Expectant management in genitourinary malignancies (prostate, bladder, kidney)

Better health awareness, access to healthcare and an improvement in diagnostic tests has led to a significant increase in the early detection and diagnosis of localised urological cancers. Expectant management or active surveillance (AS) is used in localised urological cancers and defined as the initial monitoring of tumour size and or grade, with delayed intervention only in tumours demonstrating clinical progression.

The AS of prostate cancers involves regular prostate specific antigen (PSA) blood tests, combined with intermittent biopsy and/or imaging, whereas bladder cancer surveillance involves regular flexible cystoscopy +/- biopsy and for kidney cancer this requires serial abdominal imaging with ultrasound, CT or MRI.

Whilst AS can prevent the overtreatment of low-risk disease and reduces the side effect burden of radical treatment (such as for example incontinence and impotence after radical prostatectomy), AS uptake remains suboptimal in many healthcare settings. However, conversely, some patients recommended AS may have been under-staged or under-sampled on biopsy, therefore robust AS guidelines to risk stratify patients are required.

This special series has therefore focused on the current status of AS in genitourinary malignancies, whilst highlighting the gaps for future clinical research.

Global AS protocols for prostate cancer are heterogeneous by virtue of the populations that they serve and the healthcare systems within which they exist. Shill *et al.* conducted a narrative review of recently published data, including 13 AS cohorts (1). Differences were noted in both inclusion criteria and follow-up strategies. Nevertheless, the data collected from these cohorts suggest AS is a safe approach for men with low-volume, indolent prostate cancer. However, further research is required to safely assess the long-term outcomes of an expanded inclusion criteria to benefit a subset of men with favourable intermediate-risk prostate cancer.

In acknowledgement of the heterogeneity in AS protocols, a global initiative has been established to facilitate comparisons. The Movember Foundations' GAP3 cohort was used by Crump *et al.* to test the influence of prostate biopsies on Patient-Reported Outcome (2) Measures (PROMs); erectile and urinary function. Using data from >700 patients from three different cancer centres, it was concluded that repeated biopsies as part of an AS protocol did not have a significant effect on urinary function, but did on erectile function. Whilst this indicates that post biopsy quality of life (QoL) needs to be discussed with patients when discussing AS as a management option, it also highlights the need to better understand this association by further investigating the impact of different types of biopsies (e.g., transrectal *vs.* transperineal), which is not captured as part of the GAP3 dataset. Moreover, these PROMs were only available in 3 of the 27 centres included in GAP3.

Beckmann *et al.* further investigated the use of AS for prostate cancer by aiming to understand reasons for non-adherence (3). Semi-structured interviews were conducted with 12 men from diverse socio-cultural backgrounds who had dropped out of AS without signs of disease progression. In line with the suggestions of Crump *et al.*, the key to enhancing long-term adherence to AS is effective communication aimed at building trust in patient-clinician relationships, enabling shared decision-making, along with structured information and support.

In summary, Prof. Roobol explored how the discoveries of the last 5 years may change the future of AS (4). Her narrative describes how multi-parametric MRI, targeted fusion biopsies, multivariable risk stratification nomograms and the introduction of Gleason grade groups delivers on a dynamic risk prediction technique that can be incorporated into future AS management strategies capable of achieving a balance between the burden of monitoring and the risk of disease progression.

An overview of current AS practices for bladder cancer was provided by Russell *et al.*, which as in prostate cancer concluded that there is no universally accepted protocol for endoscopic follow-up of patients with non-muscle invasive bladder cancer (5). Moreover, there is no robust guidance relating to the cystoscopic monitoring of bladder cancer patients who have undergone chemoradiation for muscle invasive bladder cancers.

In a systematic review, Nayak *et al.* found that the QoL of patients with non-muscle invasive bladder was poorly documented, concluding that a specific tool was needed to measure QoL in order to assess, understand and manage their burden of disease (6). The EORTC Quality of Life Group is currently in the process of updating and validating their existing QoL tools for non-muscle invasive and muscle invasive bladder cancer, which will in future hopefully address some of these concerns (7).

With respect to the surveillance protocols for bladder cancer, developments in new biomarker discoveries have been slower than in the prostate cancer setting. Humayun-Zakaria *et al.* reviewed the changing trends in DNA, RNA, or proteins as diagnostic urinary biomarkers over a period of 5 decades (1970–2020) and found that since 2000 the proportion of articles describing protein biomarkers has fallen to 40%, and DNA and RNA studies have increased to 32% and 28%, respectively (8). They optimistically hypothesise that, following thorough validation, a clinically useful detection test for bladder cancer based on a panel of DNA or RNA markers could become a reality within 5–10 years.

In respect to kidney cancer, Wei Cui and Sullivan presented an overview of current AS practices (9). This narrative demonstrated that AS is being applied worldwide with large similarities for selection criteria and surveillance strategies. However, the rate of renal mass biopsy and of delayed intervention through the use of AS varied significantly between studies, suggesting the diagnostic pathway for small renal masses and decision making whilst on AS vary greatly.

A short systematic review by Beyer *et al.* further investigated what factors influence patients' views on treatment decision-making in localised kidney cancer (10). It highlights the complexity of decision-making from the patient's perspective. They recommended that factors influencing the treatment decision making process (e.g., patient-physician interaction, information, risk perception) warrant further investigation to increase adherence to AS and improve patient satisfaction with this management strategy.

Whilst the above findings report on three different types of cancers, it is also interesting to note their similarities in respect to the following issues: heterogeneity in selection criteria and follow-up strategies, impact on quality of life, and the decision-making process. However, the future appears brighter in all urological tumour groups, where AS protocols are able to employ new diagnostic technology and harness new biomarker discoveries.

We would like to conclude this editorial by highlighting two other important components of this special series:

- The need for a research methodology to improve the acceptability of long-term surveillance for cancers (11);
- The need for core outcome sets in urological cancer research (12).

These two reports focus on the importance of multidisciplinary research. A mixed methods public engagement approach is optimal when answers lie in the outcomes, perceptions, views and experiences of both patients and healthcare professionals (11). Moreover, the heterogeneity in outcome reporting is problematic for urology cancer research and decision-making at many levels. Hence, with this special series we would also like recommend that interested researchers work together on a core outcome set for genitourinary cancers AS, as described by MacLennan (12). This methodology is well developed and will help reduce the inconsistencies and variability of outcome reporting into research on AS.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Translational Andrology and Urology*, for the series "Expectant Management in Genitourinary Malignancies (Prostate, Bladder, Kidney)". The article did not undergo external peer review.

Conflicts of Interest: The authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/

tau-21-453). The series "Expectant Management in Genitourinary Malignancies (Prostate, Bladder, Kidney)" was commissioned by the editorial office without any funding or sponsorship. Drs. Van Hemelrijck and Kinsella served as the unpaid Guest Editors of the series. Dr. Kinsella reports no honorariums or consulting fees received in the last 12 months, but Astellas, Janssen and Koelis for lectures and conference preparation only. The authors have no other 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. Shill DK, Roobol MJ, Ehdaie B, et al. Active surveillance for prostate cancer. Transl Androl Urol 2021. doi: 10.21037/tau-20-1370
2. Crump RT, Remmers S, Van Hemelrijck M, et al. Using the Movember Foundation's GAP3 cohort to measure the effect of active surveillance on patient-reported urinary and sexual function—a retrospective study in low-risk prostate cancer patients. Transl Androl Urol 2021. doi: 10.21037/tau-20-1255
3. Beckmann K, Cahill D, Brown C, et al. Understanding reasons for non-adherence to active surveillance for low-intermediate risk prostate cancer. Transl Androl Urol 2021. doi: 10.21037/tau-20-1254
4. Roobol MJ. Active surveillance for prostate cancer—will the discoveries of the last 5 years change the future? Transl Androl Urol 2020. doi: 10.21037/tau-20-1321
5. Russell B, Kotecha P, Thurairaja R, et al. Endoscopic surveillance for bladder cancer: a systematic review of contemporary worldwide practices. Transl Androl Urol 2021. doi: 10.21037/tau-20-1363
6. Nayak A, Cresswell J, Mariappan P. Quality of life in patients undergoing surveillance for nonmuscle invasive bladder cancer—a systematic review. Transl Androl Urol 2021. doi: 10.21037/tau-20-1333
7. Fox L, Rammant E, Van Leeuwen M, et al. First step of the Update and Validation of the EORTC quality of life questionnaires for bladder cancer: A Literature Review (2021). Poster presentation at the UK PROMs Research Conference, 16-17 June.
8. Humayun-Zakaria N, Ward DG, Arnold R, et. Trends in urine biomarker discovery for urothelial bladder cancer: DNA, RNA, or protein? Transl Androl Urol 2021. doi: 10.21037/tau-20-1327
9. Cui HW, Sullivan ME. Surveillance for low-risk kidney cancer: a narrative review of contemporary worldwide practices. Transl Androl Urol 2021. doi: 10.21037/tau-20-1295
10. Beyer K, Barod R, Nicol D, et al. Factors that influence patients' views on treatment decision-making in localised kidney cancer. Transl Androl Urol 2020. doi: 10.21037/tau-20-1317
11. Kinsella N, Van Hemelrijck M. The need for research methodology to improve acceptability of long-term surveillance for cancer. Transl Androl Urol 2020. doi: 10.21037/tau-20-1278
12. MacLennan S, Williamson PR. The need for core outcome sets in urological cancer research. Transl Androl Urol 2020. doi: 10.21037/tau-20-1323

Mieke Van Hemelrijck

Netty Kinsella

Mieke Van Hemelrijck[1]
[1]*Translational Oncology & Urology Research (TOUR), School of Cancer and Pharmaceutical Sciences, King's College London, London, UK.*
(*Email: mieke.vanhemelrijck@kcl.ac.uk*)
Netty Kinsella[2,3]
[2]*The Royal Marsden Hospital, London, UK;* [3]*Translational Oncology & Urology Research (TOUR), School of Cancer and Pharmaceutical Sciences, King's College London, London, UK.*
(*Email: netty.kinsella@rmh.nhs.uk*)
Submitted May 13, 2021. Accepted for publication May 30, 2021.
doi: 10.21037/tau-21-453
View this article at: http://dx.doi.org/10.21037/tau-21-453

Cite this article as: Van Hemelrijck M, Kinsella N. Expectant management in genitourinary malignancies (prostate, bladder, kidney). Transl Androl Urol 2021;10(6):2715-2718. doi: 10.21037/tau-21-453