EDITORIAL

Clinical

Androgen deprivation therapy, cardiovascular risk, and mortality in black prostate cancer patients: challenging established beliefs?

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Androgen deprivation therapy (ADT) is the cornerstone of treatment in high-risk and advanced prostate cancer (PCa) and has been for decades [1]. Despite its well-recognized efficacy though, ADT is not an innocuous therapy, as it could significantly increase the risk of experiencing major adverse cardiovascular events (MACE) and cardiovascular mortality [2].

Black men have higher cardiovascular disease (CVD) risk than White men in the general population [3] and disparities depending on the racial group are known when speaking of PCa and its outcomes. Indeed, Black men have higher prostate-specific antigen (PSA) values at presentation [4], a higher incidence and a greater than 2-fold increased risk of mortality compared to White patients [5].

Until recent times, the cardiovascular events and mortality risk associated with ADT in men with PCa, particularly examined by race, have remained largely unexplored.

Moul et al. [6] sought to address this gap of knowledge, by conducting a study with this objective, analyzing real-world data in the process. They reviewed data of more than 34 000 patients with PCa treated with ADT between 1991 and 2020 and explored MACE and all-cause mortality risk for Black versus White patients. Their study encompassed a wide-ranging scope, comprehending all patients that underwent ADT, regardless the stage of the disease.

Their investigation demonstrated that Black race is associated with a lower risk of MACE and improved overall survival compared to White race in men undergoing treatment with ADT.

Indeed, mortality risk after ADT initiation was 1.6% and 2.6% at 1 year and 11.7% and 18.1% at 4 years for Black and White patients, respectively. Moreover, they analyzed body mass index (BMI) of the patients, defining it as a categorical variable with a cutoff of 18.5 kg/m^2. Their results suggest that a lower BMI contributes to improved survival (and lower MACE) independent of race, but it needs to be said that a BMI < 18.5 kg/m^2 may be proxy for cancer cachexia rather than a more direct lean/obesity related mechanism.

This study contributes to a growing body of recent research that challenges previous assumptions, thereby fostering further investigations. Indeed, a 2023 review of PCa, race, and health disparity [5] reported that, of 12 phase 3 randomized clinical trials reporting outcomes by race, only one suggested a worse outcome for African American men compared to White patients [7]. Recently Wallis et al. [8] sought to evaluate the association between patient demographics and MACE risk following ADT initiation in men with PCa. While demonstrating a consistent increase in MACE risk following ADT initiation over the first four years (5% per year), they identified key risk factors for MACE, including increasing age, baseline metastasis, previous history of MACE, and treatment with antagonist vs. agonist. Interestingly, they found that MACE risk was higher for patients treated with a gonadotropin-releasing hormone (GnRH) antagonist vs. those treated with a luteinizing hormone-releasing hormone (LHRH) agonist. Moreover, a comparison of race subgroups showed that MACE risk was higher for White patients than it was for Black and Asian patients.

Socioeconomic factors play an important role in terms of patients' ability to afford and access healthcare and low socioeconomic status may be associated with higher risk of morbidity and mortality due to CVD [3]. In the results of an investigation on a cohort of PCa patients treated with ADT at a quaternary, multisite health care system, Black race was associated with a 1.38-fold increased risk of MACE, compared to White men, as defined by cause-specific proportional hazards. Mediation analysis determined that social vulnerability, specifically the socioeconomic status theme, mediated 98% of this disparity in MACE risk [9].

It is crucial to recognize that 'race' is a social construct, and any disparities associated with 'race' are likely driven by social factors such as lower socioeconomic status, food insecurity, lack of health insurance, and limited access to preventative care. So, a rightful hypothesis is that equal access to care would likely attenuate differences in survival by 'race' and is an important determinant of racial equity.

An insightful study by Lucas et al. [10], investigated a large, diverse cohort of well characterized men diagnosed with PCa, 32% of whom were Black. The study is especially significant because these men had similar access to healthcare, a rare occurrence in the U.S., as they were all part of the Veterans Affairs Healthcare System.

Their results show that Black men have similar risk of MACE as White men, when receiving ATD in combination with radiotherapy. However, for Black men, having a pre-existing CVD increases their risk for MACE by 4.2 times compared to Black men without CVD. Notably, for men with CVD at PCa diagnosis and for those who have other comorbidities, there is significant risk of a MACE, highlighting the need for CVD risk screening when treating PCa.

Further studies are required to more accurately assess and address the impact of comorbidities and social disparities on MACE risk in PCa patients undergoing ADT and to stratify patients

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based on identified predictors. Additionally, research conducted in a 'socially equitable' environment should be prioritized to control for the 'access to healthcare' factor, ensuring the most unbiased data possible. Most importantly, multilevel interventions aimed at addressing socioeconomic vulnerability should be encouraged.

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COMPETING INTERESTS

The authors declare no competing interests.