

Prostate Cancer Outcomes and Genomic-Risk differences between African-American and White Men across Gleason Scores

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Background: Gleason grade is the best independent predictor of prostate cancer outcomes. Nevertheless, the prognostic and genomic implications of Gleason grade are less clear in Black men because of disparate prostate cancer outcomes. Therefore, we investigated prostate cancer outcomes and genomic-risk differences by Gleason grade and race.

Methods: The SEER Prostate with Active Surveillance/Watchful Waiting (AS/WW) Database identified 192,224 men diagnosed with localized prostate cancer from 2010-2015 for examination of clinical outcomes. The Decipher Genomic Resource Information Database (GRID™) identified 1,240 patients with localized prostate cancer for genomic analyses. Multivariable Fine-Gray competing-risks regressions defined adjusted hazard ratios (AHRs) and associated 95% confidence intervals (CIs) for prostate cancer-specific mortality by race (Black versus non-Black) and clinical Gleason score (Gleason 6 versus 7-10). Genomic-risk scores (Decipher scores) prognostic for metastasis were calculated using a random Forest model across physician reported patient race (African-American versus white) and pathologic Gleason score (Gleason 6, Gleason 7, and Gleason 8-10). Analyses included race*clinical Gleason score interaction terms.

Results: Overall, Gleason 6 disease was associated with a lower risk of prostate cancer death compared with Gleason 7-10 disease (AHR 0.25, 95% CI 0.22-0.30, $P < 0.001$) and Black patients had a similar risk of prostate cancer death compared to non-Black patients (AHR 1.10, 95% CI 0.96-1.25, $P = 0.17$). However, Black patients with Gleason 6 disease had a higher risk of prostate cancer death (AHR 1.95, 95% CI 1.42-2.67, $P < 0.001$) compared with non-Black patients with Gleason 6 disease, while no such racial disparity was observed (AHR 1.01, 95% CI 0.87-1.16, $P = 0.94$) for Gleason 7-10 disease ($P_{\text{interaction}} < 0.001$).

In Gleason 6 disease, genomic-risk scores were significantly higher among African-American compared with white men (0.27 [IQR 0.16-0.45] vs. 0.23 [IQR 0.10-0.31]; $P = 0.028$). Genomic-risk scores were not significantly different between African-American and white men in Gleason 7 (0.30 [IQR 0.20-0.47] vs. 0.33, IQR [0.22-0.51]; $P = 0.12$, respectively) or Gleason 8-10 disease (0.42 [IQR 0.27-0.53] vs. 0.43 [IQR 0.30-0.58]; $P = 0.51$, respectively). African-American men with Gleason 6 disease were more likely to have intermediate-to high-genomic-risk scores (Decipher score ≥ 0.45)⁶ compared with white men (25% versus 13%), while there was no racial difference in the likelihood of intermediate- to high-genomic-risk scores in Gleason 7-10 disease (28% for African-American versus 37% for white men) ($P_{\text{interaction}} = 0.004$).

Conclusion: Racial disparities in prostate cancer-specific mortality and genomic risk scores were limited to low-grade disease. These data suggest underlying tumor differences may contribute to observed racial disparities in low-grade/risk disease, while the lack of racial differences in genomic risk scores in Gleason 7-10 disease suggests that disparities in more aggressive disease may be less likely to be driven by tumor differences. These findings raise important questions on how to best counsel and treat Black men with low-grade disease and suggest that further biological characterization and targeted treatment strategies merit further study.

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