Treatment for T1a Renal Cancer Substratified by Size: "Less is More"

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Abbreviations and Acronyms

CSS = cancer specific survival
CVS = cardiovascular survival
OS = overall survival
PN = partial nephrectomy
RN = radical nephrectomy
SRC = small renal cancer
TA = thermal ablation

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Purpose: Due to the widespread use of computerized tomography, the diagnosis of small renal cancers (3 cm or less) within the T1a classification continues to increase. Current treatment of these tumors includes radical nephrectomy, partial nephrectomy and thermal ablation. We used the SEER (Surveillance, Epidemiology, and End Results) Program to compare treatment modalities for these cancers based on 1 cm increments in tumor size. We examined overall survival, cancer specific survival, survival from cardiovascular disease and race based treatment disparities.

Materials and Methods: In the SEER database we identified 17,716 renal cancers 3 cm or less diagnosed from 2005 to 2010 treated with radical nephrectomy, partial nephrectomy or thermal ablation. Overall survival, cancer specific survival and cardiovascular survival were determined for each treatment group, and then substratified by size in centimeters, tumor grade, age, geographical location and ethnicity. Survival was analyzed using Kaplan-Meier methods, multivariate proportional hazards models and a propensity score weighted approach.

Results: Overall survival, cancer specific survival and cardiovascular survival were better for partial nephrectomy than radical nephrectomy in all circumstances. Thermal ablation showed equivalent overall survival to partial nephrectomy for tumors 2 cm or less. Notably, radical nephrectomy for renal tumors 3 cm or less was applied in a disparately larger number of black patients (OR 1.63, 95% CI 1.47–1.81) and Hispanic patients (OR 1.28, 95% CI 1.14–1.44).

Conclusions: Radical nephrectomy should be avoided for all tumors 3 cm or less. For renal cancers 2 cm or less partial nephrectomy and thermal ablation are equally effective. For tumors 2.1 to 3 cm partial nephrectomy is better than thermal ablation. We identified significant racial treatment disparities that negatively impact survival in black and Hispanic patients.

Key Words: kidney neoplasms, ablation techniques, nephrectomy

Historically, radical nephrectomy was the standard of care for all renal masses, with partial nephrectomy reserved for extenuating circumstances such as solitary kidney or the presence of bilateral tumors. With time, it became clear that PN was associated with a lower incidence of adverse renal outcomes[1,2] while maintaining equivalent oncologic

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outcomes for T1a renal cancers in general (ie 4 cm or less).[3] This became of even greater importance in light of recent medical data showing that chronic kidney disease in the general population leads to a decrease in cardiovascular survival.[4] Accordingly, nephron sparing treatment with PN or thermal ablation (cryoablation or radio frequency ablation) has become more widely used during the last decade.[5] Indeed, PN has become the recommended standard of care for clinical T1a renal cancers. However, RN remains a recognized alternative standard of care if PN, in the opinion of the treating urologist, is not technically feasible. In contrast, while less invasive than PN, thermal ablation, due to its lower effectiveness, is generally limited to T1a renal cancers in patients with multiple comorbidities who would be at higher risk for treatment with PN.[6]

Despite the increasing acceptance of PN as the standard therapy for small renal cancers, RN continues to be commonly used.[5] This may be due to several factors. PN is more technically challenging and has a higher complication rate than RN. TA is a relatively new technique and often requires a joint effort between urologists and interventional radiologists. Also, there is controversy as to whether PN confers a better overall survival than RN for T1a renal cancers. Indeed, there is 1 randomized trial of renal cancers 5 cm or less (ie T1a and small T1b cancers) that showed better OS with RN than PN with no difference in CSS or progression.[7] Of note, this trial was criticized for being underpowered and for having a high PN to RN crossover. In contrast, there have been multiple population based studies that have claimed superiority of PN over RN.[8–10] A recent comprehensive meta-analysis has also corroborated better cancer outcomes with PN.[11] While these studies have focused on varying aspects of survival for RN vs PN, to our knowledge no study has examined all 3 treatment modalities and all 3 outcome measures (ie OS, CSS and CVS) in a patient cohort further subdivided by tumor size in 1 cm increments up to 3 cm, as well as tumor grade, age, geographic location and patient ethnicity.

Of importance, earlier studies using the SEER database focused on 1991 data, when PN was predominantly used in patients with extenuating circumstances (ie solitary kidney, compromised renal function etc) and TA was too new to be included in any SEER based studies. Furthermore, in these studies all T1a renal cancers were lumped together over all age groups and ethnicities.

We hypothesize that the ideal treatment for T1a renal cancers 3 cm or less varies based on centimeter increments in tumor size (ie less than 1 cm, 1.1 to 2 cm, 2.1 to 3 cm). Furthermore, we are concerned that given that PN and TA are relatively recent and resource intensive procedures, a disproportionate number of disadvantaged or indigent patients may not be provided with these alternatives to RN. In this study we examine the most recent data from the SEER database to compare the treatment of small renal cancers (3 cm or less) with RN, PN and TA stratified by age, ethnicity, geography, tumor grade and tumor size between 2005 and 2010.

METHODS

Data Source and Study Population

The SEER Program of the National Cancer Institute contains approximately 97% of all incident cancer cases from cancer registries and these registries cover approximately 28% of the U.S. population. The SEER Program registries collect data on demographics, primary tumor site, tumor morphology and stage, first course of treatment, followup for vital status and cause of death. Of note, this study only deals with small renal cancer and not small renal masses, and the SEER database only includes histologically proven renal cancers. Our analysis data include cases diagnosed from 2005 to 2010 in 18 SEER registries.

Consecutive adult patients (age at diagnosis 18 years old or older) diagnosed with SRC between January 1, 2005 and December 31, 2010 were identified using the ICD-O-3 site code C649. Cases from autopsy or death certificate only were excluded from analysis. Patients who did not receive any surgical therapy were also excluded. All renal cancer pathological types were included in the analysis. The final analytic data set included 17,716 patients with small renal cancer who were treated with PN, RN or TA.

Variables and Statistical Analysis

Treatment was identified for each patient using the surgery for primary site variable provided in the SEER data, including partial nephrectomy, radical nephrectomy and thermal ablation. Other covariates included patient demographic and tumor characteristics. Patient race/ethnicity was categorized into the 5 groups of white, black, Hispanic, Asian/Pacific Islander or other/unknown. Age at diagnosis was used as a continuous variable or categorical variable with the 4 groups of less than 50 years, 50 to 59, 60 to 69 and 70 or greater. Registry region included the 4 categories of Central (Detroit, Iowa, Utah, Kentucky and Louisiana), Eastern (Connecticut, Georgia and New Jersey), Western (Hawaii, New Mexico, Seattle and Alaska) and California. Tumor characteristics included tumor grade (grade I-II, III-IV, unknown), size (1.0 cm or less, 1.1 to 2.0 cm, 2.1 to 3.0 cm), histology (clear cell or others) and tumor stage (localized, regional, distant or unknown).

Frequency distributions of patient demographic and clinical characteristics were analyzed using the chi-square or Fisher exact test for categorical variables in bivariate analysis. The time trend of treatments during