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Letter to the Editor

Re: Fatemeh Seyednasrollah, Mehrad Mahmoudian, Liisa Rautakorpi, et al. How Reliable are Trial-based Prognostic Models in Real-world Patients with Metastatic Castration-resistant Prostate Cancer? Eur Urol. 2017;71:838–40

Clinical Utility of Trial-estimated Prognostic Models

Seyednasrollah et al [1] posed a relevant question in their recent Research Letter. Once shown to be reliable enough in real-world clinical data, trial-based prognostic models could provide practical guidance in tailoring treatment strategies for patients with metastatic castration-resistant prostate cancer (mCRPC). Unfortunately, the letter missed several important points about these models and their proper application to predict overall survival of mCRPC patients, which may lead to confusion regarding their practical utility in clinical decision-making, and should therefore be addressed.

Seyednasrollah et al [1] took the open-source implementations of the three best-performing models from the recent prostate cancer DREAM challenge [2]. It should be obvious that the use of others' models without consulting the model developers will lead to suboptimal results when the models are applied to different types of patient data. For instance, as mentioned in the abstract of the DREAM challenge paper [2], aspartate aminotransferase (AST) was shared by the top-performing models as one of the most important prognostic biomarkers. However, AST was missing in this relatively limited real-world data set, along with many other key markers such as lactate dehydrogenase. To give a more balanced view of the models' performance, it would be important to understand and acknowledge the effect of the absence of these key predictors that are rarely measured in real-world prostate cancer patients.

To deal with the missing clinical variables, Seyednasrollah et al applied quite crude procedures that cannot really compensate for this lack of clinical measurements. Missing values for many laboratory tests were simply imputed using median values, even though it is known that such a procedure performs poorly in heterogeneous data sets. For instance, in our top-performing prognostic model (Team 1), we implemented and made available an improved model-based imputation method that led to the most accurate predictions in the challenge [2]. It remains unclear why Seyednasrollah et al chose to use simple median imputation instead in their closed-data results [1]. Further confusion was introduced by simply assuming that all the patients had bone lesions, even though this information was actually missing in this real-world patient data set.

The real-world patient cohort used by Seyednasrollah et al to evaluate the three prognostic models was collected on the basis of the following inclusion criteria: clinical diagnosis of prostate carcinoma (ICD10:C61), a prescription for antiandrogen therapy (ACT code G03HA), and chemotherapy with docetaxel as first-line treatment; patients with other malignancies were excluded, resulting in 289 patients. Compared to the standardized inclusion criteria of the clinical trials used in the DREAM challenge to estimate the best-performing prognostic models (histologically or cytologically confirmed prostate adenocarcinoma; metastatic disease; progressive disease while receiving hormonal therapy or after surgical castration; effective castration), it can be argued that this real-world cohort represents a rather heterogeneous patient subpopulation, making it less attractive for the application of mCRPC-specific prognostic models.

In conclusion, we commend Seyednasrollah et al for raising this important question and showing that even such suboptimal application of the trial-estimated prognostic models led to surprisingly high predictive performance for these real-world patient data, especially at the clinically important early time points. However, owing to the above issues, their letter falls short in fully addressing the question posed; instead, we are concerned it raises confusion and more questions regarding the correct application of prognostic models to real-world patient data. Better-designed studies in much larger and better-characterized mCRPC cohorts will be needed to reveal robust prognostic factors and models to help in the treatment of mCRPC patients.

Conflicts of interest: Teams led by Tero Aittokallio and Laura Elo participated the same prostate cancer DREAM challenge.

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