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Platinum Priority – Prostate Cancer

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The Impact of Local Treatment on Overall Survival in Patients with Metastatic Prostate Cancer on Diagnosis: A National Cancer Data Base Analysis

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Abstract

Background: The role of local treatment (LT) in patients with metastatic prostate cancer (mPCa) at diagnosis is controversial.

Objective: We set to evaluate the potential impact of LT on overall mortality (OM) in men with mPCa, and how this impact is influenced by tumor and patient characteristics.

Design, settings, and participants: A total of 15 501 patients with mPCa were identified in the National Cancer Data Base (2004–2012) and categorized in LT (radical prostatectomy or radiation therapy targeted to prostate) versus nonlocal treatment (NLT; all other patients).

Outcome measurements and statistical analysis: The two arms (LT vs NLT) were matched using propensity scores to minimize selection bias. To evaluate LT impact on OM in relation to baseline characteristics, first multivariable Cox regression analysis was used to predict OM in patients treated with NLT, then interaction between predicted OM risk and LT status was tested.

Results and limitations: Overall, 9.5% ($n = 1470$) of patients received LT. In the post-propensity matched cohorts, 3-yr OM-free survival was higher in the LT group versus the NLT group (69% vs 54%; $p < 0.001$). In multivariable Cox regression, the NLT group, age, and Charlson comorbidity index were predictors of OM (all $p \leq 0.03$). This model was used to predict the 3-yr OM risk. The interaction between predicted OM and LT status was significant ($p < 0.001$). The benefit of LT on OM decreased progressively as predicted OM risk increased. Specifically, the 3-yr absolute improvement in OM-free survival was 15.7%, for patients with predicted OM risk $\leq 20\%$ versus 0% for those with predicted OM risk $\geq 72\%$.

Conclusions: Men with mPCa at diagnosis benefit from LT in terms of OM. This is largely affected by baseline characteristics. Specifically, patients with a relatively low tumor risk and good general health status appear to benefit the most.

Patient summary: We used a large hospital-based database to evaluate which patients might benefit from local therapy when metastasized prostate cancer was present at diagnosis. Local therapy is associated with a survival benefit in men with less aggressive tumors and good general health.

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1. Introduction

Men who present with metastatic prostate cancer (mPCa) at diagnosis have a 5-yr survival of only 28% [1]. In these men, the first-line treatment consists of androgen deprivation therapy (ADT) [2] followed by castration-resistant tumor treatment agents [3], and/or chemotherapy. Unfortunately, these treatment modalities offer a limited improvement in patient survival and have an important economic burden [3,4]. For several other cancer entities, a survival benefit was observed, when—despite metastatic disease—the primary tumor was surgically resected [5,6]. The biological rationale for such aggressive therapy resides in the elimination of cytokine signaling, which may enhance metastatic seeding [7,8], and the elimination of the source of metastasis [9]. Despite this, there is little evidence on the use of local therapy (LT) in men presenting with mPCa. Recent Surveillance, Epidemiology, and End Results (SEER)-based reports [10–12] and an institutional series [13] demonstrated a potential survival benefit for men with mPCa who underwent LT. Unfortunately, the SEER reports [10,11] lacked important information such as comorbidity status and/or intent of treatment (palliative vs curative). Moreover, these reports were unable to examine the role of external beam radiation (EBRT) in treating men with mPCa. The only report that included comorbidity status and information on EBRT was based on SEER-Medicare and thus limited to patients >65 yr of age [12]. Likewise, the small sample size and the institutional nature of the other report [13] limits its generalizability. To circumvent these limitations, we evaluated the impact of LT on overall mortality (OM) in patients with mPCa treated within the National Cancer Data Base (NCDB). We hypothesize that the potential impact of LT on OM is influenced by tumor characteristics, as well as general patient health.

2. Methods

The NCDB, a joint program of the Commission on Cancer (CoC) and the American Cancer Society, is a nationwide oncology database that contains information about patterns of cancer care and treatment outcomes. The NCDB has collected data on newly diagnosed cancers since 1989 and includes information about more than 29 million cancers from greater than 1500 hospitals with CoC-accredited programs in the US and Puerto Rico. About 70% of newly diagnosed tumors in the US are reported to the NCDB [14].

2.1. Patient selection

Treatment naïve men aged ≥ 35 yr with adenocarcinoma of the prostate (International Classification of diseases-O-3 code: C61.9) and diagnosed as primary metastatic PCa (M1a, M1b, and M1c, respectively), based on the American Joint Committee on Cancer Cancer Staging Manual [15,16], with radiologic or pathologic confirmation of metastatic disease through the collaborative staging system of the NCDB were identified. These selection criteria yielded 38 929 mPCa patients diagnosed between 2004 and

2012. Those with missing information on Gleason Score at diagnosis ($n = 15\,907$) and/or clinical T-stage ($n = 890$; Tx was considered as unknown, but not missing), and/or prostate-specific antigen (PSA) value ($n = 6418$) were excluded from analyses. Likewise, patients receiving palliative treatment ($n = 2838$), unspecified radiation therapy ($n = 264$), chemotherapy ($n = 58$), or immunotherapy ($n = 8$) as primary treatment were excluded (details in Fig. 1). We further excluded cases with missing follow-up information ($n = 78$) and cases with less than 6 mo of follow-up as a landmark measure ($n = 1600$). This resulted in 15 501 assessable cases.

2.2. Variables and endpoint definition

Patients were stratified according to treatment type. LT was defined as radical prostatectomy, brachytherapy, and/or EBRT targeted to the prostate within 6 mo of diagnosis with or without additional ADT. Nonlocal therapy (NLT) was defined as ADT, watchful waiting, and/or EBRT not targeted to the prostate within 6 mo of diagnosis. Continuous variables consisted of age and PSA at diagnosis. Categorical variables included biopsy Gleason Score (≤ 6 , 7, and ≥ 8), clinical T-stage (cT1–cT2, cT3–cT4, and cTx), clinical N-stage (cN0/cNx and cN1), year of diagnosis (2004 to 2012), and race/ethnicity (white, black, and other), high school education status, income status, metropolitan status, geographical region, and facility type. The Charlson/Deyo Comorbidity Index (CCI) [17,18] was categorized as 0, 1, and ≥ 1 per the NCDB participant user file. Endpoint of interest was OM [19].

2.3. Statistical analyses

To compare differences in clinical and sociodemographic characteristics between the LT and NLT groups, categorical

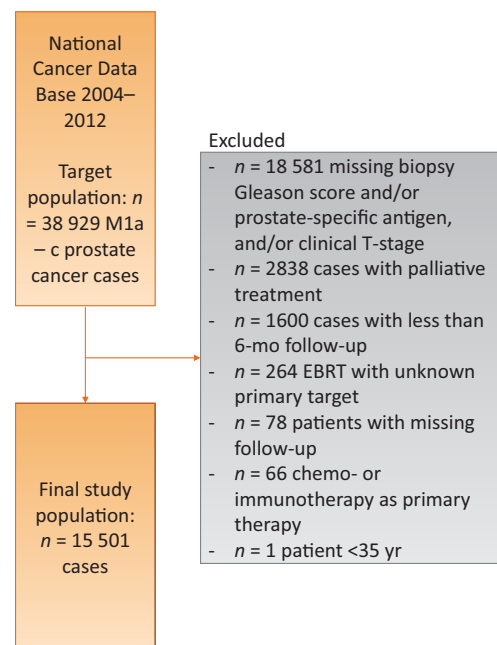


Fig. 1 – Inclusion/exclusion criteria. EBRT = external beam radiation therapy.

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