

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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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 bears 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 Γ (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 Γ 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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Ex Vivo Mercury Release from Dental Amalgam

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Editor:

This letter is regarding the article by Drs Yilmaz and Adisen, which was recently published online in *Radiology* (1). Although this article is well structured and addresses a very challenging issue, it has one shortcoming. This shortcoming

comes from emphasizing the importance of the strength of the magnetic field of MRI, while studies show that the key issue in mercury release after MRI is the radiofrequency radiation. Interestingly, Dr Yilmaz, the senior author of this article, has previously mentioned the possible role of radiofrequency radiation: “The release of mercury from amalgam by MRI is therefore, thought to occur due the radio waves, which can induce vaporization, not the static magnetic field” (2). Studies showing either increased mercury release from amalgam fillings or microleakage after exposure to other sources of electromagnetic radiation such as Wi-Fi routers (3), mobile phones (4), and light curing devices (5) have further confirmed the role of radiofrequency radiation in this phenomenon.

Considering that ex vivo results cannot be extrapolated to in vivo without caution, including several early in vivo studies that showed the increased release of mercury after MRI with lower field strengths (4,6), could improve the literature review of this article. Dr Yilmaz, in her editorial (2), has previously addressed the importance of one of these studies (4). Interestingly, Drs Yilmaz and Adisen have also observed higher mercury release in samples exposed to 1.5 T compared with control samples (172 vs 141 mg/L), but the difference was not significant. Figure 3 of their article shows a great variation of data in their control samples and possibly some outlier data points. In this light, the difference between the studies that showed increased release of mercury from amalgam fillings after 1.5-T or less MRI and that of Drs Yilmaz and Adisen can be due to statistical limitations. It is worth noting that the studies that showed increased release of mercury from amalgam fillings after 1.5-T MRI are further supported by those that showed amalgam microleakage after MRI with lower magnetic field strengths (1.5 or 3.0 T) (7,8).

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