Letters to the Editor

Management of Small Renal Masses

From
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Editor:

We commend Dr Xing and colleagues for their interesting comparative analysis of treatment modalities for small renal masses in the July 2018 issue of Radiology (1). This is clearly an important clinical question. The authors made use of propensity score–matched observational data from the Surveillance, Epidemiology, and End Results (SEER)–Medicare database adjusted for 17 variables to compare cancer-specific and overall survival with partial nephrectomy (PN), radical nephrectomy (RN), thermal ablation (TA), and active surveillance (AS).

Propensity score methods allow for the minimization of baseline imbalances across treatment groups. In particular, propensity score matching generates sets of treated and untreated subjects with similar known covariates (2). Although cancer-specific survival analyses supported PN and TA over AS in the study by Dr Xing and colleagues (1), the effect size (ie, absolute change in survival rates) is small even at 9 years (range, 1.4%–2.5%). Plus, overall survival, a surrogate for general health status, had large differences across all treatment options and AS (range, 5.9%–7.7%). This sanity check supports the existence of unknown and unaccounted confounding factors that limit the validity of the results.

Observational data may be better than no data, but we must not forget that while such quasi-experimental designs are a useful exploratory tool, only randomized controlled trials will allow for the balancing of unmeasured confounders and the estimation of unbiased causal treatment effects. Unfortunately, the only clinical trial to date to attempt a randomized comparison between AS and other treatment modalities, the SURAB study (a randomized study comparing ablation with active surveillance in the management of incidentally diagnosed small renal tumors; trial registration number ISRCTN31161700), failed to successfully recruit enough participants (3). Alternative, pragmatic trial designs, such as cohort embedded randomized studies, are needed to offer feasible alternatives to deliver high-quality unbiased evidence for the management of small renal masses.

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References

Response

From
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We thank Dr Neves and colleagues for their letter regarding our study (1). We agree that observed differences in outcomes between currently available treatment modalities for small renal masses bear comparison in randomized controlled trials or pragmatic trials to minimize unknown discrepancies at baseline. As initial management, AS is currently considered safe for older and/or sicker patients and those with very small masses (<2 cm) (2). However, given the paucity of prospective studies comparing the oncologic outcomes of AS to other modalities, observational data as presented in our study serve to provide insight into the possible benefits of intervention, including long-term outcomes, within the limitations of the database and framework of assumptions required in propensity score matching.

To better understand the impact of possible unmeasured confounding factors when comparing PN, RN, and TA with AS, we further performed formal sensitivity analysis on our findings. Based on methods set forth by Rosenbaum (3,4), we observed a high $\Gamma$ (gamma) value of greater than 5 for differences in both cancer-specific survival and overall survival when PN, RN, and TA were compared
individually with AS. Similarly high \( \Gamma \) values were observed in other direct comparisons, including PN or RN versus TA. These results suggest that the comparisons made were insensitive to unknown confounding factors.

As mentioned in our Discussion, we acknowledge that the discrepancy in the cancer-specific survival rate for PN and TA over AS (range, 1.4%–2.5%) as compared with a difference in overall survival of between 5.8% and 7.7% at 9 years may be due to the lack of clarity with regard to whether all patients designated to AS underwent adequate surveillance. Here, we are unfortunately further limited by the availability of information present in the SEER-Medicare database, which does not offer specific, standardized coding for AS. As a result, it is not possible to use registry data alone to clearly differentiate between patients who underwent AS with structured observation protocols, such as that of the Delayed Intervention and Surveillance for Small Renal Masses, or DISSRM, Registry (5), and those who delayed intervention due to other factors. Such limitations would be readily addressed in urgently needed prospective, randomized comparisons between AS and intervention, which would go a long way toward answering the questions that remain with regard to optimal therapeutic protocols for small renal masses.

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**References**


