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Research Letter

Prostate Cancer Genomic-risk Differences Between African-American and White Men Across Gleason Scores

Brandon A. Mahal [a,†,*], *Mohammed Alshalalfa* [b,†], *Daniel E. Spratt* [c], *Elai Davicioni* [d], *Shuang G. Zhao* [c], *Felix Y. Feng* [b], *Timothy R. Rebbeck* [a,e], *Paul L. Nguyen* [a,‡], *Franklin W. Huang* [b,‡]

African-American men have poorer prostate cancer-specific outcomes compared with white men [1]. Emerging evidence suggests that racial disparities in advanced stage or higher-grade disease may be predominantly accounted for by social factors and healthcare access [2,3]. In contrast, there is growing evidence to support the hypothesis that disparities in low-grade Gleason 6 disease may be in part driven by underlying tumor differences [3,4]. Although low-grade (Gleason 6) disease is considered prognostically favorable, it is associated with a diverse genomic landscape that can sometimes include aggressive genomic features [5]. As such, prognostication and management of Gleason 6 disease can be challenging, particularly for African-American men. Whether genomic-risk classifiers can help explain or predict for racial disparities in Gleason 6 disease is unknown. Thus, we examined the distribution of a prognostic 22-probeset genomic-risk classifier in African-American and white men, across Gleason scores [6].

The Decipher Genomic Resource Information Database (GRID) [6], a global expression database of prostate cancer patients treated with radical prostatectomy (NCT02609269), was used to identify patients with localized prostate cancer (histologically confirmed prostate adenocarcinoma by central pathology). The Decipher score is a 22-probeset genomic-risk classifier that is prognostic for the development of metastasis [6]. Genomic-risk scores (Decipher scores) were calculated using a random Forest model [6] across physician-reported patient race (African-American vs white) and pathological Gleason score (Gleason 6, Gleason 7, and Gleason 8–10). A race × Gleason score (Gleason 6 vs 7–10) interaction was tested for the predefined endpoint of intermediate to high genomic Decipher score (≥0.45) [6]. Statistical testing was two-sided (α = 0.05) and analyses were performed with R 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria). The Dana-Farber/Harvard Cancer Center Institutional Review Board granted permission to perform this study.

This study included 1240 men (N = 286, African American, and N = 954, white); of them, 66 African-American and 139 white men had Gleason 6 disease. In Gleason 6 disease, genomic-risk scores were significantly higher among African-American men than among white men (0.27 [interquartile range {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) or Gleason 8–10 (0.42 [IQR 0.27–0.53] vs 0.43 [IQR 0.30–0.58]; p = 0.51) disease (Fig. 1). 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% vs 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 men vs 37% for white men; $p_{\text{interaction}}$ = 0.004).

African-American men with Gleason 6 disease at surgery had higher genomic-risk scores than white men, while no racial differences in genomic-risk scores were observed in Gleason 7–10 disease. Although the overall observed racial differences in genomic-risk score for Gleason 6 disease (0.27 vs 0.24) represent an overall difference of ~1% in the risk of metastasis, African-American men with Gleason 6 disease were 12% more likely to have intermediate to high genomic-risk scores, which are associated with an atleast 15% risk of metastasis at 10 yr (Decipher score ≥0.45) [6]. These data suggest that 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 [2,3]. These data, together with recent findings [3], highlight that although racial disparities in Gleason 6 disease may be explained in part by tumor differences, absolute differences in the risk of adverse

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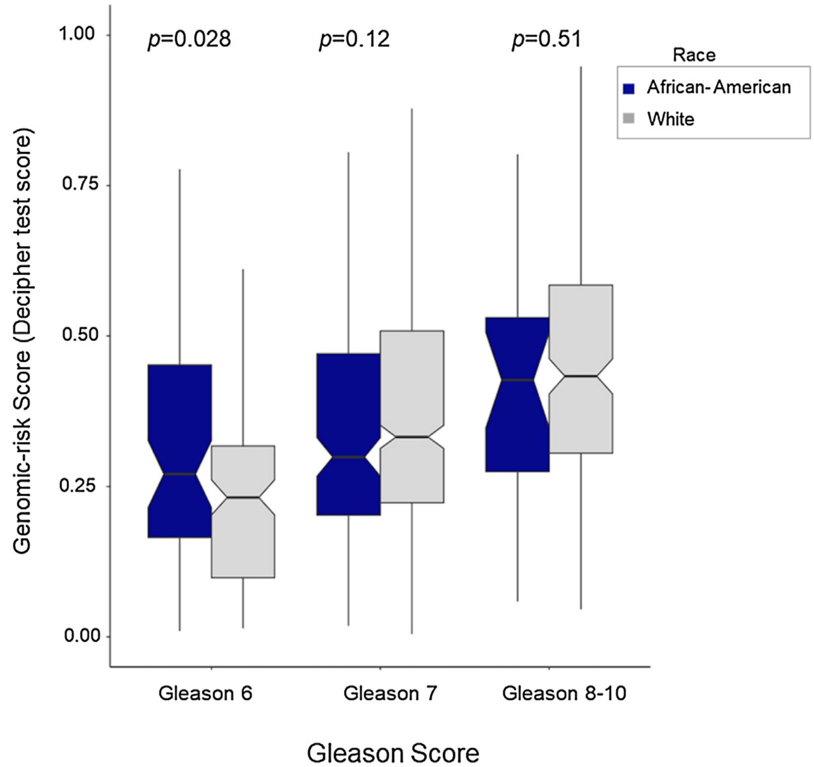

Fig. 1 – Genomic-risk score (Decipher test score) by race [a](African American vs white) and pathological Gleason score [a](Gleason 6 vs 7 vs 8–10). [a]There was a significant race × Gleason score interaction such that African-American men with Gleason 6 disease were more likely to have intermediate–high genomic-risk scores (Decipher score ≥0.45) compared with white men (25% vs 13%), but not in Gleason 7–10 disease (28% vs 37%; $p_{interaction}$ = 0.004).

prostate cancer outcome remain small, and therefore standard management options for Gleason 6 disease should be applied across race until a prospective clinical trial can definitively address active surveillance in this setting. The findings are limited by the uncontrolled retrospective design and require validation. Further research and prospective trials will be needed to determine the biological and clinical significance of the observations made in this study, and what the implications of these findings may be in contemporary five-tiered Gleason grade grouping.

Conflicts of interest: P.L. Nguyen reports personal fees from Ferring, Astellas, GenomeDx Inc., Dendreon, Nanobiotix, Augmenix, and Bayer, as well as research support for clinical trials from Astellas and Janssen, which goes toward his affiliated institution. F.Y. Feng reports consultation for Dendreon, Genzyme, Ferring Pharmaceuticals, Janssen Biotech, EMD Serono, Bayer Healthcare, Sanofi-Aventis, GenomeDx Biosciences, and Medivation/Astellas; compensation for speaking for Clovis Oncology; being a cofounder of PFS Genomics; and a patent with the University of Michigan titled "Compositions and Methods for the analysis of radiosensitivity" (patent publication number: EP3047037). E. Davicioni is an employee of GenomeDx Inc. D.E. Spratt reports being on an advisory board for Janssen and Blue Earth. These financial relationships are all outside this submitted work.

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[a]Dana-Farber Cancer Institute and Brigham and Women's Hospital, Boston, MA, USA
[b]University of California at San Francisco, San Francisco, CA, USA
[c]University of Michigan, Ann Arbor, MI, USA
[d]GenomeDx Inc., San Diego, CA, USA
[e]Harvard TH Chan School of Public Health, Boston, MA, USA

*Corresponding author. Dana-Farber Cancer Institute McGraw/Patterson Center for Population Sciences, 450 Brookline Ave., Boston, MA 02215, USA. Tel. +1 617 335 0087; Fax: +1 617 975 0912.
E-mail address: brandon_mahal@dfci.harvard.edu (B.A. Mahal).
†Equal first-author contribution.
‡Equal senior-author contribution.

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Patterns of Knowledge Acquisition Among Men Undergoing Radical Prostatectomy

*, Mikkel Fode *, Anders Frey, Peter B. Østergren, Christian F. Jensen, Jens Sønksen*

We previously conducted an extensive questionnaire-based study of patient-based outcomes among men after radical prostatectomy (RP) at Herlev and Gentofte Hospital, Denmark [1]. Among other issues, the questionnaire contained questions regarding patients' knowledge acquisition about prostate cancer before their surgery. Therefore, we read with great interest the paper by Loeb and co-workers [2] detailing the problems with prostate cancer information provided on YouTube. To the best of our knowledge, no systematic information on the proportion of prostate cancer patients who seek such information has been published, and therefore we find it appropriate to share our findings.

Questionnaires were mailed between December 2012 and February 2013 to men who had previously undergone RP [1]. A total of 386 patients were invited to participate and 316 usable questionnaires (82%) were returned. Patient demographics are presented in Table 1. Of these men, 284 (89.9%) had sought information about their cancer from sources other than their urologist. Most had used more than one source: 181 (57.3%) had consulted their family practitioner, 222 (70.3%) had sought advice from the official prostate cancer patient association, 165 (52.2%) had discussed the issue with perceived knowledgeable friends or family members, and 254 (80.4%) obtained extra information from the mainstream media. Importantly, 227 (71.8%) had looked for information online. Of this final group, 32 (14.1%) had sought information from officially recognized health care sites only, whereas 195 (85.9%) had also conducted more general searches leading them to other types of websites including YouTube. Fifty-two men (22.9%) had only visited such unofficial sites. The results are summarized in Table 2. On multivariate logistic regression analysis that included the parameters in Table 1, a higher preoperative International Index of Erectile Function-5 score (odds ratio [OR] 1.040, 95% confidence interval [CI] 1.009–10.73; $p = 0.012$) and current employment (OR 2.86, 95% CI 1.64–4.98; $p = 0.0002$) were independent predictors for seeking online information outside officially recognized sites. The main limitation of our data is that we queried patients who had chosen to undergo RP. Therefore, there might be a selection bias towards men with a relatively high degree of trust in the established medical community. The proportion of men who seek knowledge about prostate cancer on unreliable websites might be even higher than estimated here.

As shown by Loeb and co-workers [2], information about prostate cancer displayed on YouTube may be inaccurate or

Table 1 – Patient demographics ($n = 316$)

Parameter	Result
Median age at the time of the operation, yr (range)	64 (43–76)
Median time since surgery, mo (range)	17 (3–36)
Median body mass index, kg/m^2 (range)	25.5 (14.8–37.4)
In a relationship, *n* (%)	289 (91)
Currently employed, *n* (%)	128 (41)
Smoker, *n* (%)	32 (10)
Mean preoperative IIEF-5 score (95% CI)	21.5 (20.6–22.5)
Mean preoperative DAN-PSS (95% CI)	6.3 (5.2–7.5)
One or more comorbidities, *n* (%)	145 (46)
D'Amico high risk, *n* (%)	86 (27)
D'Amico intermediate risk, *n* (%)	198 (63)
D'Amico low risk, *n* (%)	32 (10)

IIEF-5 = International Index of Erectile Function-5; DAN-PSS = Danish Prostate Symptom Score; CI = confidence interval.

Table 2 – Sources of knowledge for men undergoing radical prostatectomy ($n = 316$)

Knowledge acquisition	Men, *n* (%)
Sought information from sources other than their urologist	284 (89.9)
Family practitioner	181 (57.3)
Official prostate cancer patient association	222 (70.3)
Friends and family members	165 (52.2)
Mainstream media	254 (80.4)
Online information	227 (71.8)
Both official and unofficial websites	143 (63.0)
Official websites only	32 (14.1)
Unofficial websites only	52 (22.9)