Editorial Commentary

UICC and AJCC 8th edition tumor-nodes-metastasis (TNM) classifications for patients treated with radical prostatectomy: reliable but not infallible prognostic tools

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We read with interest the article by Herden and colleagues (1) regarding the validation of the UICC and AJCC 8th edition tumor-nodes-metastasis (TNM) system on a German community-based dataset. In this study, the authors analyzed data derived from the HAROW study (n=2,957), a prospective, non-interventional, health service research study examining various treatment options for patients with localized prostate cancer (≤ cT2c). Within their study, Herden and colleagues selected all patients that underwent radical prostatectomy (RP) (n=1,738, 58.8%) with available pathologic information and follow-up data (n=515). For validation purpose, the authors stratified the patients in either cT1 or cT2, S I (≤ T2a) or S II (T2b/c), and prognostic stage group (PSG) I, PSG IIA, PSG IIB or PSG ≥ IIC according to the TNM classification and World Health Organization (WHO) grading. All groups were compared regarding proportion of organ confined disease (≤ pT2) and extraprostatic extension (≥ pT3) after RP, as well as favorable (≤2) and unfavorable (≥3) WHO grade group, or favorable (≤7a) and unfavorable (≥7b) Gleason Score after RP, respectively. Finally, biochemical recurrence free-survival (BFS) was examined and compared between groups in each classification systems.

The results showed that cT1/cT2 and S I/II subgrouping are feasible to predict a different pT-category and a favorable WHO grade after RP, but failed to predict a different BFS rates. Indeed, no BFS rate differences were found between cT1 and cT2 or SI and SII, after a median follow-up of 31.7 months. Conversely, the authors found statistically significant differences within PSG groups when pathological or BFS end-points were considered.

The main take home message of this study is that the combination rather than singular tumor characteristics may increase the prediction rate of a staging system. In other words, the combined use of TNM and Gleason grade groups performed better than TNM system alone. As the authors mentioned in the study, several models are available in clinical practice for prediction of histological finding (2,3) or survival outcomes (4) after RP. All of them have showed better accuracy when compared with TNM system or singular tumor factors. Indeed, the inclusion of more variables and the use of logistic or Cox-based models provide better discrimination power for predicting models. Nevertheless, we should always keep in mind that a model, even if it is highly accurate, should be also easy to use in the daily practice (5). Multiple input models with logarithmic variables and nomogram-based calculation might discourage the end-user from the routine use of such tool in clinical practice. Consequently, the AJCC 8th with integrated PSG grouping might represent a good compromise between accuracy and feasibility in every-day practice.

The strength of the study is the large sample size and the homogeneity of the HAROW population. Inclusion criteria and study design were also appropriate. On the other hand, the study is affected by a high drop-out rate and a short-follow-up, which might have introduced a selection

bias, as pointed out by the authors. Moreover, hard clinical end-points, such as clinical recurrence or cancer-specific mortality should be preferred over pathological finding or BFS to better discriminate the clinical utility of prognostic system, especially for patients with localized prostate cancer. Additionally, we do believe that the absence of ethnic variability (only Caucasian patients were enrolled) might have affected the results of this study. It is well known that African-American patients are not accurately classified by prostate cancer scores for Caucasian patients (6,7). Last but not least, missing information on surgical margins, seminal vesicle invasion and lymph node involvement are a major limitation, when BFS is observed. Patients with these risk factors in the RP specimen have worse oncologic outcomes (8-11). Moreover, these patients might have received further treatments after RP, resulting in various BFS.

Taken together, the study of Herden *et al.* provides interesting insights in the field of prostate cancer staging. Moreover, it underlies the need of a better staging system, which includes more tumor biological variables, but remains down-to-earth for end-users.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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