Thermal Ablation for Renal Cell Carcinoma: Current Guidelines and Supporting Evidence

A review of the recently published data that have helped to inform treatment guidelines for renal cell carcinoma.

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Treatment options for localized renal cell carcinoma (RCC) include radical nephrectomy (RN), partial nephrectomy (PN), thermal ablation (TA), and active surveillance. There is a lack of randomized controlled trials (RCTs) comparing these different RCC treatments. This article reviews current guidelines and supporting evidence behind treatment recommendations, with a particular focus on treatment of stage T1a RCC (tumors ≤ 4 cm and confined to the kidney).

AMERICAN UROLOGICAL ASSOCIATION GUIDELINE UPDATE

TA for RCC has gained recognition as a viable treatment alternative to PN. In 2017, the American Urological Association (AUA) published updated guidelines stating that "physicians should consider TA as an alternate approach for management of cT1a renal masses < 3 cm in size."[1] The AUA guidelines further stated that a percutaneous approach to TA is preferable to a surgical approach (including laparoscopic and open) to minimize complications. Limitations of existing studies underlying the recommendations were acknowledged. Other notable statements regarding TA from the updated AUA guidelines included recognition of cryoablation and radiofrequency (RF) ablation as equivalent, the recommendation that renal biopsies should be performed prior to ablation to provide pathologic diagnosis and guide surveillance after TA, and the recommendation that patients be counseled prior to ablation regarding an increased chance of residual disease or local recurrence after primary ablation compared with PN and that a recurrence or residual disease can be treated with repeat ablation.[1]

The primary support for TA as a treatment for stage T1a RCC in the updated 2017 AUA guidelines is a meta-analysis by Pierorazio et al.[2] This analysis of interventions to manage renal masses that were suspected localized RCC included 107 studies and provided strength of evidence for each comparison, ranging from moderate or low to insufficient. A total of 60 studies provided data on one or more oncologic outcome: cancer-specific survival (CSS), metastasis-free survival, or local recurrence-free survival (LRFS). The majority of the studies were cohort studies and the single RCT did not address ablation. The median follow-up time was 48.6 months for the ablation groups and 60 months for RN and PN. The majority of tumors in the analysis were T1, and no ablations were performed on T2 tumors. The median tumor size was 2.9 cm for PN and 2.5 cm for TA. CSS was between 95% and 100% for all treatment modalities; however, the strength of evidence for comparing PN and TA for T1 RCC was rated as "low," with high inconsistency and many limitations in the available studies.

Overall survival (OS) was lower in patients who underwent TA versus PN; however, this was attributed to patients in the TA group being older and having more comorbidities. TA patients were median age of

66.6 years versus 60.1 years for PN and had significantly lower mean glomerular filtration rates before treatment. Metastasis-free survival ranged from 90.5% to 100%, with no difference between PN and TA (moderate strength of evidence). There was a statistically significant difference in LRFS between PN and TA with a moderate strength of evidence. A median of 99.4% of PN patients were recurrence free at the end of follow-up versus a median of 89.3% in TA patients; however, this difference was not significant after patients underwent a second TA treatment. TA had superior perioperative outcomes when compared with PN with moderate strength of evidence. TA was associated with decreased median hospital length of stay and decreased median blood loss. The rates of urine leak, acute kidney injury, and other urologic complications were higher in PN versus TA (median percentage urine leak and acute kidney injury was 0% for both in TA and 2.6% and 2.1% for PN, respectively). Renal function outcomes were similar between PN and TA with low strength of evidence. Compared with PN, TA offers similar CSS with fewer complications for stage T1a RCC.[2]

SEER CANCER REGISTRY

Two studies based on the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) cancer registry have been published to date. Zhou et al published a SEER study comparing TA and PN in stage T1a RCC with a primary outcome of OS and secondary outcome of CSS.[3] Patients diagnosed with stage T1a RCC from 2004 to 2013 were identified. Of 4,592 patients treated for stage T1a RCC, 809 (18%) underwent TA and 3,783 (82%) underwent PN. OS was inferior with TA compared with PN both in the pooled and propensity-matched populations, although the difference in OS was less in the matched population. Patients treated with TA were an average of 10 years older than patients treated with PN (mean age, 67.7 years vs 57.2 years), and the mean tumor size was larger with TA compared with PN (24.6 mm and 23.7 mm). After propensity matching, there was no statistically significant difference in CSS with TA as compared with PN. Limitations of the study included the limitations of the SEER database such as nonreporting of potentially confounding variables including histologic subtype, number of tumors, tumor location, tumor proximity to adjacent structures, other medical conditions, as well as other treatment complications.[3]

Talenfeld et al used the SEER data to compare TA with PN and RN for stage T1a RCC.[4] Patients ≥ 66 years of age with stage T1a RCC treated between 2006 and 2011 were included. The patients were followed for a median of 42 months for RCC-specific survival. Compared with PN and RN patients, TA patients were older and sicker and had higher baseline renal insufficiency and increased cardiovascular disease. These differences were less significant between the TA and RN groups than between the TA and PN groups, confirming that similar to other analyses, patients chosen for PN tended to be healthier overall. Five-year OS was inferior with TA compared with PN (77% vs 86%), but differences in absolute survival with TA and PN were not substantial (95% vs 98%). Despite confounding variables, there was no statistically significant difference in CSS between TA and PN (although there was a trend toward significance). Five-year CSS was similar between TA and RN. As seen in other analyses, perioperative outcomes were worse in the PN group. Patients who underwent PN had statistically significant higher rates of acute renal failure and other nonurologic complications in the first 30 days after the procedure. Acute renal failure occurred in < 3% of patients undergoing TA and 7% of patients undergoing PN. Nonurologic complications, which included pulmonary embolism, deep vein thrombosis, noncardiogenic shock, respiratory failure, pneumonia, hematoma, and abscess, were 29% in PN group and 6% in TA group.[4]

AMERICAN SOCIETY FOR CLINICAL ONCOLOGY GUIDELINES

The 2017 American Society for Clinical Oncology (ASCO) guidelines on the management of small renal masses reflects the increasingly recognized role of TA.[5] Although the ASCO guidelines recommend PN for patients in whom treatment is indicated and tumor is appropriate for PN, the guidelines also state that "percutaneous TA should be considered for patients who possess tumors such that complete ablation will be achieved." As with the AUA guidelines, biopsy is recommended before or at the time of ablation to guide surveillance. The ASCO recommendation was backed by "intermediate-quality" evidence and given as a "moderate" strength recommendation.[5]

One of the studies cited is a large cohort study by Thompson et al that analyzed 1,803 patients in the Mayo Clinic Renal Tumor Registry treated for stage T1 RCC between 2000 and 2011.[6] There were 1,424 stage T1a patients. Of these, 1,057 underwent PN, 180 underwent RF ablation, and 187 underwent cryoablation. OS at 3 years for PN, RF ablation, and cryoablation was 95%, 82%, and 88%, respectively. There was no statistically significant difference in 3-year LRFS by treatment type (98% for all three groups). Five-year metastasis-free survival was excellent for all three treatment

groups (93%–100%). Limitations of the study included that it was a retrospective analysis; had heterogeneous patient follow-up, which was more robust for PN; and the median imaging after TA was < 3 years. As with other studies, selection bias of younger and healthier patients for PN was noted.[6]

CONCLUSION

There has been accelerated use of TA in the management of stage T1a RCC in the last decade, which is reflected by improved treatment outcomes and recognition of TA as a reasonable treatment option by AUA and ASCO guidelines. TA is associated with better perioperative outcomes and fewer complications when compared with surgery. Although local recurrence rates appear to be higher in patients treated with TA, this can be overcome with repeat TA treatment. Patients who undergo PN tend to have better OS; however, this effect may be attributable to PN patients being younger and healthier at baseline.

To date, there are no RCTs comparing TA with the established surgical treatments for stage T1a RCC. As a result, the level of evidence for TA for treatment of stage T1a RCC ranges from moderate to insufficient. In general, the paucity of level 1 data is an acknowledged weakness of interventional oncology. With respect to RCC, ongoing clinical trials are focused on biological agents and drugs, stereotactic radiation/radiosurgery, ablation-assisted surgery, gene- and protein-expression analysis, and assessment of other biomarkers. There is need for level 1 data directly comparing TA, PN, RN, and active surveillance with assessment of OS in addition to other clinical and cancer outcomes, with attention to histologic subtype, tumor location, tumor proximity to adjacent structures, and ablation modality.

The 2017 AUA guidelines, which support consideration of TA as an alternative to PN for cT1a RCC < 3 cm in size, have created the opportunity for an RCT. Based upon the data to date, it is expected that such a study could be pivotal for TA. Only once inherent biases in patient selection are eliminated and the treatments and their outcomes can be fully assessed will the role of TA in the management of stage T1a RCC be clearly established and accepted by the larger oncology community. ■

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