Trends in Percutaneous Thermal Ablation Therapies in the Treatment of T1a Renal Cell Carcinomas Rather than Partial Nephrectomy/Radical Nephrectomy

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Abstract

Keywords

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► radical nephrectomy
► interventional radiology

With the increased incidence of stage T1a renal cell carcinoma (RCC) has come the recognition that these lesions tend to be low grade and slow growing, with low probability of metastasis not necessarily requiring surgery. As alternatives to surgery, both active surveillance and ablation have been advocated for the management of selected patients with stage T1a renal cancers due to slow rate of tumor growth and low metastatic potential based on recent epidemiological studies. Thermal ablation also has consistently reported favorable complication and renal preservation rates compared with surgical approaches. However, most studies are single-center case series and meta-analysis of these series and comparative prospective series with long-term follow-up are lacking. The purpose of this article is to review the principal thermal ablation modalities and oncological outcomes for the treatment of stage T1 RCCs with long-term follow-up.

Over the past 30 years, the detection of stage T1a renal cancers has been increasing at 2% annually, while mortality has remained unchanged leading to the concept of overdiagnosis and overtreatment for early renal cell carcinoma (RCC).[1] With the understanding that most of these lesions are indolent, management has evolved from aggressive open radical nephrectomy (RN) to less invasive laparoscopic and robotic partial nephrectomy (PN) to minimally invasive percutaneous thermal ablation (TA), and finally active surveillance (AS). Although the latest guidelines from the American Urological Association (AUA) and National Comprehensive Cancer Network (NCCN) recommend PN as the standard of care for small renal masses (≤4 cm; clinical stage T1a), they now endorse AS and TA as acceptable alternatives for selected patients with comorbidities and preferences.[1–3] There has been recognition that most renal lesions are indolent, grow slowly, and that aggressive treatment of T1a renal lesion may actually lead to decreased renal function and chronic kidney disease (CKD) which may in turn be associated with significantly higher risk of cardiovascular mor-

bidity and mortality.[3–5] Thus, the need for finding less invasive options that preserve renal function and avoid cardiovascular risk is now the dominant paradigm. Over the past 20 years, a variety of percutaneous image-guided TA techniques have been adopted for the treatment of T1a RCCs initially for poor surgical candidates and now for all candidates with a life expectancy more than 5 years.[6–9] AS is now recognized as a management option for T1a RCCs, especially in patients with a life expectancy less than 5 years and relies on the favorable biological characteristics of these lesions including slow growth rates (2–3 mm/year), low Fuhrman grades, and low metastatic potential.[3] Although there are no widely adopted biomarkers that predict natural history of individual lesions, multiphasic computed tomography (CT) and magnetic resonance imaging (MRI) have been shown to be useful for characterization of individual lesion histology and serial lesion monitoring to detect more aggressive lesions (i.e., those with rapid growth > 1 cm per year) on AS.[10,11] Imaging with a percutaneous biopsy performed by an experienced interventional radiologist would provide a

reliable diagnosis in over 90% of cases, correlating well with final pathology.[12] AS is associated with better renal functional outcomes compared with surgery, but no prospective trials of AS with PN or TA for small renal mass (SRM) have been performed.[13] In this article, we review the oncological therapeutic and renal functional outcomes of different TA modalities in comparison with PN/RN in the treatment of T1 RCCs with long-term follow-up.

Image-Guided Thermal Ablation

Image-guided tumor ablation is a needle-based minimally invasive treatment option for early-stage renal malignancies with the following principles. First is to eradicate all malignant cells within a lesion by inducing irreversible thermal cellular injury to the target RCC. Second is to induce thermal and vascular damage to a very small surrounding margin of normal renal parenchyma, typically a surrounding ablative margin of up to 0.1 to 0.5 cm.[14] The potential to damage a minimal amount of normal renal tissue is a substantial advantage of percutaneous ablative therapies over more invasive surgical alternatives such as PN, especially in patients with renal parenchymal injury from underlying diabetes, hypertension, or other reasons for CKD.[15–17] Third, the total energy delivered has to be proportional to the radius of the target RCC and thus is exponentially greater for larger RCC, limiting its utility for stage T1b lesions. Thus, alternative strategies such as the longer ablation times, multiple sessions, probe repositioning, use of multiple probes, or combination therapy with ablation and embolization may be required.[16] Fourth, the efficacy of all thermal techniques is mitigated by the amount of surrounding blood perfused tissue and proximity to large blood vessels.[18] Thus, exophytic RCC lesions surrounded by perinephric fat will require less energy to ablate than similarly sized endophytic RCC lesions surrounded by highly perfused renal cortex and large central blood vessels.[19]

Overall ablation therapies for renal tumors are broadly divided into thermal including cold (cryoablation) and heat (electromagnetic [i.e., radiofrequency—RF, microwave, laser] or ultrasound [US]); electrical (irreversible electroporation [IRE]); radiation (brachytherapy); and direct injection (e.g., chemical, viral, small particle).[14,18,19] In this review, we will focus only on established thermal techniques which have the best reported long-term outcomes. Complete and adequate cellular destruction by percutaneous image-guided TA using either heat- or cold-based techniques requires that the entire RCC and an ablative margin be subjected to cytotoxic temperatures. Heat-based techniques result in a single-step "coagulation necrosis" wherein intra- and extracellular water evaporates and the phospholipid cell membranes, proteins, and nucleic acids, as well as extracellular all denature above 60°C.[16] Cold-based techniques result in a two-step deep freeze–thaw cycle, wherein intra- and extracellular water freezes initially with osmotic rupture of the cell membrane during thaw phase and with a second freeze and thaw cycle to ensure maximal destruction.[17]

The ability to destroy tissue by heating or cooling is equal to the energy deposited, modified by local tissue interactions, minus the energy lost before inducing thermal damage, and is proportional to the radius of the lesion.[14,17] Several strategies have been developed based on this relationship to increase the volume of coagulation necrosis, including increasing energy deposition, modifying tissue blood flow, and modulating tissue characteristics. The biggest limitations of all thermal techniques are tissue heterogeneity of limiting energy deposition, tumor volume, and the experience and skill of the operator with regards to using imaging guidance especially in cases of complex anatomy and difficult access.[16–20]

Patient Selection

In general, patients should be preprocedurally evaluated in clinic with history and physical examination and a thorough assessment of medication history and cardiovascular and pulmonary comorbidities to risk stratify patients, determine competing risks, and assess 5-year life expectancy. The ideal candidate is one with a life expectancy of at least 5 years with only mild cardiovascular and pulmonary risk factors.[21] We usually perform US during this visit to determine treatment plan and approach. We also discuss the goals of the procedure, alternative to ablation, ablation efficacy, complications, and need for at least 5 years of imaging-based follow-up in clinic.

Cryoablation

Cryoablation is an ablative technique first described for renal ablation in 1996 (►Figs. 1 and 2). It causes tissue necrosis in oncologic and nononcologic tissue by the two-step freeze–thaw cycle which leads to intra- and extracellular ice formation (visualized on CT and MRI as an "ice ball") followed by a thaw cycle leading to osmotic cellular phospholipid membrane rupture.[14] The freeze–thaw cycle is repeated twice. The goal is to have temperatures in the center and margin of the target lesion reach −140 and −20°C, respectively. Above this temperature, TA will be uneven with ineffective oncological control. Cryoprobes are 13 to 17G hollow needles inserted with CT, US, or MRI guidance into the target lesion. Using the Joule-Thomson effect, a dramatic deep freeze level cooling results along the length of the cryoprobes as compressed argon gas depressurizes along the internal tube-like shafts along the needle length.[16] Helium may be used for the thaw cycle. Up to 10 cryoablation probes can be inserted into a given lesion and individual ice balls from each cryoprobe coalesce into a larger fused ice ball.[22] Typically, cryoablation times are based on the size and location of the lesions. Small exophytic lesions require the least time and large central lesions require the most time due to extremely high thermal dissipation from surrounding circulation, known as the cold sink effect. A typical cryoablation session usually includes freeze cycles of 6 to 10 minutes, a thaw cycle of 5 minutes, followed by another similar freeze–thaw cycle. In addition to thermal injury, there is an indirect ischemic insult, because of microvascular occlusion occurring within the thawing phase of the cycle adding to the overall ablation effects.[10] However, large-volume cryoablation (> 5 cm) increases risk of complications including bleeding, cryoshock, and acute renal failure from cryoglobulinemia.
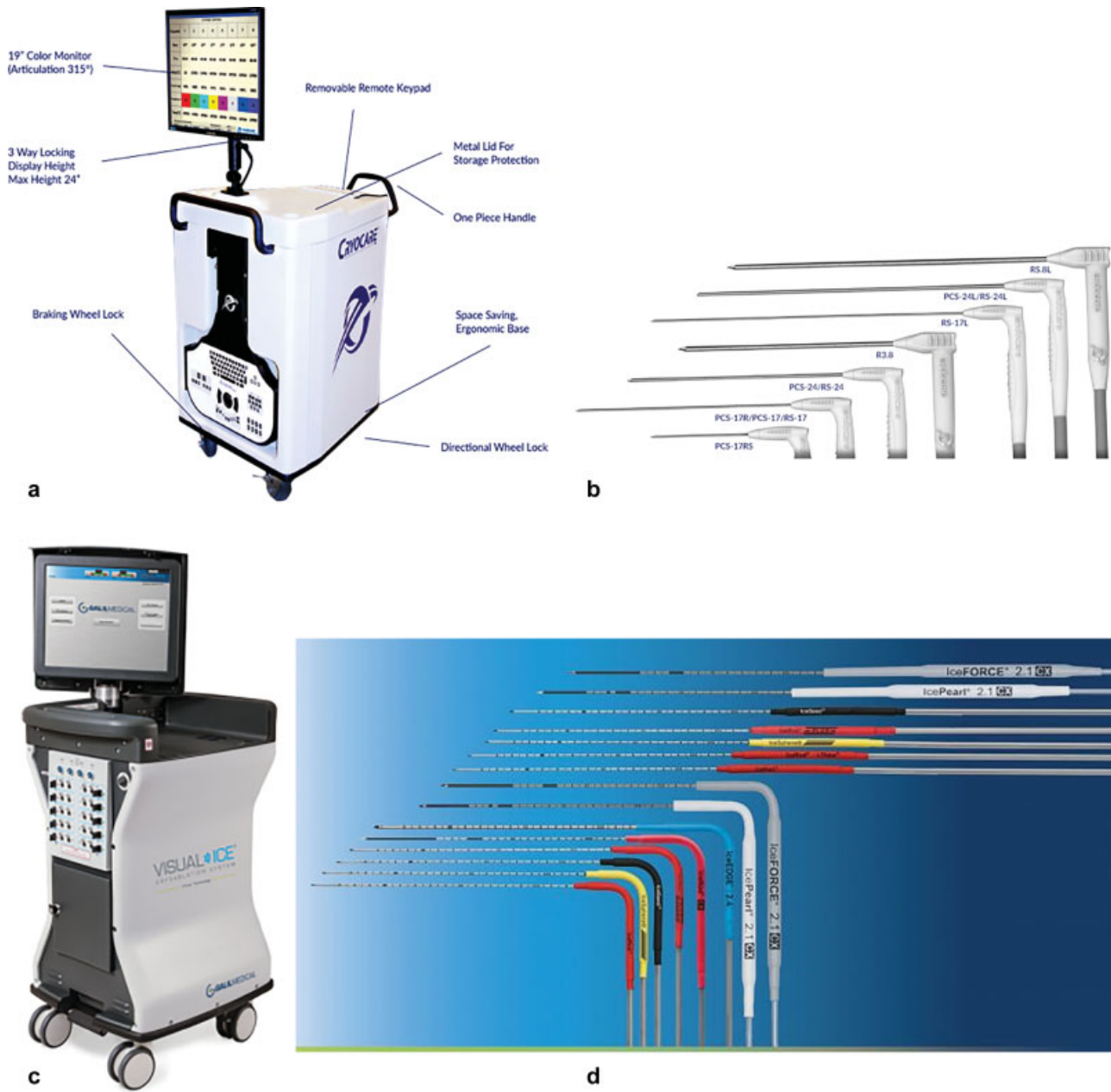
Fig. 1 Cryoablation systems: (**a, b**) Endocare systems, (**c, d**) Galil systems.
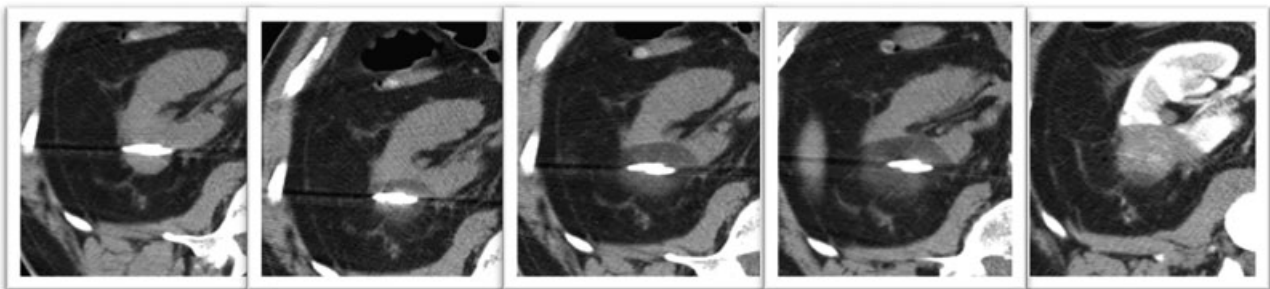
Fig. 2 Cryoablation of clear cell renal cell carcinoma (RCC) in a 71-year-old woman: unenhanced CT with cryoprobes in a posterior RCC lesion at 0, 1, 3, and 6 minutes during cryoablation, and contrast-enhanced scan postablation. The ice ball is growing over time. Postablation zone of ablation is avascular.

Image-guided cryoablation has shown to be a robust option for treatment of small renal cancers in multiple single-center series.[15,23] The most cited advantages of cryoablation are its power for treating T1a and T1b lesions by adding multiple cryoprobes and direct visualization of the growing ice ball with its precise margins with CT or MRI permitting more precise monitoring of the ablation zone.[24] Although cryoablation has theoretically been shown to be less damaging to surrounding collagen in an animal model, the translation to clinical practice has not rigorously been studied.[25] Complication rates for cryoablation are similar to other modalities with a significantly higher rate of bleeding than for heat-based modalities.[26] Precise probe positioning and operator experience are likely to affect these results.[27] Because of its controlled nature, cryoablation is also favored for the treatment of metastatic renal tumors in the renal bed, retroperitoneum, subcutaneous tissue, or near spinal column and bowel.[10,19] However, freezing into these neural and visceral structures can cause unintended significant injury. Patients are followed up with multiphasic contrast-enhanced US, CT, or MRI. Completely ablated lesions are iso- to hyperintense on CT, of low T2 and high T1 MRI, and mildly echogenic on US with no enhancement in or surrounding the ablation zone, which usually decreases in size over time. Recurrences are usually growing marginally enhancing nodular zones typically occurring within 2 years.

Radiofrequency Ablation

Radiofrequency ablation (RFA) is a current-based heating modality initially pioneered for the treatment of liver tumors[28] and was first reported in 1997 for the treatment of RCC.[16] RF energy is produced by a generator as an alternating current at 350 to 500 kHz which passes from the exposed tip of a needle-like probe into surrounding tissue, thereby oscillating water molecules in biologic tissues resulting in frictional heating to greater than 60°C. Grounding pads attached to the patient's thighs form a simple electrical circuit where in the current loop comprises a generator, cabling, electrodes, resistive tissue, and grounding pads[17] (►Fig. 3).

This closed circuit results in heat generated between 60 and 100°C by increased water friction surrounding the needle tip and produces immediate coagulative tumor necrosis by protein denaturation and causes immediate cell death. RF systems available on the market include 100 to 200 W generators with single electrodes with umbrella-type expandable tines, and internally cooled needles allowing for up to three simultaneous probe placements.[22] RF ablation also requires good guidance skills with US and/or CT to place electrodes appropriately into RCC lesions avoiding crossing vessels, bowel, and ureter.[29] During an ablation, the electrodes are placed in the deepest portion of the tumor and require retraction and repositioning to achieve a complete ablation. During the ablation, an echogenic cloud forming around the tip of the RFA electrode is visible by US and it seems as a round, hyperechoic lesion at the end of the procedure. However, on CT gas develops throughout the lesion as the ablation progresses, but this is unreliable and much less useful as a surrogate marker of efficacy than the ice ball on cryoablation.[21] The best marker is lack of enhancement of the lesion and surrounding **V**-shaped infarcted renal parenchyma on contrast-enhanced US, CT, or MRI (►Fig. 4). RF ablation efficacy is limited by carbonization of tissues immediately adjacent to the electrode resulting in increased tissue impedance from high temperatures above 100°C. To minimize inadequate treatment, several strategies such as shaft cooling and slow ramp up have been developed.[22] Like all TA, the efficacy of RFA is also limited by heat-sink effect in adjacent high-flow vascular structures above 4 mm especially centrally[28,30] (►Figs. 1 and 2). For lesions larger than 4 cm, a combination of embolization and RFA has been shown to be more effective than RF alone due to the synergistic effect of vascular occlusion.[1] RFA may interfere with cardiac pacemaker and defibrillator devices and has the potential to induce abnormal rhythms in at-risk patients. The major complication rate of RFA is approximately 4% and includes bleeding, infection, urine leak, stricture, and nontarget injury to bowel, but the overall bleeding complication rate is significantly less than cryoablation.[14,15,23,26,31,32]

Microwave Ablation

Microwave ablation (MWA), first approved for use in the United States in 2008, is electromagnetic energy in the range of 300 MHz to 300 GHz.[20] Microwaves are produced by a generator by an alternating current causing dielectric hysteresis (rotating dipoles) at either 915 MHz or 2.45 GHz from the exposed tip of a needle-like probe (antenna) into surrounding tissue, and rapidly oscillate water molecules in biologic tissues resulting in frictional heating to less than 100°C.[22] Microwave energy uses the wave property of electromagnetism to cause ionic agitation in water molecules much more robustly than RFA and cause a rapid frictional tissue heating frequently above 100°C. MWA requires no grounding pads and microwaves are not affected by carbonization or impedance[14] (►Figs. 3 and 4).

Currently, several systems are approved in the United States. Compared with RFA, MWA produces more robust, hotter, and faster thermal injury[17] (►Figs. 5 and 6). MWA ablation should not theoretically interfere with cardiac pacemakers and defibrillators or induce abnormal heart rhythms. Systems are designed for placement of either single or up to three antennae. However, some initial studies indicate that MWA may effectively ablate lesions up to 5 cm compared with the 3-cm limit for RFA.[14,32–35]

Major complications of MWA are approximately 4% and include bleeding, infection, urine leak, stricture, and nontarget ablation including skin burn if the target is within 3 cm of the skin.[20,34–39]

Other technologies including IRE, high-intensity focused US, radiosurgery, pulsed cavitational US, and laser thermal therapy remain investigational at this time.[21,29] For both RFA and MWA, ablated lesions are hyperechoic on US and hyperdense on CT with low T2 and high T1 signal on MRI without enhancement of the lesion and a surrounding margin on all modalities. MWA results in more immediate tissue shrinkage than RFA. Over time, the zone of ablation decreases in size but less than cryoablation with similar imaging properties. Recurrences tend to be growing nodular areas of marginal enhancement as with cryoablation.
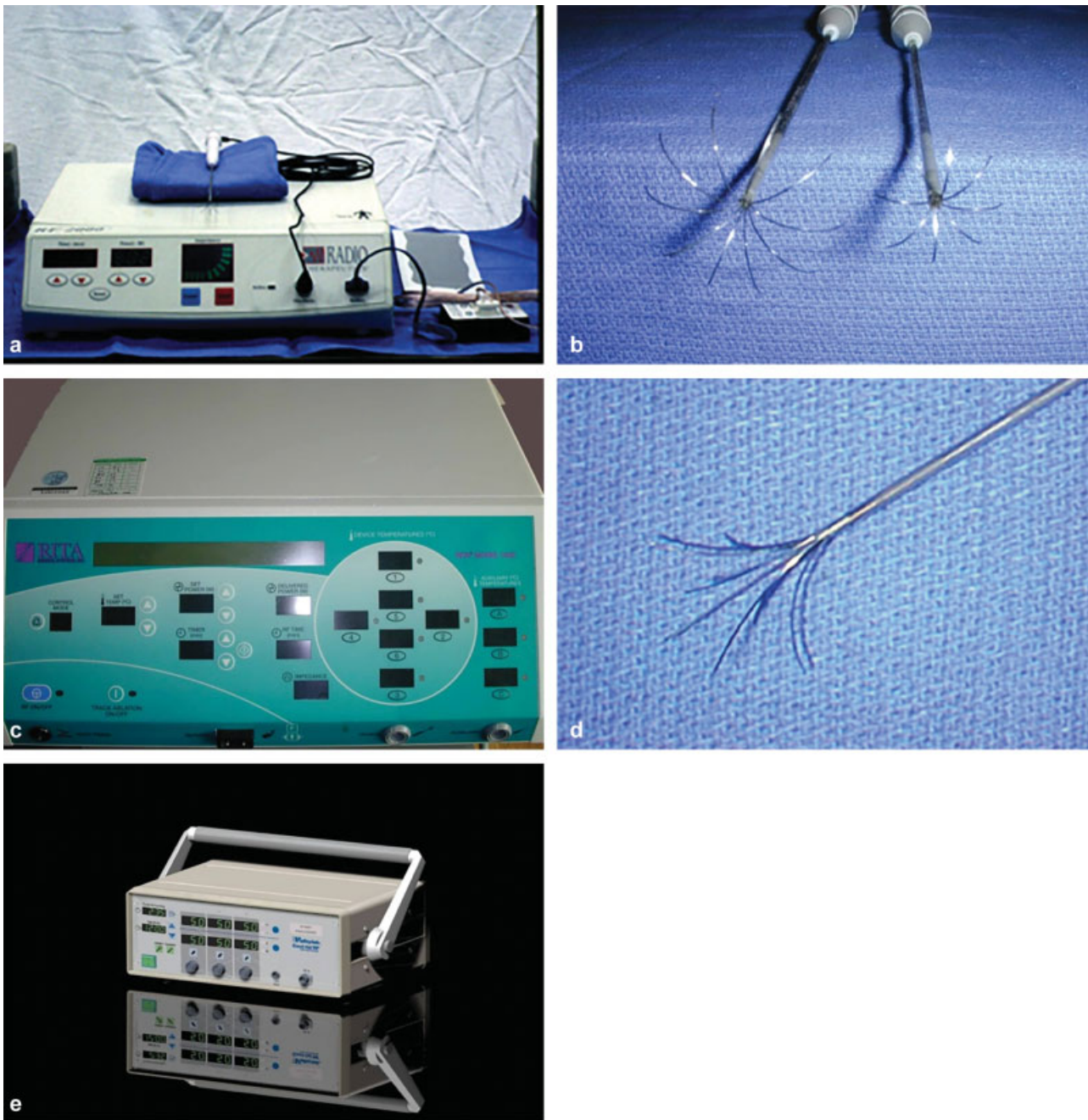
Fig. 3 Radiofrequency ablation systems available in the United States: (**a, b**) Boston Scientific RF 2100 generator with LeVeen expandable tine electrodes. (**c, d**) Angiodynamics RITA generator with Starburst expandable tine electrode. (**e, f**) Medtronic generator with Cool Tip single and cluster electrodes.

►**Figs. 7** and **8** show representative cases of MWA.

Functional Outcome

The important consideration for patients who underwent RCCs treatment is whether the kidney remains functional with relatively favorable outcomes after procedure particularly in patients with preexistent CKD. TA procedures minimize parenchymal loss and improve long-term renal function compared with PN or RN.[29]

CKD is highly prevalent (∼25–30%) among patients with small renal masses.[40] Population with risk factors including advanced age, diabetes mellitus, and hypertension are at risk of developing CKD. Patients without preexisting CKD defined as

baseline glomerular filtration rate [GFR] > 60 mL/min/1.73 m^2, no suspected proteinuria (dipstick negative or trace), and a normal contralateral kidney that is expected to provide an estimated GFR of greater than 45 mL/min/1.73 m^2. The presence or development of CKD significantly increases cardiovascular morbidity (stroke, myocardial infarction, etc.) and mortality within the general population.[21,41]

Oncological Outcomes

In accordance with the International Working Group on Tumor Ablation (IWG), the main oncological outcomes are categorized as follows: primary and secondary technical success (TS), defined as a complete ablation after one or more defined
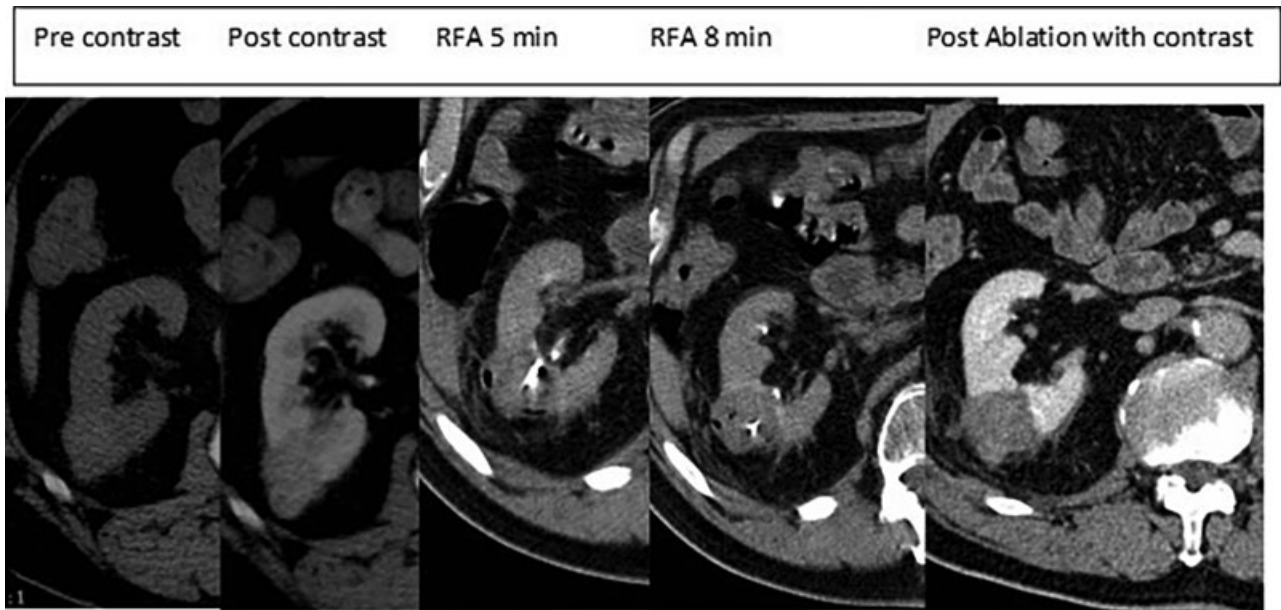
Fig. 4 Radiofrequency ablation (RFA) of posterior papillary renal cell carcinoma in a 66-year-old man. On axial CT images precontrast, lesion is characteristically hyperdense and hypoenhancing postcontrast. On RFA images, lesion with RF probe is noted at 5 minutes and becomes hypointense during ablation with gas bubbles at 8 minutes. Postablation, the lesion is markedly hypodense and nonenhancing with a wedge-shaped region of thermally induced infarction.

Fig. 5 Microwave ablation systems (left to right): Covidien Emprint, Neuwave Certus, Endocare, and HS Amica.

ablation sessions; local tumor progression (LTP) defined as the persistence of tumor focus at the edge of the ablation zone after at least one contrast-enhanced imaging study which documented adequate ablation by the absence of viable tissue in the target and surrounding ablation margin; overall survival defined as all patients alive after the procedure typically after 1, 3, 5, and 10 years of initial ablation; and disease-specific survival defined as all patients alive RCC free during that time. Complications are classified according to the Clavien–Dindo system.[14,16]

Most RCCs are detected incidentally as small renal masses and radiologists have a major role in the detection and characterization of these tumors and patient counseling. Up to 25% of SRMs less than 3 cm will be benign, mostly fat-poor angiomyolipoma and oncocytoma. Most of these lesions can be characterized with CT and MRI to determine the probability of clear cell RCC, the most aggressive cancer. The majority of T1a lesions are low grade and slow growing with little propensity to metastasize.[10,13] Cystic RCC complex lesions (Bosniak III and IV) are generally indolent but can be successfully ablated.[17]

According to the updated AUA and NCCN guidelines, AS and TA are recognized evidence-based strategies for managing stage T1a RCC in the context of favorable lesion histology, patient age, and comorbidities.[1–3,29] However, the guidelines recognize PN as the standard treatment in eligible cases.[1,29,42]

Most studies on RCC treatment are single-center case series with short-term follow-up and cross-comparison of multiple management strategies is lacking. Some recent studies provided
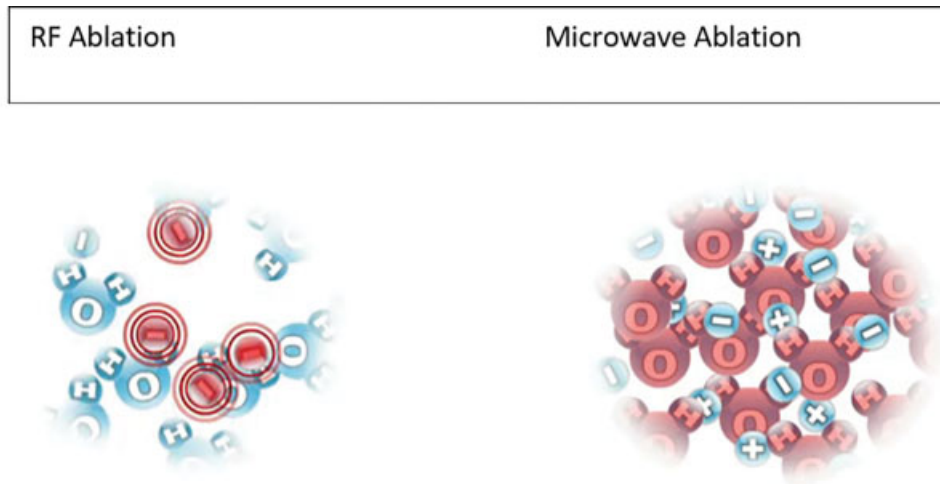
Fig. 6 Microwave ablation produces a more robust frictional heating of water molecules compared with RF ablation during an equivalent time.
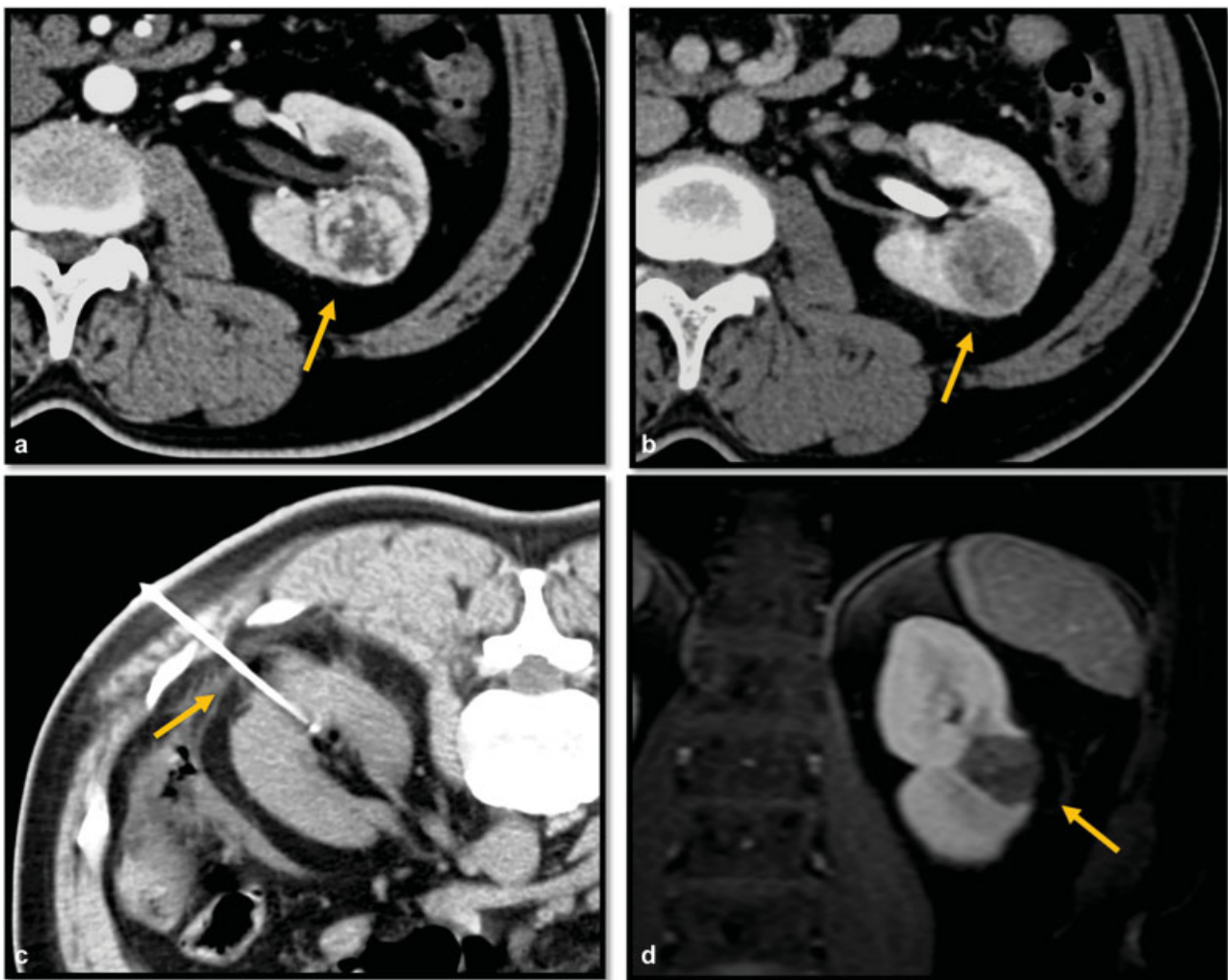
Fig. 7 A 57-year-old man with 3.3 cm *endophytic*, hypervascular, clear cell renal cell carcinoma (RCC) in the left kidney (*arrow*). Preablation CT shows typical clear cell corticomedullary hyperenhancement (**a**) and nephrographic washout (**b**). One of two microwave antennas was placed into the RCC under CT guidance (**c**). Postprocedure T1-weighted, fat-saturated, contrast-enhanced MRI shows complete ablation with smooth margins with residual enhancing tumor (**d**).
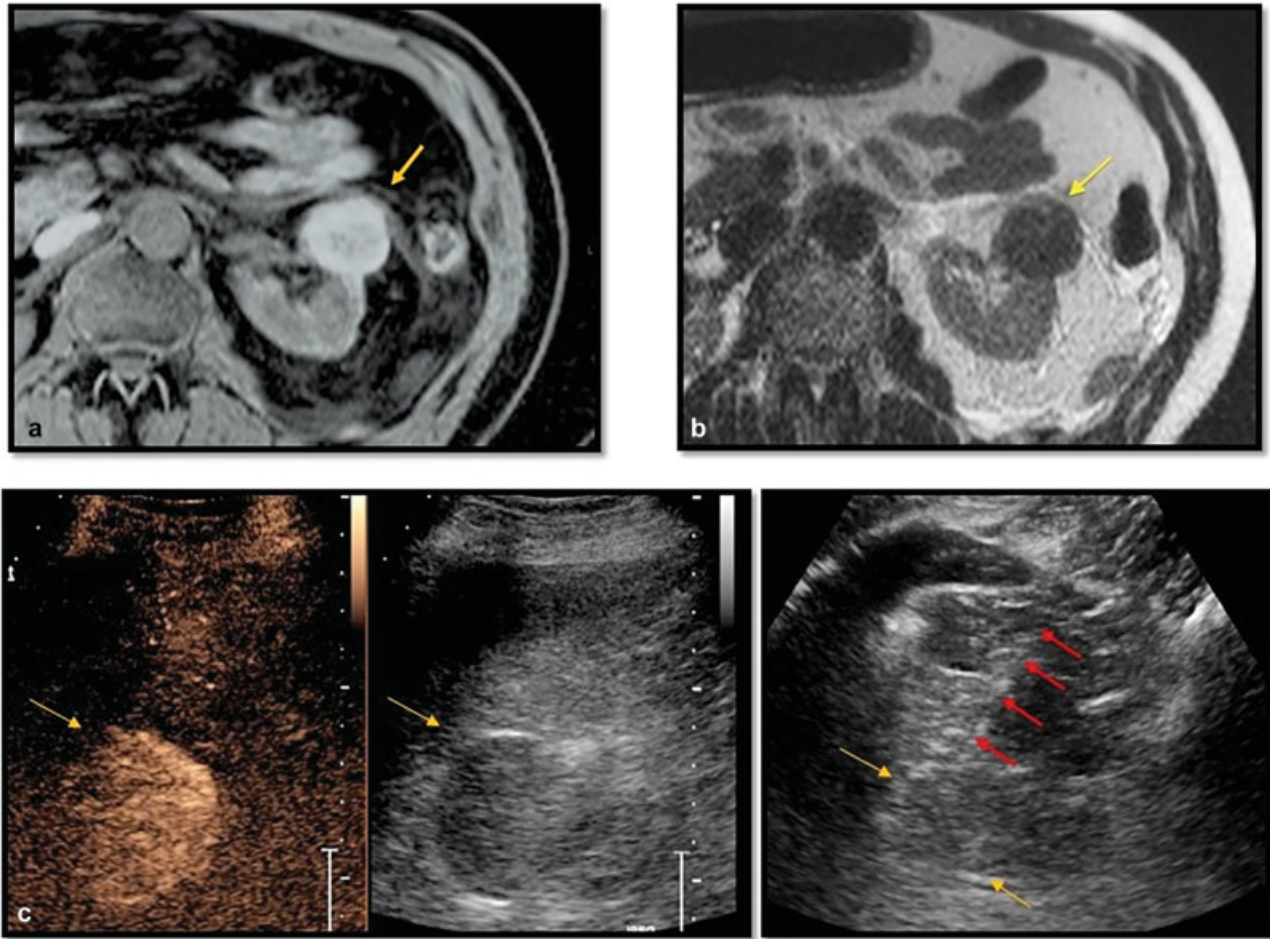
Fig. 8 Percutaneous microwave ablation of a 62-year-old man with 4-cm clear cell renal cell carcinoma partially exophytic (yellow arrow) on axial T1, T2-weighted MRI after ablation (**a, b**). Contrast-enhanced ultrasound during procedure helped to visualize lesion margins and guide more precise placement of microwave antenna (red arrow; **c**).

comparable therapeutic data to identify the potential efficacy differences among available multiple RCCs management modalities in long-term follow-up.[7,10,24,33,42–55]

In a 2019 study, Palumbo et al evaluated 3,946 patients using the Surveillance, Epidemiology and End Results database (SEER, 2004–2015) treated with cryosurgery for T1a lesions, reporting that tumor size greater than 3 cm is an independent predictor of higher 5-year cancer-specific mortality rate. Therefore, they suggested the local tumor ablation should be performed for tumors less than 3 cm.[43] As with all ablative sites, tumor diameter is the key predictive factor for local tumor control with larger lesions greater than 3 cm having greater likelihood of incomplete ablation and local recurrence[3,51] (►**Table 1**).

In a 2018 study, Xing et al retrospectively studied 10,309 patients from the SEER database (2001–2012), who underwent RN (4,522 [44.2%]), PN (2,820 [27.6%]), TA (898 [8.8%]), or AS (1,978 [19.4%]).[44] Compared with the PN subgroup, patients in the RN subgroup had significantly higher rates of renal ($p =$ 0.01), cardiovascular ($p =$ 0.01), and thromboembolic ($p =$ 0.03) adverse events within the first 30 days postprocedure, with nonsignificant differences between 31 days and 1 year postprocedure. When compared with patients in the TA subgroup, patients in the PN subgroup had significantly increased rates of

renal, cardiovascular, and thromboembolic events by approximately 2.1-, 2.3-, and 5.3-fold, respectively ($p =$ 0.001 for all), in the first 30 days after the procedure, with significant increases persistent at 31 days to 1 year ($p =$ 0 0.001) respectively.[42]

In a 2018 study, Uhlig et al evaluated 56,065 patients with T1a RCC undergoing TA (4,817, 8.6%) and PN/RN (51,248, 91.4%) with a median follow-up of 48 months and for the first postoperative year, survival was slightly higher for TA compared with nephrectomy (6-month survival for TA, 98.6%, vs. nephrectomy, 98.1%, $p =$ 0.015) with a small overall greater 5-year survival, in the nephrectomy cohort (82 vs. 76.4%, $p =$ 0.001) likely due to better unadjusted patient selection rather than differences in treatment efficacy.[52]

In a 2019 study, Zhou et al reviewed 297 T1a biopsy-proven RCCs treated with CT-guided RFA (82%), cryoablation (26.9%), and MWA (27.9%) and reported similar TS rates among the three different treatments ($p =$ 0.33).[46] Although at 1 month postablation primary efficacy was more likely to be achieved with RF ablation and MWA than with cryoablation, no significant differences in therapeutic outcomes such as local recurrence, metastatic progression, or RCC-related death or renal function were found at 2 years of follow-up.[44] They suggested that the RF ablation, cryoablation, and MWA are equivalent at 2 years for treatment of T1a RCC for therapeutic outcome and

Table 1 Characteristics of larger population-based studies comparing kidney tumor ablation to other surgical management strategies

Sl. no.	Study	No. of patients	Study population	Time period	Comparison	Outcomes
1.	Palumbo et al[45]	3,946	SEER	2004–2015	Cryosurgery vs. TA	TS > 30 mm is an independent predictor of higher 5-y CSM in TA
2.	Xing et al[44]	10,309	SEER	2001–2012	Comparison of complication rates, CSM, and OS between PN, RN, TA, and AS	TA showed CSM and OS similar to PN/RN with significantly fewer adverse outcomes at 1-y follow-up
3.	Zhou et al[46]	297	Retrospective study	2006–2016	Comparison of therapeutic effects of RFA, MWA, and cryoablation	RFA, MWA, and cryoablation are equivalent for treatment of T1a RCC for renal function, and low adverse event rate at 2-y follow-up
4.	Uhlig et al[54]	56,065	National Cancer Database study	2004–2013	Comparison of perioperative outcomes of TA vs. nephrectomy	TA showed superior perioperative outcomes with short mean hospital stay, low unplanned hospital readmission, and 30- and 90-d mortality
5.	Andrews et al[58]	1,798	Retrospective study	2000–2011	Comparison of outcomes of RFA and cryo vs. PN in T1 RCCs	TA can be used to treat the cT1 renal masses with high CSS and local recurrence free rate
6.	Atwell et al[6]	385	Retrospective study	2000–2010	Comparison of efficacy and complication rates of RFA vs. Cryo in RCCs ≤ 3 cm	Both RFA and cryo are effective in the treatment of RCCs ≤ 3 cm. Major complications are infrequent
7.	Schmit et al[29]	116	Retrospective study	2003–2010	Comparison of the efficacy and complication rates of percutaneous Cryo in T1 and T2 RCCs	Percutaneous cryoablation is effective in the treatment of T1 and T2 RCCs with the higher complication rates in large tumors
8.	Guan et al[40]	102	Prospective randomized comparison study	2004–2006	Comparison of therapeutic effects of MWA and PN in T1a	MWA provides favorable results compared with PN with high efficacy and local free recurrence rate
9.	Choi et al[59]	567 (13 articles)	Review article	2012–2017	To evaluate the technical and oncological outcomes of MWA in RCCs	MWA showed favorable technical and oncologic outcomes with a low incidence of major complications
10.	Rivero et al[60]	3,974 (15 articles)	Review article	2000–2016	Comparison of oncologic outcomes of TA vs. PN in T1 RCCs	TA is associated with a lower morbidity rate and a lesser reduction in eGFR compared with PN, but with higher CSM rates

Abbreviations: AS, active surveillance; CSM, cancer-specific mortality; eGFR, estimated glomerular filtration rate; OS, overall survival; PN, partial nephrectomy; RCC, renal cell carcinoma; RN, radical nephrectomy; SEER, Surveillance, Epidemiology and End Results database; TA, thermal ablation.

stability of renal function, with low adverse event rate.[44] Other studies have found no significant differences with regard to local recurrence rate or overall disease-free survival and distant metastases TA (RFA and MWA, excluding cryoablation) compared with PN.[47–57] Although some single-center studies have reported more local recurrences for TA compared with PN,[46,50] a recent AHRQ meta-analysis reported no significant difference in the risk ratio for local recurrence between PN and TA (RR: 1.21; 95% confidence interval: 0.58–2.5).[46]

Conclusion

In summary, with the annual increased incidence of SRM, the overall approach to these lesions has changed since up to 30%

of lesions less than 3 cm are benign and over 90% of RCC are low grade and grow slowly. AS is a recognized option for patients with a life expectancy of less than 5 years and TA is an accepted alternative to PN for most lesions less than 3 cm, due to its high rate of local control and negligible effect on renal function in single-center trials and meta-analysis irrespective of energy type. Although a large randomized controlled trial is desirable, it is unlikely to be conducted for multiple reasons.

Conflict of Interest
None declared.

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