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Archives of Nephrology and Renal Studies Mini Review

Percutaneous Ablation of Localized Renal Masses: An Updated Review

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Abstract

Introduction: Thermal ablation (TA) is increasingly used as a treatment for localized renal masses (LRMs, <4 cm) especially in older or comorbid patients. Our previous article by Mershon et al., highlighted the safety and efficacy of TA for treatment of LRMs in select patients. In this presentation, we update that work and discuss new frontiers for TA including patient selection, procedural improvements, and outcomes.

Evidence acquisition: A structured literature review was conducted on PubMed using the keywords: “renal cell carcinoma,” “renal mass,” and “ablation” as well as “complication,” “renal function,” “outcomes”, “cost”, “solitary kidney”, “propensity score” and/or “partial nephrectomy”. Additional papers were cross referenced via citation review.

Evidence synthesis: TA is technically suited for small and less complex tumors in older patients or patients with multiple co-morbidities especially chronic kidney disease, solitary kidney or multiple renal masses. Percutaneous technique allows for decreased length of stay and faster recovery time due to the minimally invasive nature of TA. No prospective or randomized trials to compare TA to partial nephrectomy. Comparative studies demonstrate lower complication rates, preservation of renal function, and similar cancer specific survival when compared to partial nephrectomy.

Conclusions: TA is a safe and effective management option for SRM in select patients especially older patients with multiple other co-morbidities.

Keywords: Carcinoma, Renal cell, Ablation techniques, Radiofrequency ablation, Cryosurgery, Microwaves

Abbreviations: LRM: Localized Renal Mass; TA: Thermal Ablation; SEER: Surveillance, Epidemiology, and End Results; AUA: American Urologic Association; EAU: European Association of Urology; eGFR: Estimated Glomerular Filtration Rate; RCC: Renal Cell Carcinoma; CKD: Chronic Kidney Disease; T1a: less than 4 centimeter diameter localized renal mass; T1b: greater than 4 centimeter localized renal mass; RFA: Radiofrequency Ablation; CA: Cryoablation; MWA: Microwave Ablation; RFS: Recurrence Free Survival; CSS: Cancer Specific Survival

Introduction

With readily available cross-sectional imaging, asymptomatic localized renal masses (LRMs) are often incidentally found. The standard management for LRM has been surgical resection, however, detection of masses that are benign or with low metastatic risk has led to interest in minimally invasive alternatives such as percutaneous thermal ablation (TA) or active surveillance. The increasing adoption of TA heralds more data and novel uses. Our previous article by Mershon et al. highlighted the safety and efficacy of TA for treatment of LRMs in select patients [1]. In this presentation, we update that work and discuss new frontiers for TA including patient selection, procedural improvements, and outcomes.

Patient Selection

Decision-making for treatment of localized LRM must balance several competing priorities. TA has gained popularity due to its favorable oncologic efficacy and complication profile. When comparing papers on PubMed from 2000 to 2007 versus 2008 to 2015 using systematic review per Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, Pietropaolo et al. reported a change of +109% (P = 0.002) and +78% (P = 0.036) was seen for cryoablation (CA) and radiofrequency ablation (RFA), respectively [2]. Shi et al. reported an increase in TA from 8.1% in 2004 to 14.9% in 2016 using the retrospective Surveillance, Epidemiology, and End Results (SEER)-Medicare associated databases [3]. The American Urologic Association (AUA) and European Association of Urology Association (EAU) guidelines suggest TA as an alternative for patients with LRMs 3 centimeters or smaller that have a contraindication or unwillingness to undergo surgical resection [4,5]. However, no additional criteria for patient selection have be endorsed by current guidelines.

Many studies document that patients undergoing thermal ablation are significantly older with more comorbidities including hypertension, diabetes, chronic kidney disease, cardiovascular disease, and lower baseline estimated glomerular filtration rates (eGFR) than those undergoing partial nephrectomy (PN) [3,6-11]. According to Doolittle et al. patients between 70 and 79 were far less likely to undergo PN and far more likely to undergo either ablation or active surveillance as compared to patients under 40 years of age [12]. In addition to the risks associated with biologic age, clinicians must weigh competing causes of mortality versus benefit of treatment for renal cell carcinoma (RCC). Age has been shown to be the strongest predictor of mortality, especially non-RCC related mortality [13]. In comorbid patients who present with a LRM, it is often difficult to assess the risk of competing co-morbidities. A state-transition microsimulation by Kang et al. mathematically weighted competing oncologic and non-oncologic risks for mortality. Life expectancy was driven by comorbidities, especially renal function, and associated risks from worsening renal function projected with intervention. Partial nephrectomy was indicated for patients with chronic kidney disease (CKD) stage 1 and 2, particularly those with less complex masses (RENAL nephrometry score <7). TA extended life expectancy in patients with CKD stage 3A, RENAL nephrometry score less than 7 and Charlson comorbidity index greater than or equal to 1. Patients with more aggressive tumors (RENAL nephrometry score ≥ 7) and CKD stage 3B benefited from watchful waiting or MRI surveillance to detect papillary type 1 RCC (i.e., well-circumscribed cortical masses with T2-weighted hypointensity and low-level enhancement) which would have minimal oncologic benefit with treatment due to low probability of tumor progression [14].

Management of LRMs in patients with anatomically or a functionally solitary kidney poses additional challenges. Partial nephrectomy generally requires renal hilar clamping and ischemia time which can further damage renal function. Consideration should be given to future eGFR decline secondary to concomitant medical comorbidities to preserve renal function and avoid end-stage renal disease and dialysis, which is associated with significant morbidity and 43% 5 year survival [15]. Meta-analysis by Yang et al. reported outcomes for 628 patients undergoing TA in a solitary kidney which showed less change in creatinine and eGFR as well as decreased new onset of chronic kidney disease and a trend toward less postoperative dialysis as compared to partial nephrectomy [16]. Similarly, in a review by Favi et al. 89 transplant patients with T1a (less than 4 centimeter diameter LRM) or T1b (greater than 4 centimeter diameter LRM) masses, graft loss was seen in 5 (6%) patients, but graft function remained stable in most patients [17].

Patients with hereditary RCC often present at a younger age with bilateral and/or multifocal tumors with high risk of additional tumor formation in the future. TA is minimally invasive, renal parenchymal sparing, and repeatable – all of which are highly advantageous for patients with hereditary RCC. Matsui et al. treated 6 patients with a total of 29 renal masses (range 1-16) secondary to Birt-Hogg-Dubé disease over 20 TA sessions. At a median of 54 months (range: 6–173 months), all 6 patients were alive without local tumor progression and no distant metastasis. The mean decrease in eGFR during follow-up was 10.7 mL/min [18]. TA has also been described for patients with multiple clear cell RCC associated with Von Hippel Lindau disease [19-23].

The use of TA has been described as a treatment option after a variety of RCC treatments. Brassier et al. reported lower complication rates and similar disease recurrence, local recurrence and distant metastasis when comparing TA (n=42) versus surgical resection (n=39) in 81 patients with isolated local recurrence after partial nephrectomy [24].

Procedural Considerations

Although consensus is still emerging, renal tumor biopsy should be considered to confirm or rule out malignancy even if pathognomonic imaging features are present. One of the major concerns in use of TA is the lack of histopathology. Although biopsy pathology can help counsel patients on prognosis, the timing of biopsy remains controversial. Staged biopsy prior to TA has been shown to result in a decreased rate of TA for benign lesions which could result in cost savings and prevention of unnecessary intervention in benign masses [25,26].

TA technical success is dependent upon mass characteristics and establishing safe percutaneous access with sufficient margins. Uncorrectable coagulopathies remain contraindications to TA. Practical procedure planning algorithms have been proposed, including the ABLATE approach (A, axial tumor diameter; B, bowel proximity; L, location within the kidney; A, adjacency to the ureter; T, touching renal sinus fat; and E, endophytic or exophytic position) [27]. TA is technically best suited for LRM less than 4 centimeters (i.e., T1a tumors); however, a few case series have expanded to larger and more complex tumors [28-34]. Tumor diameter is of great importance for planning the number of probes, especially for larger (T1b) renal masses. Precise probe placement and distribution within the LRM is crucial to obtaining complete ablation and decreasing bleeding risk [35,36]. Care is taken not to traverse the pleura in upper pole tumors in order to prevent pneumothorax. Timing needle puncture with breath holds from anesthesia can be helpful. Oblique needle trajectories through the kidney are favored to prevent damage to the renal collecting system and prevent urinoma. Positioning adjustments (i.e., prone or ipsilateral decubitus position) and hydro-dissection can be used to isolate the kidney from surrounding structures, including bowel or liver. Similarly, pyeloperfusion can be deployed in which a ureteral stent with cold saline irrigation is used to protect the collecting system and ureter in patients undergoing RFA or MWA [27,28]. The method of image guidance ranging from ultrasound, CT or even MRI should be carefully chosen to best visualize the probes, tumor, and surrounding structures.

Various TA techniques have been described for treatment of renal tumors including radiofrequency (RFA), cryoablation (CA), and microwave (MWA). Although MWA has gained increasing acceptance, most of the literature has focused on RFA and CA, and only RFA and CA are mentioned as ablation options in AUA guidelines [4]. MWA systems with higher power can achieve higher temperatures exceeding 100°C and thus are less affected by the "heat-sink" effect created by blood vessels in a vascularized renal target. Furthermore, MWA is also less affected by increased impedance from desiccated tissue and thus able to produce larger ablation volumes in a shorter time. MWA required less sedation than CA and RFA. Despite these theoretical advantages, multiple studies report similar outcomes for varying TA modalities [6,35,37,38].

Immediately following the ablation procedure, contrast-enhanced cross-sectional imaging, if permitted by patient's baseline renal function, allows assessing for complete TA and ruling out complications. In carefully selected patients, contrast used during CT imaging for this evaluation has not been shown to impact the patient's renal function [39].

Perioperative Outcomes

The minimally invasive approach to TA complements the overall low reported complication rates. We reported minor complication rates (i.e., requiring no intervention or only medical intervention) range from 7 to 24 percent, including most commonly probe site pain, hematoma, hematuria, venous thromboembolism, wound complication, urinoma, acute kidney injury and ileus. Major complications (requiring more than medical intervention) range from 0 to 7 percent and include pneumothorax and thermal damage to surrounding structures[1]. Similar complication rates for CA (8-20%) were reported in a recent systematic review[40]. Given this favorable risk-benefit profile, most patients can be discharged on the day of the TA procedure or the first post-procedure day.

Perioperative outcomes for TA compare favorably to partial nephrectomy. Multiple studies, including meta-analyses, report lower blood loss, length of stay and complications with TA than for PN [6,36,41-46]. Renal, thromboembolic, and cardiovascular events occurred at similar rates in TA and PN [8]. A meta-analysis by Patel et al. reported no differences in renal functional outcomes for TA or PN with both resulting in a decrease in eGFR around 1.0 mL/min per 1.73 mL^2 with eGFR remaining stable postoperatively [47]. Regardless of technique (TA vs. PN), complications and local recurrence are associated with dimensions and complexity of the tumor [15,48]. Furthermore, patients at highest risk for complications following PN are ideally defined candidates for TA [8]. Interestingly, Zhou et al. reported no increased risk of disease-free survival or complication rates for overweight or obese patients undergoing TA [49].

Oncologic Outcomes

Follow up with cross-sectional imaging (CT or MRI) is the cornerstone for evaluation of ablation success. In our institution, we use follow up renal protocol enhanced MRI (or CT if MRI contraindicated) at 6 months after ablation then at 12 months or annually based upon AUA guidelines [4]. Residual or recurrent disease is indicated by persistent or newly enhancing or enlarging nodule(s) in the ablation zone.

Five -year survival above 95% has been reported for all TA modalities. Recurrence -free survival (RFS) is inferior when only comparing single TA session to PN. Many studies demonstrated secondary efficacy of TA with repeat ablation bringing RFS up to 97 to 100%, and differences between PN and TA were no longer significant [36]. AUA guidelines specifically note the higher risk of recurrence with stage T1b renal masses treated with TA [4]. High rate of comorbidities in patients undergoing TA can have competing-cause mortality and are often cited as causes

Publication	Years	Study Type	Patient population	Modality	Survival Reporting	Complications	Recurrence-Free Survival (%)	Overall survival (%)	Cancer-Specific Survival (%)
Takaki (2010) [52]	2002-2008	Retrospective	cT1a	51 RFA	5 years	0% (Major)	98.0%	75.0% ∵	100%
				10 PN		0% (Major)	75.0%*	100%	100%
				54 RN		7.4% (Major)	95.0%	100%	100%
Olweny (2012) [53]	1998-2005	Retrospective	pT1a	37 RFA	5 years	NR	91.7%	97.2%	97.2%
				37 PN		NR	94.6%	100%	100%
Anglickis (2019) [54]	2012-2019	Retrospective	pT1, >70 yo	15 MWA	5 years	0%	93.3%	100%	100%
				18 PN		0%	100%	100%	100%
Talenfeld (2018) [6]	2006-2011	Retrospective (SEER)	cT1a	456 TA	5 years	6%	NR	77%	95%
				1748 PN		29%	NR	86%	98%
Park (2017) [9]	2008-2016	Retrospective (PSM)	pT1a	63 RFA	2 years	4.7% (Major)	95.2%	NR	NR
				63 PN		4.7% (Major)	100%	NR	NR
Xing (2018) [7]	2002-2011	Retrospective (SEER, PSM)	cT1a	691 TA	9 years	NR	NR	88.6%	96.3%
				691 PN		NR	NR	91.1%	96.4%
Zhou (2018) [55]	2004-2013	Retrospective (SEER, PSM)	cT1a	809 TA	5 years	NR	NR	86.3% ∵	NR but no significant difference
				3,783 PN		NR	NR	91.0%	
Yu (2020) [45]	2006-2017	Retrospective (PSM)	cT1a	185 MWA	5 years	2.2% (Major)	82.9%	86.3%	NR but no significant difference
				1770 PN		4.9% (Major)	91.4%	91.9%	
Shi (2020) [3]	2004-2016	Retrospective (SEER, PSM)	cT1	4,656 TA	10 years	NR	NR	56.6% ∵	92.4% ∵
				33,499 PN		NR	NR	64.2%	96.1%
Thompson (2015) [44]	2000-2011	Retrospective	cT1a	180 RFA	3 years	NR	98%	82%	NR
				187 CA		NR	98%	88%	NR
				1057 PN		NR	98%	95%	NR
			cT1b	53 CA	3 years	NR	97%	74% ∵	NR
				326 PN		NR	96%	93%	NR

Liu (2017) [56]	2005-2014	Retrospective	pT1 ccRCC	93 RFA	10 years	15.1% T1a 30% T1b	82.8%	84.9%	NR
				120 PN		11.5% T1a 15.2% T1b	88.3%	88.3%	NR
			pT1 non-ccRCC	22 RFA	10 years	25% T1a 10% T1b	100%	86.4%	NR
				29 PN		25% T1a 15.4% T1b	100%	86.2%	NR
Andrews (2019) [57]	2000-2011	Retrospective (PSM)	cT1a	180 RFA	5 years	NR	94.5%	72%	95.6%
				187 CA		NR	93.4%	77%	100%
				1055 PN		NR	97.4%	92%	99.3%
			cT1b	52 CA	5 years	NR	90%	56%∵	91%
				324 PN		NR	94%	90%	98%
Takaki (2014) [58]	2002-2012	Retrospective	cT1b	21 RFA	10 years	8.0% (Major)	NR	48% ∵	94%
				39 RN		5.1% (Major)	NR	97%	100%
Chang (2015) [59]	2006-2010	Retrospective	cT1b	27 RFA	5 years	11.1% (Major)	81.0%	85.5%	92.6%
				29 PN		10.3% (Major)	89.7%	96.6%	96.6%
Rembeyo (2020) [34]	2010-2016	Retrospective (PSM)	cT1b	55 CA + 11 RFA	2 years	0% (Major)	NR	92.6%	96.8%
				36 PN		0% (Major)	NR	96.3%	96.3%
Xing (2018) [7]	2002-2011	Retrospective (SEER, PSM)	cT1a	691 TA	9 years	NR	NR	88.6%	96.3%
				691 PN		NR	NR	91.1%	96.4%
Shapiro (2020) [30]	2000-2018	Retrospective	cT1b	40 MWA	5 years	10% (Major)	94.5%	NR	100%
				74 PN		5.4% (Major)	97.9%	NR	97.6%
				211 RN		3.3% (Major)	99.2%	NR	95.5%

SEER: Surveillance, Epidemiology, and End Results-Medicare linked database; PSM: Propensity Score Matching; cT1a: clinical T1a (<4 cm LRM); pT1a = pathologic T1a (<4 cm LRM); cT1b = clinical T1b (>4 cm LRM); yo: years old; PN: Partial Nephrectomy; RN: Radical Nephrectomy; NR: Not Reported; Major: Major complications (Clavian Dindo ≥ 3)

*3 years

∵ Significant difference in survival when compared to partial nephrectomy

Table 1: Comparison of Complications and Oncologic Outcomes for Studies Comparing LRM Treated with TA vs Surgical Resection.

for decreased overall survival as compared to cancer specific survival [43,45]. Bhindi et al. reported similar local recurrence, distant metastasis and cancer specific survival (CSS) at a median follow up of 47 months when comparing patients with solitary LRM undergoing CA or PN using inverse probability of treatment weighting based on propensity to receive treatment [15]. Another recent retrospective review of 10,2018 patients with T1aN0M0 RCC during a 9 year follow up period reported similar overall and cancer-specific survival (96%) for patients undergoing TA as well as partial and radical nephrectomy [7]. Further detailed comparisons of TA and PN are detailed in Table 1. To date, there has been no prospective, randomized comparison of ablation and PN. A recent review done by the EAU RCC Guideline Panel found that there was high risk of bias due to the retrospective, observational nature of most studies with poorly matched controls and limited follow up. Further, it is difficult to compare studies with variable oncologic outcomes reported and heterogenous patient populations with some reports including benign tumors in their cohorts. They concluded that "the current data are inadequate to make any strong and clear conclusions regarding the clinical effectiveness of TA for treating T1N0M0 renal masses compared with PN. Therefore, TA may be cautiously considered an alternative to PN for T1N0M0 renal masses, but patients must be counselled carefully regarding the prevailing uncertainties" [50].

Future Directions

There has been an increased acceptance of TA, but it is typically reserved for the morbidity-burdened population with LRMs. The question of the effect of ablation on health-related quality of life remains unanswered. Some evidence suggests that ablation could be a cost-effective option for many patients [8,41,45,51]. However, a cost comparison including active surveillance and PN arms remains to be done. Additional questions remain in how to best assess competing co-morbidities to direct the patient to the best individualized treatment strategy.

Conclusion

TA is an important addition to the urologist's established armamentarium of surgical resection for management of renal masses. There are no prospective or randomized studies comparing efficacy of ablation and PN. Patient selection is highly subject to bias as patients that are currently targeted for percutaneous TA are often older and burdened with multiple comorbidities but have smaller and less complex masses as compared to patient selected for PN. When compared to partial nephrectomies, retrospective comparative series report similar oncologic outcomes and often improved complication profiles. Other specific patient populations well suited for ablation including those with a solitary kidney, CKD, or multiple masses where preservation of renal function is of the utmost priority. Percutaneous image guided TA is an attractive treatment option providing local tumor control, fewer complications, and better preservation of renal function.

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