EDITORIAL

Clinical Research

Nomograms in PCa: where do we stand

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Prostate cancer management represents a fertile field for the development of predictive models and nomograms. The development of predictive models, as stated by Steyeberg et al., requires a certain number of steps including: data inspection, coding of predictors, model specification and estimation, evaluation of model performance, internal validation and model presentation [1]. Thereafter the model should be externally validated. The keys to develop a good nomogram are efficacy, availability and easy of use.

In this issue, Fiori et al. developed a clinical nomogram to predict LNI in patients undergoing mp-MRI and targeted biopsies only. The authors included 461 patients in a nomogram including the following variables: DRE, PI-RADS, seminal vesicle invasion, PSA and worst GS at I and II target lesions. According to their results the nomogram presented a predictive accuracy of 0,74 and they established a 60-points cut-off corresponding to a risk of LNI of 7%. The authors have the merit of exploring an interesting area of research using a very accurate methodology. However, the study presents some limitations common to the available nomograms.

In the past decade several models have been proposed in the diagnosis and management of PCa however most of them lack external validation and remain poorly used (Table 1). In the available literature there are over 100 nomograms however in the EAU guidelines only 16 nomograms are recommended and very few of them are used by clinicians [2–6]. The development of a nomogram should be based ideally on randomized clinical trials or at least on prospective data in large cohorts to minimize sources of bias. Moreover, when selecting a nomogram clinicians should always consider that the nomogram will probably apply to the population in exam therefore external validation and calibration is essential to guarantee the predictive abilities of the model [7].

Applicability should be always in mind when developing a predictive model. Nowadays there is an ongoing debate on whether patients should undergo only targeted biopsies or should perform standard biopsies as well [8]. To date EAU guidelines only allow targeted biopsies alone in a second biopsy setting while first set biopsies still require standard random biopsies. Growing evidence is supporting the use of only targeted biopsies to reduce complications and diagnosis of indolent tumors however evidence is still needed to achieve this goal. Moreover, some authors suggest that avoiding random biopsies may lead to an increase in upstaging and upgrading events [8].

The availability of the nomogram is of outmost importance. Graphic nomograms are not always available specially if published in non-open access journals while web-based and mobile phone apps may be easier to access. The advances in technology have promoted the use of electronic models which have pros and cons. Web based and mobile phone apps have the advantage of having user friendly interfaces, may include explanations and enable clinicians to use only the available data on the patient to calculate the risk. On the other hand, some of these models are not free, some may be based on poor evidence and some clinicians may not have access to them. Although we are moving toward a web-based medicine to date there is no evidence confirming the superiority of web-based models vs graphic models.

Important questions remain unanswered: Do nomograms improve outcomes? What is the effect of nomograms on patients care?

The clinical utility of nomograms is unclear and the available literature does not answer these questions. Over 22 studies comparing nomograms to clinical judgement only 59% of the studies showed a superiority of the nomogram over clinicians judgement based only on AUC data. However, superiority of AUC does not imply a superiority in patients management. A study evaluating the role of nomograms in PCa showed that under 30% of probability threshold the nomogram was harmful for the patient. Hence, nomograms can lack clinical utility despite having good performance, and assessing whether a nomogram improves patient and physician satisfaction, quality of life, and oncologic outcomes is often ignored. It also follows that if the AUC of nomogram A is greater than the AUC of nomogram B, it does not mean nomogram A is more clinically useful. If clinical utility of nomograms is uncertain we wondered how cited are nomograms in the literature. As a matter of fact, 131 nomograms on PCa are cited more than 100 times according to Scopus highlighting an important role of nomograms in the academic careers of authors. Overall medicine is moving through a personalized patients centered medicine and the effect of a poor probability on a patients and families may be deleterious [9]. The impact of nomograms on patients 'expectations is largely unknown and should be part of the evaluation of the clinical usefulness of a nomogram. The advance in technology is moving together with the growing of artificial intelligence models and the genomic/proteomic profiling of patients [10]. In the future, we will probably be able to estimate the exact risk of every single patient based on the available data but more importantly AI models can integrate new data without the need of updating models.

Table 1. Nomograms available in Pubmed and in the EAU guidelines.

	PUBMED	EAU guidelines
PCa Diagnosis	195	1
Lymphnode invasion	96	5
Extracapsular Invasion	64	3
Upgrading	37	1
Survival	240	6

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Notwithstanding all these limitations, some nomograms have a significant role in the decision-making process of PCa patients. Hopefully the implementation of genetic biomarkers and AI will overcome most of the limitations of the current nomograms and open a new era of personalized diagnosis and treatment.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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