Are the long-term outcomes of percutaneous ablation for clinical stage T1 renal tumors similar to those of partial nephrectomy?

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A better understanding of the natural history of small renal masses and the adverse effects of radical nephrectomy on long term renal function and subsequent morbidity and mortality led to a surge in the use of nephron sparing surgery and surveillance for the treatment of clinical stage T1 renal masses (1-3). Nephron sparing treatment options include predominantly partial nephrectomy (PN), however reports have shown the feasibility of percutaneous thermal ablation methods, including cryoablation and radiofrequency ablation (RFA), as possible alternatives (4). Initially used for patients who were unfit for surgery, the indications for these techniques have expanded to include a larger group of patients with small renal masses that are amendable to complete ablation (5,6). While percutaneous ablative therapies are less invasive and result in superior functional outcomes compared to radical nephrectomy, it is uncertain whether they provide equivalent oncologic outcomes (7-9). To date, thermal ablative techniques were not compared to PN in a randomized prospective manner. The CONSERVE trial comparing PN with thermal ablation was terminated early due to poor accrual, and an ongoing trial (Clinicaltrials.gov identifier: NCT03094949) has not resulted yet (10). With the lack of randomized prospective studies comparing the oncological and functional outcome of ablative treatments and PN, current guidelines rely on non-randomized studies which are limited mostly by selection bias and a relative short follow-up which may not be sufficient to show differences in oncological outcomes (11-15).

In the current retrospective analysis, Andrews *et al.* compared local recurrence free survival, metastatic free survival and cancer-specific survival of PN and percutaneous ablation using either RFA or cryoablation for a large group of 1,798 patients treated at the Mayo Clinic for a cT1N0M0 renal mass (16). Median follow-up for the cohort was above 6 years. Among 1,422 patients treated for a cT1a tumor, ≤4 cm in diameter, 1,055 underwent PN, 180 RFA and 187 cryoablation. No significant differences were found when comparing PN to either RFA or cryoablation on all evaluated outcomes with reported 5-year CSS rates of 99%, 96% and 100% for PN, RFA and cryoablation, respectively. Within the subgroup of 376 patients with cT1b tumors, between 4 to 7 cm in diameter, no significant difference was found when comparing PN (n=324) and cryoablation (n=52); however, cancer related death after cryoablation was more common with a 5-year CSS rate of 91% compared to 98% in patients treated with PN (16).

Previous studies comparing the oncologic outcomes of PN and percutaneous ablation were limited by the heterogeneity of the cohorts evaluated, selection bias, and relatively short follow-up periods. The current study, a large single center study with long follow-up, concluded that for patients with a cT1a tumor, clinically relevant differences in treatment outcomes are unlikely. While these results support the role of thermal ablation for cT1a tumors, they were obtained with substantial patient selection as evident

by the different numbers of patients treated in each group and significant differences in patient characteristics between the treatment groups including younger age and lower Charlson comorbidity score among patients who underwent PN. In addition, overall survival rates of patients who underwent RFA and cryoablation were significantly lower than those of patients treated with PN, consistent with the older age and higher rate of comorbidities in the groups treated with ablation. The authors did not report additional reasons for selecting patients to receive a certain treatment; however previous studies suggest that patients treated with ablative therapies for tumors with a higher RENAL nephrometry score suffer a higher rate of adverse outcomes and may be less suitable for ablative procedures (17,18). Camacho *et al.* reported that a RENAL nephrometry score >8 significantly predicted early tumor recurrence and complications after percutaneous ablative therapy for stage T1a RCC (17). Similarly, Schmit *et al.* found that patients with local recurrence and major complications after ablation were more likely to have a higher RENAL score (18). The selection bias, apparent in the current as well as previous studies, emphasizes the importance of conducting a prospective randomized comparison in order to truly understand the difference in treatment outcome when treating patients with cT1a renal tumors. Nevertheless, the similar long-term oncologic outcome suggests that with appropriate selection, thermal ablation may have a role in treating patients with renal masses less than 4 cm in size.

The conclusions of the study are less definitive for patients with cT1b tumors. A previous study looking at patients with cT1b tumors treated with cryoablation has shown a significant benefit to the use of PN with regards to local recurrence (11). While not statistically significant, in the current study, the outcome for patients treated with cryoablation was inferior to that of PN. As stated in the conclusions, future studies should evaluate the role of ablative treatments in this group of patients.

Considering the results of the current as well as previous studies, ongoing efforts should focus on optimizing the treatment for each individual patient, balancing between the oncologic and functional outcomes while considering the patients age and comorbidities and the tumor characteristics. A better understanding of the tumor's molecular features may aid in this decision process. A recent report by Manley *et al.* showed that patients with small renal masses that harbor a *KDM5C* mutation have inferior survival from either recurrence or death of their disease (19). Since patients who undergo ablation are recommended to have a renal mass biopsy before treatment—in the future, molecular characteristics of the tumor may guide us regarding the optimal treatment for this group of patients (10).

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Footnote

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