Editorial Commentary

Safety and delayed intervention rates of active surveillance for small renal masses in an elderly population

Brian T. Kadow, Marc C. Smaldone

Fox Chase Cancer Center, Philadelphia, PA, USA

Correspondence to: Marc C. Smaldone, MD. Fox Chase Cancer Center, 8 Huntingdon Pike, 3rd floor, Rockledge, PA 19046, USA.
Email: Marc.Smaldone@fccc.edu.

Provenance: This is an invited article commissioned by the Section Editor Dr. Xiao Li (Department of Urology, Jiangsu Cancer Hospital, Jiangsu Institute of Cancer Research, Nanjing Medical University Affiliated Cancer Hospital, Nanjing, China).

Comment on: Whelan EA, Mason RJ, Himmelman JG, *et al.* Extended Duration of Active Surveillance of Small Renal Masses: A Prospective Cohort Study. J Urol 2019;202:57-61.

Submitted Jul 05, 2019. Accepted for publication Jul 19, 2019.
doi: 10.21037/atm.2019.07.68
View this article at: http://dx.doi.org/10.21037/atm.2019.07.68

The incidence of incidentally detected renal masses thought to represent renal cell carcinoma (RCC) has increased with widespread utilization of cross-sectional imaging, with many of these lesions being considered small renal masses (SRMs), ≤4 cm in maximal diameter (1,2). These lesions were historically treated surgically, with either radical nephrectomy or nephron-sparing surgery (NSS), or with percutaneous ablation. Over the last two decades, however, there has been a paradigm shift towards active surveillance (AS) as an initial treatment option for patients who present with SRMs, particularly in the elderly or those with significant competing risks of mortality (3). The goals of AS are to minimize overtreatment of indolent renal lesions, avoid the potential morbidity of surgical or percutaneous intervention, and to weigh the risks of disease progression/metastasis versus the risks of intervention, taking into the account the patients' co-morbidities. Patients on AS can be offered delayed intervention based on SRM growth kinetics, competing risks, or patient preference (4). Current AUA guidelines state that AS should be considered as an option for the initial management of small solid renal masses, particularly those <2 cm in maximal diameter (5). While multiple AS cohort studies have been published in recent years documenting low rates of metastases, these have generally had short median follow-up and/or small sample sizes (6-9).

Adding to the literature, Whelan *et al.* recently reported results from a prospective cohort study enrolling 103 patients (median age 75) at a single center from January 2001 to December 2011 with renal masses <6 cm in maximal diameter who elected to undergo primary AS of their lesion (10). At median follow-up of 55.5 months, they found that only 17 (16.5%) patients required delayed surgical or percutaneous intervention of their lesion. Intervention was predominately due to patient preference, however 9 patients (8.7%) required treatment because of development of symptoms, or due to radiographic progression thought to represent clinically significant disease.

The group found that patients with a centrally located tumor were statistically more likely to undergo delayed intervention of their lesion (P=0.006). Mean tumor growth rate for the cohort was 0.21 cm/year, while those undergoing delayed intervention had a mean growth rate of 0.37 cm/year. Notably, 48 (46.6%) of the patients included for study died of unrelated causes at median follow-up. Fifty-three (51.5%) of patients remained on AS, and 2 (1.9%) of patients developed metastatic disease while on AS. Of the two patients who developed metastatic disease, one died of RCC, while the other died of unrelated causes.

The authors concluded that with almost 5 years median follow-up, the majority of SRMs in patients on AS in their cohort displayed indolent behavior and the risk of progression to metastatic disease was very low at 1.9%. Furthermore, almost 50% of enrolled patients died of other causes while on AS for their SRM, highlighting the importance of contextualization of competing

risks when counseling patients who present with an incidentally discovered SRM, Strengths of this study include its prospective nature and long-term follow-up. A limitation of the study is the older median age of the study population [75], which makes the findings difficult to generalize to a younger or healthier patient population.

This study adds to the previous literature showing that AS appears to be an appropriate management strategy for patients presenting with SRMs, particularly those who are elderly or have significant competing risks of mortality. In this series, the rate of progression to metastatic disease was 1.9%, which is similar to prior published reports (11).

McIntosh and colleagues recently published a retrospective, single-institution analysis of 457 patients undergoing AS for SRMs with a median follow-up of 67 months (12). They evaluated the rates of delayed intervention in the AS cohort, as well as overall survival (OS). They found that the cumulative incidence of delayed intervention after 5 years on AS was 42% (95% CI, 37–48%). OS at 5 years was noted to be 89% (95% CI, 85–92%), and delayed intervention did not appear to have an effect on OS. Eight (1.8%) patients in this cohort progressed to metastatic disease and five patients subsequently died from RCC. The discrepancy of intervention rates between Whelan and McIntosh's studies may be related to the difference in the median age of the cohorts (75 versus 70 years), as age can affect competing risks of mortality and risks of surgical intervention.

In conclusion, these data support the use of AS as an initial management strategy, particularly in the elderly or those with significant competing risks. It has now been well demonstrated that AS is safe with very low rates of disease progression (with short and intermediate term follow up) and that delayed intervention is effective with acceptable oncologic outcomes. Current gaps in the literature include uniform selection criteria for AS, consistent imaging surveillance schedules, and criteria for definitive intervention (4). Moving forward, prospective multi-institutional registries such as the Delayed Intervention and Surveillance for Small Renal Masses (DISSRM) may be the most effective data source to identify and validate such measures across institutions which will further enable utilization of AS in community practice and reduce over treatment.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Hollingsworth JM, Miller DC, Daignault S, et al. Rising incidence of small renal masses: a need to reassess treatment effect. J Natl Cancer Inst 2006;98:1331-4.
2. Kane CJ, Mallin K, Ritchey J, et al. Renal cell cancer stage migration: analysis of the National Cancer Data Base. Cancer 2008;113:78-83.
3. Kutikov A, Egleston BL, Wong YN, et al. Evaluating overall survival and competing risks of death in patients with localized renal cell carcinoma using a comprehensive nomogram. J Clin Oncol 2010;28:311-7.
4. Ristau BT, Kutikov A, Uzzo RG, et al. Active Surveillance for Small Renal Masses: When Less is More. Eur Urol Focus 2016;2:660-8.
5. Campbell S, Uzzo RG, Allaf ME, et al. Renal Mass and Localized Renal Cancer: AUA Guideline. J Urol 2017;198:520-9.
6. Jewett MA, Mattar K, Basiuk J, et al. Active surveillance of small renal masses: progression patterns of early stage kidney cancer. Eur Urol 2011;60:39-44.
7. Pierorazio PM, Johnson MH, Ball MW, et al. Five-year analysis of a multi-institutional prospective clinical trial of delayed intervention and surveillance for small renal masses: the DISSRM registry. Eur Urol 2015;68:408-15.
8. Pierorazio PM, Johnson MH, Patel HD, et al. Management of Renal Masses and Localized Renal Cancer: Systematic Review and Meta-Analysis. J Urol 2016;196:989-99.
9. Uzosike AC, Patel HD, Alam R, et al. Growth Kinetics of Small Renal Masses on Active Surveillance: Variability and Results from the DISSRM Registry. J Urol 2018;199:641-8.
10. Whelan EA, Mason RJ, Himmelman JG, et al. Extended Duration of Active Surveillance of Small Renal Masses: A Prospective Cohort Study. J Urol 2019;202:57-61.
11. Smaldone MC, Kutikov A, Egleston BL, et al. Small renal masses progressing to metastases under active surveillance:

a systematic review and pooled analysis. Cancer 2012;118:997-1006.
12. McIntosh AG, Ristau BT, Ruth K, et al. Active Surveillance for Localized Renal Masses: Tumor Growth, Delayed Intervention Rates, and >5-yr Clinical Outcomes. Eur Urol 2018;74:157-64.

Cite this article as: Kadow BT, Smaldone MC. Safety and delayed intervention rates of active surveillance for small renal masses in an elderly population. Ann Transl Med 2019;7(Suppl 6):S182. doi: 10.21037/atm.2019.07.68

