EDITORIAL

Disparities in prostate cancer diagnosis and management: recognizing that disparities exist at all junctures along the prostate cancer journey

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Prostate cancer (PCa) is the most common non-cutaneous malignancy in American men with the second highest rate of annual cancer-related mortality [1]. Despite PSA screening, well-established disease management options, and ongoing advances in cancer risk-stratification with more novel imaging and biomarkers, there continues to be a wide range of cancer treatment outcomes largely attributed to disparities in underlying biology, access to screening, risk stratification tools used, and treatments employed. These recognized disparities have been reported and proposed as racial disparities in the disease biology impacting prognosis, genetic predisposition and characterization based on race and ethnic background of patients, and access-to-care which impacts disease stage at time of diagnosis as well as biomarker, imaging, and management offerings. In this online collection, the editors of PCAN have selected key papers that have been published in the last several years in our journal, which highlight the important aspects of such recognized disparities that exist in the diagnosis and treatment of prostate cancer in the United States.

Race-based disparities have attracted attention from both society and medical research in patients with PCa as Black individuals often present with higher cancer stages and experience worse cancer-specific and overall survival. However, more often we only focus on the phenomenon that Black men suffer more commonly from PCa and are recommended to undergo screening starting at an earlier age. The specific biological aspects impacted by racial disparity are not well-defined nor are the weight of importance contributed to by each of these potential underpinnings of cancer risk and aggressiveness determinants. Thus, it is of great interest to sort out the existing disparity so that targeted measures can be taken to narrow the difference, whether it be inherently biological risk differences or simply social determinants of health from which the disparities in diagnosis and outcomes are derived.

Definitive treatment with curative intent is the most impactful way to affect cancer-specific survival in cases of clinically-significant prostate cancer, in addition to earlier treatments in the setting of biochemical recurrence or advanced staged metastatic disease. Multiple studies have shown that patients with different racial and ethnic backgrounds seem to have variable preferences regarding therapeutic options at all junctures of treatment decision-making. In the PROCEED study cohort, Black men performed better than white men with prostate cancer when treated with sipuleucel-T, especially at lower PSA values, which may be attributed to the innate responsiveness of the immune system and the effectiveness of immunotherapy at the level of the tumor microenvironment [2]. Nevertheless, a significant under-representation of non-white participants in FDA drug registration trials of PCa treatments over the last fifteen years was found, with 76.3% White, 7.9% Asian, 2.9% Black, 0.5% American Indian or Alaskan Native, and 10.5% unknown racial background enrolled in these reported clinical trials [3]. Recruitment of black and other classically underrepresented minority participants in these trials should be a research priority as the representation of the diverse population would improve our scientific understanding and guide the emerging standard-of-care treatment pathways we recommend. Besides treatment decision-making, access to medical care is another aspect that can seriously affect the disease prognosis based on differential time to screening and continuum of care. This has been shown to be significantly influenced by racial disparities. Krimphove and colleagues found that access-related variables explained 84.7% of the excess risk of death in Black men with prostate cancer, suggesting that initiatives to improve access to care may reduce disparities in PCa associated outcomes [4].

Furthermore, the variability in the biological underpinnings of PCa, which has been proposed to be reflective of genomic differences seen across different races and ethnic backgrounds, is a point of ongoing investigation amongst those studying disparities in prostate cancer. Most recently, the mutation of homologous recombination repair (HRR) genes and pathways has attracted extensive attention in the pathogenesis of, and follow-up treatments for, prostate cancer. Novel targeted drugs like Olaparib and Niraparib have presented options to patients with homologous recombination deficiencies. However, it should be noted that mutation rates, especially those harboring variants of unknown significance (VUS), vary widely across different racial backgrounds. Black patients more frequently carried BRCA1/2 VUS compared to white patients (4.6% versus 1.6%, respectively) [5]. Similarly, the VUS among Hispanic men were significantly higher than non-Hispanic white men in a retrospective analysis of two separate cohorts of men diagnosed with PCa (21.5% versus 16.6% and 20.6% versus 7.2%, respectively) [6]. The disparity in genomic mutations among different races highlights the need for improved access to germline testing in minority populations, classically underrepresented in large studies that have defined the distribution of hereditary mutational analyses. More encouragement for guideline-driven germline testing for men at increased risk of harboring hereditary risk of prostate cancer can potentially help close the gap in cancer care disparities of these minority populations and improve screening and early diagnosis for relatives of affected men. Developing prognostic models based upon gene profiling for risk stratification has become a hotspot of research inquiry. However, the mainstream available genomic tests to predict oncological outcomes in PCa patients: Decipher, Oncotype Dx, and Prolaris were all developed and validated

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primary in populations of white men. Howard and colleagues validated Decipher genomic testing in a large Veteran Affairs cohort with findings that Decipher genomic profiling overall performed well in Black men, with the caveat that certain genes may prove to be more predictive of outcomes in one race over another [7]. Based on these findings it can be suggested that race-specific biomarkers could be explored in the future to generate an even more accurate risk classifier for prostate cancer outcome prognostication than those currently available.

To assess the impact of racial disparities on the overall course of prostate cancer patients more comprehensively, the differences in early diagnosis and postoperative monitoring should also be taken into account. The adoption of novel imaging modalities and novel biomarkers are moving toward earlier diagnoses of clinically-significant prostate cancers. Hoge and colleagues found that Black men were less likely to undergo mutiparametric magnetic resonance imaging-ultrasound fusion biopsy (FBx), a promising modality for the detection of PCa, when presenting with PCa suspicion (22.5% versus 51.5%, respectively) [8]. More concerningly, using Stockholm3 tests, an excess risk of Grade Group ≥ 2 PCa was found among Black men from an American cohort than risk-matched white patients from the STHLM3 study [9]. Such data suggest that new clinical prediction variables and techniques were not well promoted in minority populations and were not sufficient enough to explain the excess risk of high-grade PCa found in Black men at the time of biopsy. Since the AUA updated the standard operating procedure for the use of mpMRI in 2019, the recognized gap in the rate of utilization across different racial and ethnic groups may be narrowed in the future which is conducive to minimizing the overall discrepancies in diagnostic yields, treatments offered, and ultimately outcomes across races. Although novel biomarkers are attractive and promising, recalibration is needed before prediction tools are developed based on data derived, and often validated on, largely white patient cohorts, when there is application of such biomarkers to men of other races, underrepresented in the development of these tools. In the aspect of post-treatment surveillance of treatment success versus disease recurrence, PSA monitoring is the most wildly accepted and utilized. Rising PSA levels after treatment are often the first indicator of recurrent PCa. Asiriet and colleagues retrospectively studied individual patient-level data from the SEER Medicare linked database and found that Black men were more likely to not receive guideline-concordant PSA surveillance testing after definitive treatment for localized PCa during the first 4 years post-treatment [10]. However, the disparity in PSA testing was not observed in the higher income subgroups suggesting that socio-economic factors, strongly associated with racial disparity in the United States, drove deviation from standard PSA monitoring following primary definitive therapy for prostate cancer.

As long as the racial disparities among prostate cancer patients still exist, the ongoing exploration of its causes and efforts to eliminate these differences, is critical. Most disparities can be attributed to social determinants of health such as socioeconomic status, access to health care, insurance coverage, and countless implicit biases. These factors can certainly influence the timing and use of screening tools for early diagnosis, choice amongst treatment options and the prevalence of postoperative surveillance, as well as the genetic differences that may account for the biological character of cancer and its sensitivity to various therapies. Further research should focus on a spectrum of ways to narrowing disparities caused by non-genetic factors such as improving the representativeness of minority in clinical trials, standardizing the operational approaches of early diagnosis and postoperative surveillance on a population level, validating and adjusting the existing predictive models to meet the characteristics of ethnic minorities, as well as increasing the diversity in the body of medical practitioners to mitigate the subconscious biases against minority populations.

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DATA AVAILABILITY

There is no primary data related to this manuscript.

REFERENCES

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72:7–33.
2. Sartor O, Armstrong AJ, Ahaghotu C, McLeod DG, Cooperberg MR, Penson DF, et al. Survival of African-American and Caucasian men after sipuleucel-T immunotherapy: outcomes from the PROCEED registry. Prostate Cancer Prostatic Dis. 2020;23:517–26.
3. Lythgoe MP, Krell J, Savage P, Prasad V. Race reporting and diversity in US food and drug administration (FDA) registration trials for prostate cancer; 2006–2020. Prostate Cancer Prostatic Dis. 2021;24:1208–11.
4. Krimphove MJ, Cole AP, Fletcher SA, Harmouch SS, Berg S, Lipsitz SR, et al. Evaluation of the contribution of demographics, access to health care, treatment, and tumor characteristics to racial differences in survival of advanced prostate cancer. Prostate Cancer Prostatic Dis. 2019;22:125–36.
5. Petrovics G, Price DK, Lou H, Chen Y, Garland L, Bass S, et al. Increased frequency of germline BRCA2 mutations associates with prostate cancer metastasis in a racially diverse patient population. Prostate Cancer Prostatic Dis. 2019;22:406–10.
6. Pan E, Shaya J, Madlensky L, Randall JM, Javier-Desloges J, Millard FE, et al. Germline alterations among Hispanic men with prostate cancer. Prostate Cancer Prostatic Dis. 2022;25:561–7.
7. Howard LE, Zhang J, Fishbane N, Hoedt AM, Klaassen Z, Spratt DE, et al. Validation of a genomic classifier for prediction of metastasis and prostate cancer-specific mortality in African-American men following radical prostatectomy in an equal access healthcare setting. Prostate Cancer Prostatic Dis. 2020;23:419–28.
8. Hoge C, Verma S, Lama DJ, Bergelson I, Haj-Hamed M, Maynor S, et al. Racial disparity in the utilization of multiparametric MRI-ultrasound fusion biopsy for the detection of prostate cancer. Prostate Cancer Prostatic Dis. 2020;23:567–72.
9. Vigneswaran HT, Discacciati A, Gann PH, Grönberg H, Eklund M, Abern MR. Ethnic variation in prostate cancer detection: a feasibility study for use of the Stockholm3 test in a multiethnic U.S. cohort. Prostate Cancer Prostatic Dis. 2021;24:120–7.
10. Asiri IM, Chen RC, Young HN, Codling J, Mandawat A, Beach SRH, et al. Race and prostate specific antigen surveillance testing and monitoring 5-years after definitive therapy for localized prostate cancer. Prostate Cancer Prostatic Dis. 2021;24:1093–102.

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SRB and YZ both provided conceptualization, primary authorship, critical review, and revisions for this manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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