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Role of Androgen Deprivation Therapy in Early Salvage Radiation Among Patients With Prostate-Specific Antigen Level of 0.5 or Less

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Abstract

In this study, we examine the benefit of adding androgen deprivation therapy (ADT) to salvage radiotherapy in modern patients followed with ultrasensitive prostate-specific antigen (PSA). In these 108 patients who received radical prostatectomy and salvage radiation at a PSA of 0.5 or less, we found that ADT was associated with a decreased risk of recurrence. This benefit appeared limited to men with negative margins, which suggests that men with positive margins and PSA ≤ 0.5 may be good candidates for salvage radiation alone.
Background: The Radiation Therapy Oncology Group 96-01 randomized trial demonstrated the benefit of adding androgen deprivation therapy (ADT) to salvage radiotherapy for an increasing prostate-specific antigen (PSA) after prostatectomy, but it is unknown whether modern patients followed with ultrasensitive PSA and salvaged at a low PSA (ie, ≤ 0.5) also benefit from ADT. **Patients and Methods:** The cohort comprised 108 patients who received radical prostatectomy (RP), were followed by ultrasensitive PSA, and received salvage radiotherapy at a PSA of 0.5 or less. Sixty patients had negative margins, and 48 patients had positive margins at RP. Cox multivariable regression analysis was performed to identify factors associated with time to secondary PSA failure and included PSA at salvage, year of treatment, Gleason score, ADT use, margin status, T stage, and PSA doubling time. Occurrence of distant metastases was documented. **Results:** Median follow-up after radiation was 63.09 months. A total of 24 patients had a distant metastasis. In all patients, ADT use was associated with a decreased risk of recurrence (hazard ratio [HR], 0.44; 95% confidence interval [CI], 0.25-0.79; $P = .006$). On subgroup analysis, ADT was associated with a decreased risk of failure among patients with negative margins (HR, 0.27; 95% CI, 0.12-0.61; $P = .002$), but not among men with positive margins (HR, 0.78; 95% CI, 0.29-2.10; $P = .63$). **Conclusions:** Even patients followed with ultrasensitive PSA and salvaged early with a PSA ≤ 0.5 seem to benefit from the addition of ADT to salvage radiation. However, this benefit seemed to be limited to men with negative margins; thus, men with positive margins and PSA ≤ 0.5 may be good candidates for salvage radiation alone.

Introduction

Among patients who undergo radical prostatectomy (RP) as definitive treatment for localized prostate cancer, approximately 20% to 40% may experience a prostate-specific antigen (PSA) recurrence.[1-3] Salvage radiotherapy in this setting has been associated with reductions in prostate-cancer specific and overall mortality in select patients.[4] The Radiation Therapy Oncology Group (RTOG) 96-01 randomized trial of salvage radiotherapy with or without 2 years of bicalutamide (Casodex; AstraZeneca Pharmaceuticals LP, London, UK) has suggested that androgen

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Table 1 Patient Baseline Characteristics

Characteristic	Entire Cohort n = 108 No. (% or Range)	ADT n = 43	No ADT n = 65	Positive Margin n = 48	Negative Margin n = 60
Baseline PSA (before RP)					
0-10	81 (75%)	35 (81.4%)	46 (70.8%)	33 (68.7%)	48 (80%)
10-20	21 (19.4%)	5 (11.6%)	16 (24.6%)	12 (25%)	9 (15%)
>20	2 (1.9%)	1 (2.3%)	1 (1.5%)	2 (4.2%)	0 (0)
Unknown	4 (3.7%)	2 (4.7%)	2 (3.1%)	1 (2.1%)	3 (5%)
Maximum Gleason score (biopsy)					
<6	5 (4.6%)	3 (7%)	2 (3.1%)	3 (6.3%)	3 (5%)
6	24 (22.2%)	11 (25.6%)	13 (20%)	15 (31.2%)	9 (15%)
7	55 (51%)	20 (46.5%)	35 (53.8%)	21 (43.7%)	34 (56.6%)
8-10	21 (19.4)	9 (20.9%)	12 (18.5%)	8 (16.7%)	13 (21.7%)
Unknown	3 (2.8%)	0 (0)	3 (4.6%)	1 (2.1%)	1 (1.7%)
Clinical T-category					
Tx	10 (9.3%)	4 (9.3%)	6 (9.2%)	7 (14.6%)	3 (5%)
T1b	1 (0.9%)	1 (2.3%)	0 (0)	1 (2.1%)	0 (0)
T1c	68 (63%)	31 (72.1%)	37 (57%)	26 (54.2%)	42 (70%)
T2a	28 (25.9%)	6 (14%)	22 (33.8%)	14 (29.1%)	14 (23.3%)
T3a	1 (0.9%)	1 (2.3%)	0 (0)	0 (0)	1 (1.7%)
Age at salvage RT	61 (47-75)	61 (47-73)	61 (49-75)	62 (47-73)	61 (48-75)
Median time from RP to salvage RT	24.80 mo	29.01 mo	24.31 mo	19.72 mo	29.95 mo
Median PSA (at salvage)	0.24 (0.01-0.5) ng/mL	0.24 (0.04-0.5) ng/mL	0.24 (0.01-0.50) ng/mL	0.28 (0.03-0.05) ng/mL	0.20 (0.01-0.5) ng/mL
PSA at salvage					
0.01-0.04	3 (2.8%)	1 (2.3%)	2 (3.1%)	1 (2.1%)	2 (3.3%)
0.05-0.09	2 (1.9%)	0 (0)	2 (3.1%)	1 (2.1%)	1 (1.6%)
0.10-0.19	23 (21.3%)	14 (32.6%)	9 (13.8%)	10 (20.8%)	13 (21.7%)
0.20-0.29	36 (33.3%)	12 (27.9%)	24 (37%)	12 (25%)	24 (40%)
0.30-0.39	23 (21.3%)	9 (20.9%)	14 (21.5%)	16 (33.3%)	7 (11.7%)
0.40-0.50	21 (19.4%)	7 (16.3%)	14 (21.5%)	8 (16.7%)	13 (21.7%)
Maximum Gleason score (pathologic):					
<6	2 (1.8%)	0 (0)	2 (3.1%)	0 (0)	2 (3.3%)
6	5 (4.6%)	2 (4.6%)	3 (4.6%)	4 (8.3%)	1 (1.7%)
7	72 (66.7%)	29 (67.4%)	43 (66.2%)	31 (64.6%)	41 (68.3%)
8-10	29 (26.9%)	12 (28%)	17 (26.1%)	13 (27.1%)	16 (26.7%)
ADT					
Yes	43 (39.8%)	43 (100%)	0	25 (52.1%)	42 (70%)
No	65 (60.2%)	0	65 (100%)	23 (47.9%)	18 (30%)
Margins					
Positive	48 (44.4%)	18 (41.9%)	23 (35.4%)	48 (100%)	0
Negative	60 (55.6%)	25 (58.1%)	42 (64.6%)	0	60 (100%)
Pathologic T-category					
pT2	54 (50%)	20 (46.5%)	34 (52.3%)	18 (37.5%)	36 (60%)
pT3a	29 (26.9%)	14 (32.5%)	15 (23.1%)	16 (33.3%)	12 (20%)
pT3b	25 (23.1%)	9 (21%)	16 (24.6%)	14 (29.2%)	12 (20%)

Abbreviations: ADT = androgen deprivation therapy; PSA = prostate-specific antigen; RP = radical prostatectomy; RT = radiotherapy.