

## PROSTATE CANCER THE HIGH-RISK DICHOTOMY

Men with high-risk localized prostate cancer, according to the National Comprehensive Cancer Network (NCCN) criteria, experience highly variable cancer-specific outcomes. Such variability in metastasis-free survival (MFS) and time to biochemical recurrence, for example, hinders patient prognostication and can affect treatment decisions. Now, researchers at Johns Hopkins University argue that dichotomizing these patients into 'high-risk' and 'very-high-risk' subgroups is possible, and might help in counselling and recruiting for trials.

"For the first time, we can define this group of patients into two subgroups of men with very distinct outcomes," explains lead investigator Edward Schaeffer. The researchers interrogated the Johns Hopkins patient database to identify men with NCCN high-risk prostate cancer (Gleason sum 8–10, PSA >20 ng/ml, clinical stage  $\geq$ T3), identifying >750 men treated in the PSA era. They then conducted univariate analyses between 28 possible very-high-risk definitions (including primary pattern 5, multiple NCCN high-risk features and number of biopsy cores with high Gleason sum), looking for associations with metastasis, cancer-specific mortality and all-cause mortality.

The definitions in the highest quartiles for association with MFS and cancer-specific survival were then subject to multivariate analysis, which enabled researchers to determine the best definition of very high risk. They report that patients presenting with primary Gleason pattern of 5,  $\geq$ 5 biopsy cores with Gleason sum 8–10 or those with at least two NCCN high-risk features should be considered to have very-high-risk prostate cancer.

The new subgroup, which comprised 15% of the cohort, included those with particularly poor outcomes. For example, men in the very-high-risk group were at more than threefold risk of cancer-specific mortality compared with the rest of the cohort. Furthermore, the probability of 10-year MFS was 0.37 for these men, much lower than the 0.78 for the remainder of the high-risk group.

The goal is to identify men who are most likely to gain from additional multimodal treatments. "We are currently validating our findings in another large cohort of patients, and will report these soon," concludes Schaeffer.

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