

Long-term results of adjuvant versus early salvage postprostatectomy radiation therapy: a large single institutional experience

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Background: To evaluate freedom from biochemical failure (FFBF), freedom from androgen deprivation therapy (FFADT), freedom from distant metastases (FFDM), and overall survival (OS) after adjuvant radiation therapy (ART) versus early salvage radiation therapy (ESRT) in men with prostate cancer and adverse pathologic features (pT3 and/or positive surgical margins).

Methods: Of 718 patients consecutively treated with postoperative radiation therapy (RT) for prostate cancer between 1992 and 2013, we retrospectively identified 171 men receiving ART and 230 receiving ESRT (RT delivered at PSA ≤ 0.5 ng/ml) who had adverse pathologic features. Post-irradiation FFBF (BF was defined as PSA rise to ≥ 0.2 ng/ml), FFADT, FFDM, and OS were compared using Kaplan-Meier and Cox regression methods. Propensity score (PS)-matching was performed to estimate treatment effects while accounting for covariates predicting treatment allocation. We performed a sensitivity analysis to address the limitation that an unknown proportion of the patients in the ART group who did not develop BF may have already been cured by surgery alone. Among patients in the propensity-score matched cohort, we randomly selected an increasing number of patients treated with ART who did not develop BF at the last follow-up visit (i.e., were assumed to have been cured by surgery alone), and compared actuarial BF rates between the ART and ESRT groups, using log-rank test.

Results: Median follow-up was 7.4 and 8.0 years for patients treated with ART and ESRT, respectively. Ten-year FFBF (69% versus 56%, $p=0.003$) and 10-year FFADT (88% versus 81%, $p=0.046$) rates were higher after ART; however, FFDM and OS did not significantly differ. After PS-matching, ART was associated with improved FFBF ($p<0.0001$), FFADT ($p=0.0001$), and FFDM ($p=0.02$). Findings were confirmed in multivariable analyses in unmatched and PS-matched cohorts. In the sensitivity analysis, we found that the decreased risk of BF associated with ART lost statistical significance only when more than 38% of ART patients were assumed to have been cured by surgery alone.

Conclusions: Postoperative RT confers excellent long-term cancer control. These results suggest ART may be associated with improved FFBF, FFADT, and FFDM, but comparable OS. In our sensitivity analysis, the statistical significance of the benefit associated with ART was lost only after 38% of patients were assumed to have been cured after surgery and excluded from the analysis. Recognizing that statistical power is also progressively limited in this model as increasing numbers of patients without BF are excluded, this corresponds with the upper bound of the proportion of patients with adverse pathologic features who were only observed after surgery in prior randomized trials. Given the retrospective study design, these findings should be interpreted with caution. Optimal timing of postoperative RT further awaits results of ongoing trials.

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