Letters

COMMENT & RESPONSE

In Reply We thank Dr Bianchi and colleagues for reiterating the importance of external validation for any prediction tool. Decision support tools such as clinical nomograms are important components of individualized decision making and patient care. Currently, many nomograms are available for different clinical scenarios. Decision making in the prebiopsy setting is of utmost importance because suboptimal decisions can lead to unnecessary biopsies and ultimately overtreatment. Patients with clinically significant prostate cancer, however, need to undergo a biopsy procedure and receive treatment according to their risk profile.

We acknowledge that controversy surrounds the definition of clinical significance and that current prediction tools are limited. Besides Gleason score or, more recently, grade group, several staging parameters such as extraprostatic extension, seminal vesicle invasion, and lymph node involvement correlate with cancer-specific survival. However, Gleason score remains the strongest predictor of adverse outcome. Staging parameters, on the other hand, cannot be determined with high accuracy by either digital rectal examination or multiparametric magnetic resonance imaging.[1] There are convincing data demonstrating that patients with Gleason 6 prostate cancer rarely develop metastases or die of prostate cancer.[2] We therefore defined presence of any Gleason pattern 4 or higher as clinically significant prostate cancer in our analysis,[3] although we are aware that interreader variability among pathologists and mismatch of biopsy and final Gleason score are important limitations. Hopefully, in the future genomic markers will add predictive value to the Gleason score.

The point that prediction tools need to be tested across broad populations of patients is valid. Clinical nomograms based on logistic regression perform best in patient populations with similar demographic characteristics and a priori probabilities of outcome variables.[4] Our training cohort resembles the US population in the prostate-specific antigen screening era. Although the validation cohorts did not differ from the training cohort with respect to age, ethnicity, and family history, they did differ in history of prior negative systematic biopsy results, prostate volumes, biopsy Gleason scores, and Prostate Imaging Reporting and Data System (PI-RADSv2) categories. Moreover, while the training cohort was scanned at a research institution with a consistent workflow and single dedicated prostate radiologist, scans at the second validation cohort were read by 7 different radiologists in a more clinically oriented daily routine. Our model remained robust despite these differences. However, it is undeniable that the ultimate value of a prediction tool can only be determined after it has been tested in many different populations of patients.

Sherif Mehralivand, MD
Joanna Shih, PhD
Baris Turkbey, MD

Author Affiliations: National Cancer Institute, National Institutes of Health, Bethesda, Maryland (Mehralivand); Division of Cancer Treatment and Diagnosis: Biometric Research Program, National Cancer Institute, National Institutes of Health, Rockville, Maryland (Shih); National Cancer Institute, Bethesda, Maryland (Turkbey).

Corresponding Author: Baris Turkbey, MD, National Cancer Institute, 9000 Rockville Pike, Bethesda, MD 20892 (ismail.turkbey@nih.gov).

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