A simplified prostate cancer grading system

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Developed nearly 50 years ago, the Gleason scoring system for prostate cancer assigns grades 1–5 based on histologic features and, as prostate cancer can be heterogeneous, a total score representing the sum of the first and second most common patterns is calculated. Together with serum PSA level and tumour stage,1–2 Gleason sum is used for risk stratification and to guide treatment decisions. Concerns regarding the utility of PSA screening have centred on the overtreatment of screen-detected prostate cancer, which might have been a result of misclassification owing to the random nature of conventional biopsy strategies and limitations of the existing Gleason scoring system.3

In a new study, Epstein et al.4 address the latter issue and provide an alternative, simplified prostate cancer grading system that seems to improve risk stratification and, consequently, clinical decision making.

Using biochemical recurrence (BCR) of prostate cancer after treatment as a surrogate end point to define aggressive disease, the authors propose a new five-grade group system that is based on the modified Gleason scoring system. Grade group 1 includes previously described Gleason sum 6 or lower, grade group 2 includes Gleason 3 + 4 = 7, grade group 3 includes Gleason 4 + 3 = 7, grade group 4 includes Gleason sum 8, and grade group 5 includes Gleason sum 9 or higher. When compared with conventional three-tiered risk stratification (low risk, Gleason sum 6 or lower; intermediate risk, Gleason sum 7; high risk, Gleason sum 8 or higher),2 the five-grade group system provided better prediction of BCR, using both biopsy and radical prostatectomy pathology. With biopsy Gleason sum 6 or less (grade group 1) as the referent, multivariate hazard ratios (HR) for BCR were 2.5 (grade group 2), 5.7 (grade group 3), 9.1 (grade group 4), and 13.8 (grade group 5), compared with 3.4 (Gleason sum 7) and 10.3 (Gleason sum 8 or greater) for the traditional Gleason system. Using radical prostatectomy pathology, multivariate HRs for BCR were 1.9 (grade group 2), 5.1 (grade group 3), 8.0 (grade group 4), and 11.7 (grade group 5), compared with 2.7 (Gleason sum 7) and 8.5 (Gleason sum 8 or greater).

The improved risk discrimination seen with the five-grade group system is a direct result of two important changes: firstly, separation of Gleason sum 7 into two distinct risk groups, and secondly, separation of Gleason sum 8 from Gleason sum >9. Previous studies have demonstrated heterogeneity among Gleason 7 prostate tumours, with Gleason 4 + 3 tumours significantly associated with extraprostatic extension, risk of disease progression, risk of metastatic disease, and, ultimately, prostate cancer mortality, compared with Gleason 3 + 4 disease.5 Despite this evidence, traditional classification systems combine all Gleason sum 7 prostate cancer into a single intermediate risk group.2 By dividing Gleason sum 7 into grade group 2 (Gleason 3 + 4) and grade group 3 (Gleason 4 + 3), the authors distinguish this considerable difference in prognosis. Furthermore, they confirm the difference in prognosis between these two groups by demonstrating significant differences in adjusted HRs of BCR after prostatectomy (grade group 3, HR 5.1 versus grade group 2, HR 1.9).

Also, taking into consideration the existing evidence that patients diagnosed with Gleason sum >9 prostate cancer are at a significantly higher risk of metastasis and prostate-cancer-related death than those with Gleason sum 8 prostate cancer,6 the authors separate these patients into grade group 4 (Gleason sum 8) and grade group 5 (Gleason sum >9).

Another potential advantage of the five-grade group system is that of patient perception, which could be as powerful as the objective improvements in prognostic discrimination. Although the change of the lowest risk prostate cancer group from ‘Gleason sum 6’ to ‘grade group 1’ seems one of semantics, the authors assert that this new nomenclature more appropriately conveys to the patient their degree of prostate cancer risk. Studies have established that patient satisfaction during prostate cancer care is strongly influenced by uncertainty and perception of risk.7 Clearly communicating to patients the true extent of danger associated with their diagnosis—essentially that there is no risk of metastatic disease with Gleason sum 6 prostate cancer diagnosed in the modern era—is critical to successfully managing these patients on active surveillance.8
The study is not without limitations, such as the use of BCR as the study end point rather than metastasis or survival. As the existing Gleason system was introduced in 2005, the follow-up period is too short to capture clinical disease recurrence, development of metastases, and disease-specific mortality. The study period of 2005–2014 raises another limitation, as additional modifications made to the Gleason system in 2014 are not reflected in this study. Cribriform architecture found on pathology has been associated with poor clinical prognosis, such that the Gleason system revisions in 2005 reclassified many of these glands from Gleason 3 to Gleason 4. More recent revisions to the Gleason system in 2014 have reclassified all cribriform glands to Gleason 4. Although difficult to anticipate how this change would affect the five-grade group system, the improvement in prognostic discrimination for the Gleason score would likely be reflected in the five-grade group system as well, potentially improving its accuracy even further. Future prospective studies using the five-grade group system will be needed, both to correlate risk of clinical disease progression, metastasis, and prostate-cancer-related death to the grade group assignment, and to demonstrate any improvements in patient understanding of their prognosis and satisfaction with treatment decision making.

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Competing Interests
G.L.A. declares that he is an investigator with Johnson and Johnson, Medivation, and Traxxson, and acts as a consultant for Augmenix, Bayer, Genomic Health, and Myriad Genetics. E.H.K. declares no competing interests.


