A Single-center, Retrospective Observational Study of Current Management Practices of Localized High-/Very-High-Risk and Advanced Hormone Sensitive Prostate Cancer Patients

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Background: The decision of the most suitable primary treatment is critical for high-/very high-risk localized non-metastatic and advanced hormone-sensitive prostate cancer (HSPC) due to the increased risk of progression to metastatic and castrate-resistant disease with limited life expectancy. This single-center analysis evaluates the impact of diverse treatment modalities, including novel hormonal therapies, on patient outcomes in this cohort. We compared the efficacy of radical prostatectomy (RP) versus definitive radiation therapy (RT) with androgen deprivation (ADT) and/or androgen receptor signaling inhibitors (ARSI) in the localized high-and very high-risk patient population. Additionally, we evaluated the use of ADT with and without ARSI in the treatment of advanced hormone-sensitive prostate cancer.

Methods: Non-metastatic prostate cancer patients classified as high- very high-risk according to NCCN guidelines, treated with RP or RT+ADT/ARSI at the Upstate University Hospital and affiliated tertiary centers, were included. Overall survival (OS), time to biochemical recurrence (BCR), and time to metastasis were evaluated from initial treatment to the last known follow-up (minimum follow-up $>$ 6 months). Additionally, we assessed HSPC patients, specifically studying the time required for the development of castrate-resistant prostate cancer (CRPC) using Kaplan-Meier curves and univariate/multivariate Cox proportional hazard models.

Results: A total of 376 patients with non-metastatic prostate cancer, categorized as high-risk or very high-risk according to the National Comprehensive Cancer Network (NCCN) guidelines, were identified for this study. These patients had received either RP (N = 290) or RT+ADT (N = 86) as their primary treatment modality. Multiple pathological and clinical variables (age, race, Charlson Comorbidity Index (CCI), AJCC stage, PSA, ECOG, and Gleason score) were significantly associated with initial treatment type ($p < 0.05$). Patients who received RP demonstrated a significantly higher survival probability of 87% compared to 71% for RT +ADT at 8 years post-treatment (log-rank $p = 0.02$). However, multivariate analysis for overall survival revealed no significant benefit of RP over RT+ADT, with ECOG performance status emerging as the primary and only predictor of outcome ($p = 0.005$). Interestingly, patients receiving RT+ADT demonstrated a significantly longer time to recurrence in multivariate analysis (HR=0.34, $P < 0.001$) compared to those undergoing RP alone. In 92 HSPC patients, ADT+ARSI demonstrated a significant benefit in delaying the progression to castration-resistant prostate cancer and metastatic disease, outperforming both ADT alone and ADT with chemotherapy in Kaplan-Meier analysis (log-rank <0.05).

Conclusions: In this single-center study, high- and very high-risk prostate cancer patients treated with definitive RT demonstrated significantly lower survival compared to the patient group who was treated by radical prostatectomy in univariate analyses but not in multivariate analyses. This likely reflects the impact of baseline patient characteristics, such as older age, higher CCI, PSA values, ECOG scores, and proportion of African Americans in the group of patients treated with RT+ADT. Additionally, in the HSPC cohort, ADT+ARSI was associated with a longer time to CRPC and metastasis compared to other treatment regimens. Larger studies are needed to confirm this benefit and refine treatment strategies for advanced prostate cancer.

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