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Editorial

Current perspectives on active surveillance for patients with small renal masses

Small renal mass (SRM) incidence has been increasing over last decades due to the widespread access to diagnostic tools and is now accounting for 48%–66% of all renal cell carcinoma (RCC) diagnoses [1]. The optimal management of SRM is still debated since approximately 25% of T1a is benign lesions. The role of active surveillance (AS) and the problem of SRM overtreatment are widely described in the current literature. However, RCC mortality has remained stable over the last 2 decades. The major strength of AS is the "tetrafecta" concept as it brings renal function preservation, safe oncological outcomes, and no surgical complications, and it maintains quality of life. AS is nowadays considered as a safe strategy for many SRMs.

Several issues have jeopardized AS in the past. First, AS definition was not well-stablished initially; therefore, a mixture of watchful waiting and AS patients might be included in those series. Secondly, progression labelling is equivocal and triggers for intervention have evolved with improvement on characterization of SRM biology. Third, progression or recurrence within the first 6 months of AS is currently not considered as that due to the likelihood of prior existence; however, that might not have been the case on initial series. Last, retrospective published series provided short follow-up outcomes (mean follow-up 24–36 months) [2].

Two prospectively maintained AS registries for SRM have recently updated their long-term follow-up outcomes [3]. The Canadian registry reported on 5-year follow-up for AS patients. A total of 136 were included, 49 (36%) remaining on AS at 5 years. All patients included in the current report underwent a SRM biopsy for proof of RCC. Several interesting findings were to be highlighted. Growth rates for biopsy-proven SRM were slow (mean: 0.19 cm per year) and extremely variable over the first year on surveillance. Only six patients developed metastatic disease and 29 died (three cancer-related deaths). From the Delayed Intervention and Surveillance for Small Renal Mass (DISSRM) registry, the 10-years outcomes have been recently published. A total of 495 patients were enrolled on the AS arm; only 110 had a biopsy-proven RCC; the 5-year progression-free survival rate on AS group was 67%, like the Canadian series and mostly driven by elevated growth rates. The 5-year recurrence-free survival rate for patients on AS was 93%, similar to patients that had chosen a primary intervention pathway. To highlight that, the long-term cancer-specific survival outcomes at 7-year were similar amongst primary intervention and AS. Therefore, the prospective registries are excellent in terms that provide strong evidence to support the role of AS for SRM without hesitation. The oncological outcomes remained similar to primary intervention and the likelihood of metastatic disease was minimal. Nevertheless, the selection of patients that would mostly benefit from AS is still unclear. Most series are reporting on patients with very SRMs (<2 cm) and high comorbidity burdens. American Urological Association guidelines suggest AS for renal masses <2 cm while European Association of Urology guidelines encourage AS to frail and/or comorbid patients with T1a tumors. Patient selection with tailored approaches according to patient needs and tumor biology might bring some light on optimal decisions.

Moreover, standardized follow-up schemes and AS progression definitions represent an open issue. Most common follow-up schemes consist of monitoring the mass size by serial abdominal imaging (ultrasound, computed tomography, or magnetic resonance scheduled every 6–12 months) with delayed intervention reserved for tumors showing clinical progression. Most authors define progression based on a growing mass, adopting it as a trigger for active treatment (growth rate over 0.5 cm per year and/or absolute tumor size >4 cm) [4].

However, recent retrospective long-term series have shown how increased initial growth rate did not impact on overall survival outcomes. In fact, no (<1 mm per year), low (1–<5 mm per year), moderate (5–10 mm per year), and high (>10 mm per year) growth groups presented similar overall survival rates ($p=0.4$) [5]. These data are in line with a recent analysis from cancer-specific survival which found that most SRMs with significant growth rate variability in the first 6 months on AS do not always

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demonstrate persistently elevated growth rates and commonly have positive outcomes with continued follow-up and repeat imaging. Clinically relevant progression definitions remain to be elucidated.

Percutaneous renal mass biopsy allows for patient stratification. SRM biopsies were reported diagnostic in up to 80% of patients with a minimal risk of major complications. On the current literature, less than 30% of patients on AS had a biopsy proven RCC, a key point in the management of SRM that needed to be addressed in the future [6]. Moreover, pathology might aid to tailor surveillance imaging schedules since a significant difference in growth and progression among different RCCs [7].

Quality of life (QoL) of patient on AS also requires maximal attention. QoL of patients undergoing immediate intervention versus AS has also been assessed on DISSRM registry. Patients undergoing immediate intervention had higher QoL scores at baseline, specifically for physical health. The perceived benefit in physical health persisted for at least 1 year following intervention; however, mental health, which includes domains of depression and anxiety, was not adversely affected while on AS [8].

Looking forward, the main concern is risk stratification either at diagnosis or during follow-up. RCC biomarkers remain on their infancy as they are still not ready for prime time. SRM biopsy aids on decision making, but it still lacks power of discrimination. The lack of stratification precludes also tailored follow-up schedules. Currently not evidence-based schedules are suggested at guideline publications, only expert statements. The future of AS holds a combination of clinical, imaging, and biological tools to help tag decisions on the right time without jeopardizing outcomes. The main goal of treatment strategies should include weighing patient-specific prognosis relative to their competing health risks and their QoL status.

In summary, AS is defined as initial observational management for SRM including the monitoring of renal tumor size. Long-term registries showed proof of oncological safety of AS for SRM. AS follow-up protocols commonly include enhanced abdominopelvic computed tomography scan or renal ultrasound. Progression is defined as a linear growth rate greater than 0.5 cm per year, diameter greater than 4 cm, or presence of metastasis.

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Conflicts of interest

The authors declare no conflict of interest.

References

[1] Volpe A, Panzarella T, Rendon RA, Haider MA, Kondylis FI, Jewett MAS. The natural history of incidentally detected small renal masses. Cancer 2004;100:738—45.
[2] Siu W, Hafez KS, Johnston WK, Wolf JS. Growth rates of renal cell carcinoma and oncocytoma under surveillance are similar. Urol Oncol 2007;25:115—9.
[3] Finelli A, Cheung DC, Al-Matar A, Evans AJ, Morash CG, Pautler SE, et al. Small renal mass surveillance: histology-specific growth rates in a biopsy-characterized cohort. Eur Urol 2020;78:460—7.
[4] Rebez G, Pavan N, Mir MC. Available active surveillance follow-up protocols for small renal mass: a systematic review. World J Urol 2021;39:2875—82.
[5] McIntosh AG, Ristau BT, Ruth K, Jennings R, Ross EE, Smaldone MC, et al. Active surveillance for localized renal masses: tumor growth, delayed intervention rates, and >5-yr clinical outcomes. Eur Urol 2018;74:157—64.
[6] Mir MC, Capitanio U, Bertolo R, Ouzaid I, Salagierski M, Kriegmair M, et al. Role of active surveillance for localized small renal masses. Eur Urol Oncol 2018;1:177—87.
[7] Ball MW, An JY, Gomella PT, Gautam R, Ricketts CJ, Vocke CD, et al. Growth rates of genetically defined renal tumors: implications for active surveillance and intervention. J Clin Oncol 2020;38:1146—53.
[8] Pierorazio P, McKiernan J, Allaf M. 633 Quality of life on active surveillance for a small renal masses versus immediate intervention: interim analysis of the dissrm (delayed intervention and surveillance for small renal masses) registry. J Urol 2013; 189:e259. https://doi.org/10.1016/J.JURO.2013.02.185.

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