tissues.[13] It should be mentioned that this complication was observed in a patient with a complete endophytic lesion, close to the collecting system, thus representing a high-risk case for every percutaneous procedure. Moreover, neither procedure led to a substantial long-term decline in glomerular filtration rate, which is consistent with previous studies demonstrating that thermal ablation is safe in patients affected by CKD.[14] Length of stay was shorter in the CA group, though the observation may be related to differences in hospital protocols. In fact, a recent single center series has shown the feasibility of same day discharge after percutaneous MWA.[15] In terms of oncologic outcomes, recurrence and survival rates were similar among groups, which is coherent with data from comparable studies.[16,17] De Cobelli et al.[18] showed a 6% tumor persistence rate after MWA, which is lower compared to our results. Aarts et al. reached an 89% primary efficacy rate in T1a lesions after MWA, with a significant number of subsequent secondary ablations.[19] It should be noted that ablated tumors can show enhancement for up to 3 to 6 months even in the absence of residual disease,[20] thus recommending caution when evaluating early follow-up imaging. In addition, most of the persistent lesions in our MWA cohort could be managed conservatively. As mentioned, one patient experienced local recurrence after CA along the cryoprobe tract. As for renal mass biopsy, disruption of the tumor surface during TA may indeed determine neoplastic cell seeding. To this regard, coagulation of the probe tract at the end of MWA could theoretically reduce the risk of such event.[21]

Strength of our study is the novelty of the results, showing that MWA is a safe and effective procedure with comparable outcomes compared to CA. Furthermore, the increasing detection of small renal masses and the need to treat an increasing number of frail patients with high comorbid burden by minimally invasive and safe procedure, such as MWA, provide our results a strong characterization in the everyday clinical practice.

Our study is not devoid of limitations. First the retrospective nature of this study did not allow for control for confounding variables determined by the diverse management of each case. Of clinical importance, there was a non-negligible number of patients who underwent thermal ablation for benign lesions. Frequently, the decision to treat was based on imaging and patients' history alone, and RMB was hence performed at the time of the procedure in these cases. Of note, the EAU guidelines strongly recommend that a biopsy should be taken prior to, and not concurrent, to the procedure, although it does not state the same for nephron-sparing surgery.[7] Therefore, RMB is not recommended before invasive surgery, such as partial nephrectomy which harbor the risk of kidney loss, with possible benign pathology postoperatively. This discrepancy is most likely due to the risk of a nondiagnostic sample when performing RMB. On the other hand, while considering biopsy prior to thermal ablation as the best option, the AUA guidelines suggest that the timing of RMB should be chosen on an individual basis, as a staged approach may increase the costs and the risk of complications.[8] This is particularly true in patients with single kidney or with multiple complications, which are usually candidate for thermal ablation. Nevertheless, tumors such as oncocytomas, though benign, may still grow to a significant extent, thus requiring a more invasive approach if not treated in the early stages. Because of the introduction of a new internal protocol, since January 2022, RMB are performed before thermal ablation in 96% of cases. Lastly, the limited number of events (eg, recurrence, mortality) did not allow testing for variables influencing oncological outcomes by means of multivariable Cox regression analysis.

Conclusion

Results of this study show that microwave ablation is comparable to cryoablation in terms of safety, preservation of renal function and oncologic outcomes. MWA was associated with shorter procedural time than CA. Even though larger and prospective studies are needed to completely evaluate MWA outcomes, this technique shows valid results for the treatment of localized small renal masses.

Clinical Practice Points

Percutaneous thermal ablation of renal masses (RM) is a valid alternative to surgery in specific patients bearing small tumors. While cryoablation (CA) is supported by a wider body of literature, microwave ablation (MWA) of renal tumors is still regarded experimental. In this study we showed that patients treated with MWA had similar perioperative outcomes, rates of complications, kidney function impairment and survival outcomes than those treated with CA. MWA was associated with shorter operative time. Since MWA showed comparable outcomes and shorter procedural time than CA, it should be considered as a valid alternative minimally invasive procedure for selected patients with small renal tumors.

Authors' Contributions

Luca Boeri: Project development; Data analysis; Manuscript writing and editing.

Gianpaolo Lucignani: Project development; Data analysis; Manuscript writing and editing.

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Andrea Piasentin: Data collection; Manuscript editing.

Elisa De Lorenzis: Data collection.

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Michele Bertolotto: Data collection.

Gianpaolo Carrafiello: Final approval of the version to be submitted.

Emanuele Montanari: Final approval of the version to be submitted.

Disclosure

The authors have stated that they have no conflicts of interest.

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