**Comparative Effectiveness of Prostatectomy and Radiation Therapy (RT) in Gleason 9-10 Prostate Cancer**

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**Purpose/Objective(s):** Prostate cancers with a Gleason Score (GS) of 9 or 10 are biologically aggressive. Recent data suggest that extremely dose-escalated radiation therapy delivered using external beam radiation therapy (EBRT) and a brachytherapy (BT) boost results in superior biochemical failure free survival (BFFS) and metastasis free survival (MFS) in these patients compared to radical prostatectomy (RP). We sought to validate these findings among patients cared for in the Veterans Administration (VA) and hypothesized that we would find similar results.

**Materials/Methods:** Patients diagnosed with GS 9-10 prostate cancer in the VA system between January 2000 and December 2010 were identified. Patients with an unknown initial PSA or metastases prior to treatment were excluded. Kaplan Meier analysis and multivariable cox regression modelling were used to compare BFFS, MFS, cancer specific survival (CSS), overall survival (OS), and time to salvage therapy by treatment modalities.

**Results:** In total, 1951 patients were treated with either RP (n=682), EBRT (n=1146), EBRT+BT (n=62), or BT (n=61). Median age in each group was 62, 67, 65, and 67 years, respectively. Median initial PSA was 17.6, and 56% of patients had ≤ T2a disease. Neoadjuvant and/or concurrent androgen deprivation therapy (ADT) was utilized in 59%, 75%, 73%, and 77% respectively (p<0.0001). Salvage therapies, defined as radiation and/or ADT after BF, were utilized in 31%, 21%, 18%, and 16% respectively (p<0.0001). Of the RP patients, 11% received adjuvant EBRT. Median follow up was 74 months (IQR 21-102mo). On multivariable analysis, after adjusting for age at diagnosis, GS, T stage, race, and PSA, EBRT (HR 0.61, p<0.0001) and EBRT+BT (HR 0.54, p=0.006) demonstrated superior BFFS compared to RP, with BT nearing significance (HR 0.63, p=0.06). Compared to RP, there was significantly superior MFS for EBRT (HR 0.35, p<0.0001), EBRT+BT (0.261, p=0.02) and BT (HR 0.23, p=0.04) and prolonged salvage free survival for EBRT and EBRT+BT. Patients treated with EBRT had worse CSS and OS and those treated with EBRT+BT has worse OS compared to RP (Table 1).

**Conclusion:** Radiation therapy-based approaches for patients with GS 9-10 prostate cancer were associated with superior BFFS, MFS, and prolonged time to salvage therapy compared to RP. Comparisons of overall survival were considered unreliable, given a historical preference to recommend RP in patients with longer life-expectancies. The costs and consequences of upfront RP for patients with GS 9-10 prostate cancer warrants further investigation.