PROSTATE CANCER

Independent validation of the five-tier grade group system

Recent proposals to change the way in which prostate cancer is graded to a five-tiered system, rather than by classical Gleason grade, have been validated in a new study published in *BJU Int*.

Although Gleason scores between 2 and 10 can be described histologically, scores <6 are now rarely reported, and studies suggest that Gleason 6 prostate cancer might not be clinically significant. Thus, subsequent alterations to the Gleason system, introduced since it was first proposed in the 1960s, have stratified patients into three risk groups, based on Gleason score 6, 7 or 8–10. However, this system of stratification does not distinguish between Gleason 3+4 and Gleason 4+3 cancers, which have different clinical prognoses, and does not take into account the adverse effect of the presence of Gleason 5 pattern cancer. Thus, in 2013, a team from Johns Hopkins Hospital proposed a new, five-tier model of grade grouping, which classified tumours as Group 1 (Gleason score ≤6), Group 2 (Gleason score 3 + 4 = 7), Group 3 (Gleason 4 + 3 = 7), Group 4 (Gleason score 8) or Group 5 (Gleason score 9–10).

Now, a team from the University of Michigan have validated this system in an independent surgical cohort, with nearly double the median follow-up duration previously studied, to increase the confidence that the newly proposed prostate cancer grade grouping system remains prognostic in an independent dataset with longer follow-up duration. Medical records of 3,715 men who received radical prostatectomy between 1994 and 2013 were reviewed. Biopsy and surgical specimens were assigned a Gleason score, and were then further stratified according to their grade group in the new model. Biochemical-recurrence-free survival (bRFS) was the primary end point, defined as two consecutive serum PSA measurements of <2 ng/ml. Univariable and multivariable Cox regression, as well as Kaplan–Meier analysis, was used to determine the association between the new grade group and bRFS.

Median follow-up duration across the study was 52.7 months, with 5-year bRFS of 94.2%, 89.2%, 73.1%, 63.1% and 54.7% across groups 1–5, respectively ($P < 0.001$), determined using biopsy samples. Hazard ratios (HRs) for biochemical recurrence increased in line with grade group, with HR relative to group 1 of 2.1, 4.8, 6.9, and 10.6 for groups 2–5, respectively. Adjusting for clinical stage, preoperative PSA level, and year of treatment still showed a significant increase in the adjusted HR for biochemical recurrence across the grade groups. Using the grade groupings as determined using radical prostatectomy samples showed a similar pattern, with bRFS for grade groups 1–5 of 96.1%, 93.0%, 74.0%, 64.4% and 49.9%, respectively. “We demonstrate that the new grade grouping system is prognostic both on univariable and multivariable analyses based on the biopsy grade as well as the prostatectomy grade,” lead author Daniel Spratt told *Nature Reviews Urology*.

Area under the curve (AUC) analyses were used to compare the discriminatory power of the new five-tier system with the three-tier Gleason scoring system. AUCs for both biopsy and prostatectomy samples were improved by use of the new system (0.65 versus 0.67 and 0.66 versus 0.72, respectively). The difference was apparent both in men diagnosed and treated before 2005, when the International Society of Urological Pathology update occurred, and after 2005. “We were able to show that the new system has improved discriminatory value for patients graded before 2005, as well as afterwards. Furthermore, the discriminatory value of the new grade grouping system was even higher when used with patients who were originally graded after 2005,” explains Spratt. “Future studies will focus on the impact of the new grade grouping system on more meaningful end points other than biochemical failure, such as distant metastases and prostate-cancer-specific mortality. Furthermore, the system will need to be validated with long-term follow-up in radiotherapy-treated patients, which our group is actively investigating.”

Annette Fenner

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ORIGINAL ARTICLE Spratt, D. E. *et al.* Independent surgical validation of the new prostate cancer grade grouping system. *BJU Int*. <http://dx.doi.org/10.1111/bju.13488> (2016)

FURTHER READING Kim, E. H. & Andriole, G. L. Prostate cancer: A simplified prostate cancer grading system. *Nat. Rev. Urol.* **12**, 601–602 (2015)