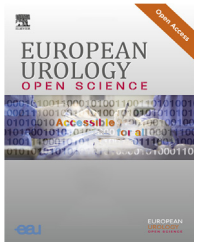
available at www.sciencedirect.com
journal homepage: www.eu-openscience.europeanurology.com



European Association of Urology

Letter to the Editor

Re: Manolis Pratsinis, Christian Fankhauser, Katerina Pratsinis, et al. Metastatic Potential of Small Testicular Germ Cell Tumors: Implications for Surveillance of Small Testicular Masses. Eur Urol Open Sci 2022;40:16–18

Should We Be Afraid of Surveillance? Clinically Meaningful Reasons Why Offering Surveillance for Incidentally Detected Small Testicular Masses Remains a Safe Approach

We read with great interest the article by Pratsinis et al. [1] regarding a cohort of 849 patients who underwent orchiectomy for a malignant germ cell tumor and their specific analysis for masses <10 mm. Among the 25 such masses, five presented with metastases and two cases with initially localized disease experienced relapse. The authors conclude that these data "raise the question of whether active surveillance for small testicular masses is safe."

We would like to respectfully share our thoughts on issues regarding this conclusion and our perspective on surveillance for small testicular masses (STMs). First, we feel it is unfair to examine a cohort of patients, all of whom underwent orchiectomy and all for malignant germ cell tumors, and draw conclusions about surveillance of undifferentiated STMs.

Patients who underwent orchiectomy did so for a reason: either their surgeon was concerned or they were concerned about the malignant potential of their testicular mass. This concern may have come from the presence of elevated tumor markers, lesion growth on serial ultrasound, or certain lesion characteristics [1]. To assume that this highly selected set of STMs can be extrapolated to the behavior of all STMs is inaccurate.

The perception that all incidentally found STMs are malignant has shifted in the last decade [2–5]. Previously, every testicular mass, regardless of size, characteristics, or tumor marker status, was treated with radical orchiectomy on the understanding that 95% of such masses were malignant [2]. However, we have learned that the malignancy rate for these STMs is much lower than traditionally thought and could be as low as 13–21% [2–5].

Assessing the safety of STM surveillance is best done using a surveillance series. Two large retrospective series have done so. The first study, by Toren et al. [3], examined 46 patients with an incidentally detected impalpable STM of $\leq$1 cm. Three patients (7%) underwent immediate surgery, but the remainder were observed. In five additional cases (11%) the mass was excised after a period of observation. In total, only 1/46 lesions (2%) were found to be malignant during the study [3]. Bieniek et al. [4] updated follow-up for the Toren series and added a further 81 patients meeting similar criteria. Among the 120 patients in the study, 18 underwent orchiectomy, of whom six (33% of the orchiectomy cases but 5% of the total cohort) had malignant pathology. Thus, 85% of the patients remained on surveillance at follow-up [4]. Finally, a recent systematic review including 11 studies confirmed that 229 patients (81%) with an incidentally diagnosed nonpalpable STM of $\leq$2 cm were found to have a benign tumor [5].

Our second issue is that one-third of the patients in the study by Pratsinis et al. had elevated tumor markers [1]. Of the seven patients they described with metastatic disease, five (71%) had elevated markers. No one would advocate surveillance for patients with STMs and elevated tumor markers, so it is biased to draw conclusions about a de novo marker-negative STM population. In a similar vein, the median tumor size in the study was 8 mm [1]. This is substantially larger than the size observed by Toren et al. (4.3 mm) [3] and Bieniek et al. (4.1 mm) [4], again speaking to the fact the cohort analyzed by Pratsinis et al. should not be extrapolated to all newly presenting STMs.

Similar unintentional errors of bias occurred early in the adoption of surveillance for low-grade prostate cancers and small renal masses: series of patients with surgically excised specimens were examined and a subset who would have met surveillance criteria were identified, with demonstration that they had adverse pathology or behavior [6–8]. Subsequent dedicated surveillance series for both kidney and prostate cancers have demonstrated that surveillance is safe for appropriately selected patients [9,10].

Unfortunately, no features of STM presentation have been found to date for accurate discrimination between benign and malignant masses. Lesion size, growth rate, calcification, and vascularity on ultrasound have all been described, but reliable discrimination has not been proved for any of these parameters [11,12]. Until we have the means to differentiate which tumors are malignant, a valid approach would be to surgically resect these STMs. However, we feel that initial surveillance of STMs with negative markers is safe, in part because of the low rate of malignancy and the even lower rate of metastases from those small lesions that are actually malignant. A number of questions remain unanswered. What is the optimal

https://doi.org/10.1016/j.euros.2022.08.022

follow-up protocol? For how long should these patients be followed? And what are the triggers for surgical intervention?

As a final remark, it should be noted that despite the increase in the incidental detection of STMs, most physicians are still reluctant to offer surveillance to these patients, which makes it more difficult to prospectively recruit patients for surveillance clinical trials. Moreover, while we agree that we should not base our decisions on tumor size alone, we believe that for all of us researchers in this field it should become a priority to start prospectively recruiting patients with STMs into surveillance protocols and start using biomarkers or imaging features to help discriminate which patients benefit from immediate surgery and which patients can safely opt for surveillance.

Conflicts of interest: The authors have nothing to disclose.

References

[1] Pratsinis M, Fankhauser C, Pratsinis K, et al. Metastatic potential of small testicular germ cell tumors: implications for surveillance of small testicular masses. Eur Urol Open Sci 2022;40:16–8.
[2] Goldberg H, Klaassen Z, Chandrasekar T, Fleshner N, Hamilton RJ, Jewett MAS. Germ cell testicular tumors—contemporary diagnosis, staging and management of localized and advanced disease. Urology 2018;125:8–19.
[3] Toren PJ, Roberts M, Lecker I, Grober ED, Jarvi K, Lo KC. Small incidentally discovered testicular masses in infertile men—is active surveillance the new standard of care? J Urol 2010;183:1373–7.
[4] Bieniek JM, Juvet T, Margolis M, Grober ED, Lo KC, Jarvi KA. Prevalence and management of incidental small testicular masses discovered on ultrasonographic evaluation of male infertility. J Urol 2018;199:481–6.
[5] Ory J, Blankstein U, Gonzalez DC, et al. Outcomes of organ-sparing surgery for adult testicular tumors: a systematic review of the literature. BJU Compass 2021;2:306–21.
[6] Choo R, Klotz L, Danjoux C, et al. Feasibility study: watchful waiting for localized low to intermediate grade prostate carcinoma with selective delayed intervention based on prostate specific antigen, histological and/or clinical progression. J Urol 2002;167:1664–9.
[7] Inoue LY, Trock BJ, Partin AW, Carter HB, Etzioni R. Modeling grade progression in an active surveillance study. Stat Med 2014;33:930–9.
[8] Kunkle DA, Crispen PL, Li T, Uzzo RG. Tumor size predicts synchronous metastatic renal cell carcinoma: implications for surveillance of small renal masses. J Urol 2007;177:1692–7.
[9] Klotz L, Vesprini D, Sethukavalan P, et al. Long-term follow-up of a large active surveillance cohort of patients with prostate cancer. J Clin Oncol 2015;33:272–7.
[10] 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.
[11] Brown D, Tsampoukas G, Petkov E, Aldin Z, Moussa M. The role of radiological surveillance in the conservative management of incidental small testicular masses: a systematic review. Arab J Urol 2021;19:179–85.
[12] Scandura G, Verrill C, Protheroe A, et al. Incidentally detected testicular lesions <10 mm in diameter: can orchidectomy be avoided? BJU Int 2018:575–82.

Julian Chavarriaga *
Robert Hamilton

Division of Urology, Department of Surgery, Princess Margaret Cancer Centre, Toronto, Canada

*Corresponding author. Division of Urology, Department of Surgery, Princess Margaret Hospital Cancer Centre, Toronto, Canada.
E-mail address: julian.chavarriaga@uhn.ca (J. Chavarriaga).

August 5, 2022