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Risk factors for biochemical recurrence after a tissue-ablative prostate-specific antigen <0.2 ng/mL

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ABSTRACT

PURPOSE: A prostate-specific antigen (PSA) nadir <0.2 ng/mL is generally considered as tissue ablative and at low risk for recurrence. After attaining such a low PSA nadir, we analyzed risk factors for recurrence.

METHODS AND MATERIALS: We identified patients from our institutionalized database with either D'Amico low- or intermediate-risk prostate cancer that was treated with either low-dose-rate prostate brachytherapy or external beam radiotherapy as monotherapy. We compared patients who attained a nadir <0.2 ng/mL and subsequently developed biochemical failure to patients who did not experience biochemical failure by using χ^2 test and Student t test. Survival analysis was performed using the Kaplan–Meier method (log-rank test).

RESULTS: Of 892 patients, 560 (63%) achieved a nadir <0.2 ng/mL. Only 23 (4.1%) later developed a biochemical recurrence. The 7-year Kaplan–Meier biochemical recurrence-free survival after a PSA nadir of <0.2 ng/mL was 96%. Patients who later experienced biochemical recurrence were more likely to have Cancer of the Prostate Risk Assessment Score intermediate- or high-risk cancer: (74% vs. 40%, $p < 0.001$). Patients were more likely to have a diagnostic PSA >6.0 ng/mL: (66% vs. 43% $p < 0.001$) and have a Gleason score $\geq 3 + 4$: (52% vs. 34%, $p = 0.005$). They were also more likely to be older ($p = 0.003$): mean (SD) 70.3 (6.4) vs. 66.2 (6.5) and have a time to PSA nadir that was significantly shorter ($p = 0.013$): mean (SD) 51.8 (29.6) vs. 65.2 (25.1).

CONCLUSIONS: Biochemical recurrence after attaining a PSA nadir <0.2 ng/mL is rare and more frequent in patients with intermediate risk cancer and older patients. These patients can benefit from a prolonged followup with specialized physicians.

Keywords: Prostate cancer; Radiotherapy; Brachytherapy; Tissue-ablative PSA; PSA Nadir; Biochemical failure

Introduction

Patients achieving a low prostate-specific antigen (PSA) nadir (<0.2 ng/mL) are generally considered at low risk for biochemical failure (bF); however, the transfer of patients to their general practitioner is often met with doubt. They may be ideal candidates to have their followup with their general practitioner, thus avoiding a return visit to [1] a specialist [1].

We analyzed risk factors for recurrence after attaining such a low PSA nadir, which is often considered as tissue ablative. Such knowledge could help reassure patients and identify those who do not need a followup by a specialist.

Methods

We identified 892 patients from our institutionalized database with either D'Amico classification of low- or intermediate-risk prostate cancer that was treated with either low-dose-rate prostate brachytherapy (LDR-PB) or external beam radiotherapy (EBRT) as monotherapy. Patients treated with neoadjuvant or adjuvant androgen

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deprivation therapy were excluded. Institutional ethical review board approval was obtained.

bF was defined according to the Phoenix definition (nadir + 2 ng/mL) [2]. All patients without any bF had a minimum followup of 48 months.

We separated patients into three different treatment groups: (*1*) normofractionation was defined as receiving 1.8−2.0 Gy per day in daily treatments to a total dose of 70.2−80 Gy, (*2*) hypofractionation was defined as receiving either 60 Gy in 3 Gy daily fractions, five times a week, or alternatively 45 Gy in once weekly fractions of 5 Gy [3], or 36.25 Gy in once weekly fractions of 7.25 Gy, and (*3*) patients treated with LDR-PB of 144−160 Gy.

Patient data were entered into the database prospectively. Patients for whom no regular visits were scheduled were regularly called throughout the year as to obtain information on their PSA.

Statistical analysis

We compared patients who subsequently developed bF to patients without failure using χ^2 test for categorical variables and Student *t* test to compare means. Multivariate analysis was adjusted for treatment type to avoid bias for LDR-PB. Survival analysis was performed using the Kaplan−Meier method (log-rank test). The analysis was performed using SPSS 25.0 for Windows (IBM SPSS, Chicago, Illinois). *p*-value ≤ 0.05 was deemed significant.

Results

Of 892 patients, we report the results of 560 (63%) patients who achieved a nadir <0.2 ng/mL (Table 1). In the normofractionation group, 38% achieved a nadir <0.2 ng/mL (12% of our study population), 31% in the hypofractionation group (7% of study population), and 77% in the LDR-PB group (81% of study population).

The median followup in patients without recurrence was 78 months (interquartile range 56−102). The median of the last PSA reported in patients without bF was 0.05 ng/mL (interquartile range 0.02−0.10).

Thus far, 28 patients (5%) have died; 3 patients, who were treated with EBRT died from prostate cancer. Mean and median time to recurrence was 53.2 months (standard deviation [SD] 38.2) and 46.0 months, respectively. Fig 1 illustrates the time to bF in all patients who had a PSA nadir <0.2 ng/mL.

Only 23 (4.1%) of the 560 patients developed a biochemical recurrence. This occurred more frequently ($p < 0.001$, X^2 test) in the normofractionated group (11/68 patients; 16.2%) than in the hypofractionated group (4/38; 10.5%) or the LDR group (8/446; 1.8%).

The 7-year Kaplan−Meier analysis for biochemical recurrence−free survival after a PSA nadir <0.2 ng/mL was 96% for all patients and better after LDR-PB (98%) than that after normofractionation (90%) and hypofractionation (91%) ($p < 0.001$, log-rank test between treatment modalities). This difference remained after stratification

Table 1
Comparison of patients with a PSA nadir of <0.2 mg/mL according to treatment received

Univariate analysis	Normofr (n = 68)	LDR-PB (n = 454)	60 Gy/20 (n = 9)	1×/week (n = 29)	Intergroup comparison *p*-value[a]	Log-rank test
Age >70 years	63	22	89	52	**<0.001**	**<0.001**
Median (IQR)	72 (66−74)	66 (62−70)	76 (73−79)	71 (65−73)	**<0.001**[b]	
CAPRA score					**<0.001**	**<0.001**
1−2 (low)	15	66	0	64		
3−5 (intermediate)	78	34	78	36		
6−7 (high)	7	0.2	22	0		
PSA (ng/mL)					**<0.001**	**<0.001**
0−6	56	60	33	45		
6−10	29	35	44	52		
10−20	25	6	22	3		
Gleason					**<0.001**	**0.013**
6	13	71	0	97		
3 + 4	60	26	44	3		
4 + 3	27	2	56	0		
Biopsy >33%	56	38	33	61	**0.006**	**0.043**
T-stage, % T2	41	24	33	28	**0.027**	0.10
T1 vs. T2						
Time to PSA nadir >48 mo	77	82	67	66	0.09	**0.001**
Median (IQR)	66 (48−90)	60 (48−84)	48 (36−84)	72 (40−78)	0.47[b]	
Followup patients without bF						–
Median (IQR)	102 (78−114)	72 (56−96)	81 (72−102)	108 (75−108)	**<0.001**[b]	

Results shown as percentages. Bold indicates $p < 0.05$.

CAPRA = Cancer of the Prostate Risk Assessment; Normofr = normofractionation group; LDR-PB = low-dose-rate prostate brachytherapy; IQR = interquartile range; PSA = prostate-specific antigen; bF = biochemical failure.

[a] χ^2 test.

[b] Kruskal−Wallis nonparametric test.