**Multi-institutional Outcomes of Postprostatectomy Adjuvant Versus Early Salvage Radiation Therapy in Prostate Cancer Patients With Adverse Pathologic Features**

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**Purpose/Objective(s):** Prostate cancer patients (pts) with adverse pathologic features (pT3 and/or positive surgical margins) after prostatectomy may be managed with adjuvant radiotherapy (ART) or surveillance followed by early salvage radiotherapy (ESRT) for biochemical recurrence. The purpose of this study is to evaluate freedom from biochemical failure (FFBF), freedom from distant metastases (FFDM), prostate-cancer specific survival (PCSS), and overall survival (OS) after ART versus ESRT. **Materials/Methods:** Individual data from 1566 pts with adverse pathologic features who underwent either post-prostatectomy ART (n = 371; PSA < 0.1 ng/mL or undetectable by assay) or ESRT (n = 1195; 0.1 ≤ PSA ≤ 0.5 ng/mL) between 1987 and 2013 at 10 academic centers were pooled. Post-RT BF was a PSA rise to ≥ 0.2 ng/mL. All outcomes were measured from surgery date to address lead-time bias. FFBF, FFDM, PCSS, and OS were compared using Kaplan-Meier and analyzed using Cox regression methods. Propensity score (PS) 1:1 matching was used to account for covariates associated with treatment selection including age, year of surgery, Gleason score, T stage, margin status, and use of post- operative androgen deprivation therapy (ADT). A sensitivity analysis was completed to address the limitation that an unknown proportion of pts in the ART group who did not develop BF may have been cured by surgery alone.

**Results:** Median time from surgery to RT was 4.4 vs 23 months and median follow-up was 5.4 vs 7.7 years for the ART and ESRT groups, respectively. Ten-year FFBF (75% vs 59%, P = 0.0001) and PCSS (99% vs 97%, P = 0.01) were significantly higher after ART whereas FFDM (95% vs 92%, P = 0.28) and OS (93% vs 91%, P = 0.21) were not significantly different. After PS matching, ART was associated with higher 10-year FFBF (75% vs 53%, P < 0.0001) but not FFDM (95% vs 93%, P = 0.25), PCSS (99% vs 99%, P = 0.58), or OS (93% vs 86%, P = 0.05). On multivariate analysis, ART remained significantly associated with decreased risk of BF (HR 0.45 [95% CI, 0.31 - 0.69]; P < 0.001). Higher Gleason score as a continuous variable (HR 1.81 [95% CI, 1.51 - 2.17]; P < 0.0005), pT3b vs pT2 (HR 1.75 [95% CI, 1.07 - 2.86]; P = 0.027), and omitting pelvic nodal RT (HR 5.13 [95% CI, 2.44 - 10.7]; P < 0.0005) were independent unfavorable prognostic features. The use of postoperative ADT was not independently associated with outcomes on multivariate analysis. The sensitivity analysis demonstrated that the decreased risk of BF associated with ART only lost sta- tistical significance when more than 39% of ART pts were assumed to have been cured by surgery alone.

**Conclusion:** The optimal timing of postoperative RT is unknown pending ongoing randomized trials. In this large multi-institutional retrospective study, adjuvant RT was associated with improved freedom from biochemical failure but did not demonstrate a clear benefit in terms of survival or avoiding distant metastases compared to early salvage RT.