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The Next Generation of Prostate Cancer Risk Calculators

Thomas Hermanns *, ***Cédric Poyet***

Department of Urology, University Hospital Zürich, University of Zürich, Zürich, Switzerland

Multivariable prediction models are superior to conventional decision-making based solely on prostate-specific antigen (PSA) testing or digital rectal examination (DRE) in predicting the outcome of prostate biopsies [1]. Therefore, several prostate cancer risk calculators (RCs) have been developed with the aim of minimizing the number of unnecessary biopsies and reducing overdetection and overtreatment of insignificant prostate cancer. External validations have confirmed the utility of several RCs, and thus their use in clinical practice is increasingly recommended [2].

However, the performance of current RCs is still suboptimal, as evidenced by significant variation in RC performance in different patient cohorts [3]. Strategies to improve current RCs include recalibration of existing RCs to adjust for local cohort characteristics [4]. Using data from contemporary clinical cohorts to create novel RCs could be another option for building more accurate up-to-date decision aids. Including biomarker data or results from multiparametric magnetic resonance imaging (mpMRI) are further ways to potentially improve RC performance [5].

In this issue of *European Urology*, Radtke and colleagues [6] evaluate whether RCs using a combination of clinical parameters and mpMRI data (ie, Prostate Imaging-Data and Reporting System [PI-RADS] v.1.0 score) improves the prediction of significant prostate cancer compared to PI-RADS score alone or RCs based only on clinical parameters.

They used prospectively collected data for their patient series of 1015 men (660 biopsy-naïve and 355 prebiopsied men) who underwent mpMRI before combined fusion targeted biopsy and transperineal systematic saturation biopsies to develop a risk model (RM) that included clinical parameters and PI-RADS scores. Clinical parameters evaluated for model inclusion were those already used for the RCs of the Dutch arm of the ERSPC (RC3 for biopsy-naïve men and RC4 for prebiopsied men). Furthermore, they compared the performance of their novel RM with the performance of the original ERSPC RC3 and RC4, of the ERSPC RCs refitted to their cohort characteristics, of a combination of the original ERSPC RCs with PI-RADS scores, and of the PI-RADS score alone.

Performance of their novel RM was good, with an area under the receiver operating characteristic curve (AUC) of 0.83 for biopsy-naïve men and 0.81 for prebiopsied men. Furthermore, both models showed the highest rate of reduction in unnecessary biopsies in decision analyses. However, the performance of the original ERSPC RCs with PI-RADS scores was comparable to their novel RM (AUC 0.84 for biopsy-naïve and 0.78 for prebiopsied men). Both models including clinical and PI-RADS data were superior to the models including only clinical data (ERSPC RCs and refitted ERSPC RCs) or PI-RADS score alone.

The authors are to be congratulated for their effort to create a contemporary prostate cancer RC that includes mpMRI data and is based on a current patient cohort undergoing modern biopsy procedures. This is an important step towards more precise risk prediction with the goal of further reducing unnecessary biopsies and overdetection and overtreatment of insignificant prostate cancer.

mpMRI is unique compared to other approaches as it covers two important aspects that are useful for prostate cancer risk assessment and diagnosis. First, it can identify men who are likely or unlikely to have prostate cancer by detecting or not detecting suspicious lesions in the prostate. Second, it can improve the accuracy of prostate biopsies by making cancerous lesions visible and thus targetable.

The utility of these two aspects of prostate MRI has already been investigated. In a recent pilot study, Nam and

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* Corresponding author. Department of Urology, University Hospital Zürich, Frauenklinikstrasse 10, 8091 Zürich, Switzerland. Tel. +41 44 2551111; Fax: +41 44 2554555.
E-mail address: thomas.hermanns@usz.ch (T. Hermanns).

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colleagues [7] showed that prostate MRI as a primary screening test was better in predicting prostate cancer than PSA measurement. In addition, a meta-analysis revealed that prostate MRI and subsequent MRI-targeted prostate biopsies improved the diagnostic accuracy for significant prostate cancer [8]. More recently, Ahmed and colleagues [9] showed in a prospective multicenter study that mpMRI, used as a triage test for prostate biopsy in men presenting with elevated PSA, improved the accuracy of prostate biopsies for significant prostate cancer, and allowed a quarter of all biopsies to be avoided. Given these findings, it seems more than reasonable to incorporate mpMRI results into prostate cancer RCs.

However, what price are we willing to pay for improved risk prediction? Should mpMRI become a standard investigation for all men with elevated PSA or a suspicious DRE? The use of this approach would take advantage of both of the above-mentioned benefits of mpMRI. However, although fewer unnecessary biopsies would be performed and fewer men with significant prostate cancer would be missed, a relevant number of men would undergo unnecessary mpMRI, which is a time-consuming and costly investigation.

Should we not instead evaluate a stepwise and probably more cost-effective work-up for our patients and health systems? Alberts and colleagues [10] have recently shown that half of all mpMRI scans could be avoided in men with a previous biopsy if RC-based patient selection was performed. If upfront selection recommends further work-up, MRI findings could still be incorporated into risk prediction models to decide whether to perform a biopsy or not.

The results presented in the current study nicely illustrate the benefit of improved risk prediction by addition of mpMRI results. However, given the comparable performance of the novel RM and the RM based on the ERSPC RCs and PI-RADS data, it remains unclear which RM should be used in clinical practice. External validation of the two RMs would probably help to determine the preferred model for risk prediction. However, the current study does not give answer whether we should simply add PI-RADS data to a well-validated and robust RC that is based on historical data (ie, ERSPC RC) or if it would be better to use novel RCs, which include mpMRI data and are based on contemporary clinical but rather small patient cohorts.

The work by Radke and colleagues shows us how important it is to work on the development of next-generation prostate cancer prediction models based on contemporary cohorts, up-to-date biopsy regimens, and promising novel parameters. It should motivate us to support large-scale multi-institutional databases (eg, of the Prostate Biopsy Collaborative Group). These projects are most likely to provide data robust enough to determine the best pathways and optimal RMs for prostate cancer risk prediction in the future.

Conflicts of interest: The authors have nothing to disclose.

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