Impact of diabetes on cardiovascular outcomes in prostate cancer survivors receiving androgen deprivation therapy

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Background: Diabetes is a major comorbidity for prostate cancer (PC) survivors (prevalence 20%) and associated with increased mortality. In PC survivors, diabetes is a major risk factor for cardiovascular disease (CVD), the leading cause of death in PC survivors. Androgen deprivation therapies, particularly gonadotropin-releasing hormone agonists (GnRHa), are known to increase CVD risk in locally advanced PC survivors. In cancer patients, cardiotoxic cancer treatments and diabetes have been shown to interact to further increase CVD events. However, how both GnRHa and diabetes impact specific CVD outcomes in PC survivors has not been studied.

Methods: We conducted a retrospective analysis using Surveillance, Epidemiology and End Results cancer registry data linked to Medicare claims. We included patients ≥66 years old diagnosed with locally advanced PC between 2008 and 2017 and excluded patients with preexisting CVD. Preexisting diabetes and CVD (myocardial infarction [MI], ischemic heart disease [IHD], coronary artery disease [CAD], congestive heart failure [CHF] diagnoses, and GnRHa treatment (within year of PC diagnosis) were based on claims data. We used inverse probability treatment weighting (IPTW) with propensity scores to match those who received GnRHa vs. no GnRHa based on sociodemographic and clinical characteristics. Time-dependent Cox regression was used to assess the impact of diabetes, GnRHa, and their interaction on CVD event incidence.

Results: Of 22,030 locally advanced PC survivors, 11,297 (52%) did not have underlying CVD and were included for analysis. Median age was 71 years (interquartile range [IQR] 68-75). 8316 (75.1%) were White, 1070 (9.7%) Black, 971 (8.8%) Hispanic, and 706 (6.4%) Other race. 10,718 (94.9%) had high-risk localized PC (according to NCCN risk criteria, N0) and 579 (5.1%) had regional PC (N1). 4,782 (42.3%) received GnRHa. 2,228 (20.3%) had preexisting diabetes. 667 (5.9%) PC survivors had incident MI, 767 (6.8%) had incident IHD, 2661 (23.6%) had incident CAD, and 667 (5.9%) had incident CHF. Median follow up was 5.1 years. Diabetes increased risk of total CVD events (Hazard Ratio [HR] 1.41, 95% confidence interval [95%CI] 1.30-1.54), IHD (HR 1.37, 95%CI 1.11-1.69), CAD (HR 1.58, 95%CI 1.42-1.75), and CHF (HR 1.78, 95%CI 1.56-2.03). GnRHa also increased risk of total CVD events (HR 1.10, 95%CI 1.04-1.17), MI (HR 1.21, 95%CI 1.05-1.40), IHD (HR 1.25, 95%CI 1.09-1.57), CAD (HR 1.11, 95%CI 1.03-1.19), and CHF (HR 1.13, 95%CI 1.03-1.25). The diabetes-GnRH interaction terms did not significantly increase any CVD event risk.

Conclusions: Both diabetes and GnRHa therapy in a large cohort of PC survivors significantly increase incident CVD events separately, but they do not interact to further increase CVD risk. Future research should develop strategies to mitigate CVD risk in PC survivors with diabetes receiving GnRHas. Optimizing use of novel diabetes medications that improve CVD outcomes should be further investigated in PC survivors.

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