

Improved biochemical disease-free survival with immediate irradiation after radical prostatectomy with positive surgical margins-a match-paired analysis

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Introduction

EORTC trial 22911 demonstrated that immediate postoperative irradiation after radical prostatectomy (RP) improved biochemical outcome compared to surveillance alone in patients with pT2-3 tumors and pathological risk factors (Bolla et al., Lancet 2005). After analyzing by risk factor subgroups, the benefit of this approach has been shown across all patient groups (Collette et al., Eur J Cancer 2005). However, little is known about the influence of the location and type of positive surgical margins in this modality of treatment. We performed a retrospective match-paired analysis of prostate cancer patients treated non-randomly with RP vs RP plus immediate irradiation for positive surgical margins.

Methods

We reviewed the charts of 723 patients who underwent RP for cT1-2N0M0 prostate cancer. We analyzed 140 patients (pT2-3, positive margins, undetectable postoperative PSA level), 70 of whom were treated to immediate irradiation (median 64 Gy, range 60-66 Gy, 2 Gy fractions, start before 3 months post-op). The patients were matched with age, initial PSA, Gleason score, clinical and pathological stage, margin status and follow-up [Table 1]. Biochemical relapse was defined according to the ASTRO criteria. An analysis for the cumulative risk of biochemical failure was performed.

Table 1. Baseline characteristics for match-pair analysis between irradiated and non-irradiated patients

	RT	No RT
N	70	70
Age	65.0 (62.8,67.6)	64.0 (61.8,65.4)
Initial PSA (ng/mL)	9.3 (9.2,13.5)	9.4 (8.9,11.3)
<10	42 (60%)	40 (57%)
≥10	28 (40%)	30 (43%)
Gleason score		
<7	44 (63%)	45 (64%)
≥7	26 (37%)	25 (36%)
Clinical stage		
T1	44 (63%)	41 (59%)
T2	26 (37%)	29 (41%)
Pathological stage		
T2	27 (39%)	25 (36%)
T3	43 (61%)	45 (64%)
Positive margin status		
Focal	52 (74%)	52 (74%)
Multiple	18 (26%)	18 (26%)
Follow-up (months)	50.0 (46.4,57.6)	49.0 (34.7,56.9)

Data are number (%) or median (95% CI of mean)

All differences were not significant

Conclusions

Although the limitation of a non-randomized study, our results demonstrated an improved biochemical disease-free survival with immediate irradiation after RP for prostate cancer with positive surgical margins. In our experience, this approach benefits pT3, Gleason score < 7 and multiple surgical margins patients despite their anatomical location. Longer follow-up is needed to assess the endpoint of clinical disease-free survival.

Results

Immediate irradiation improved biochemical disease free survival in positive surgical margins patients (7-year biochemical control rate 69% vs 78%, p=0.04) [Figure 1]. The median time until biochemical failure increased 20 months in the irradiated patients (73.0 months, 95% CI 61.0-85.0 vs 93.0, 82.0-104.0) [Figure 2]. In univariate analysis by Kaplan-Meier method, pT3, Gleason score < 7 and multiple

surgical margins patients [Figure 3-5] have improved biochemical outcome while location of surgical margin has not [Table 2]. In the multivariate Cox proportional hazards regression model, these three variables were significantly associated with the biochemical disease free survival. The estimates from the final model including the significant covariates are given in table 3.

**Figure 1. Overall PSA progression-free survival time in relation to immediate irradiation
Log Rank (Mantel-Cox): Chi-Square 4.067, p=0.04**

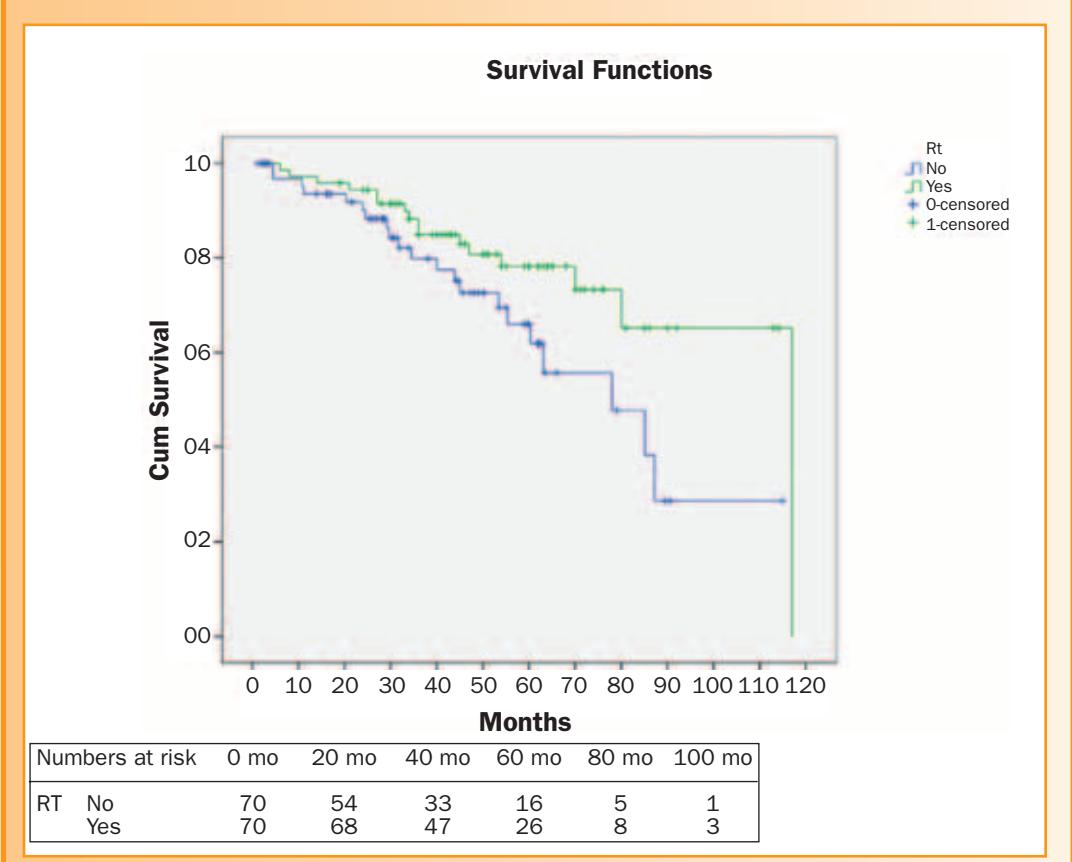


Figure 2. The median time until biochemical failure increased significantly in the irradiated patients

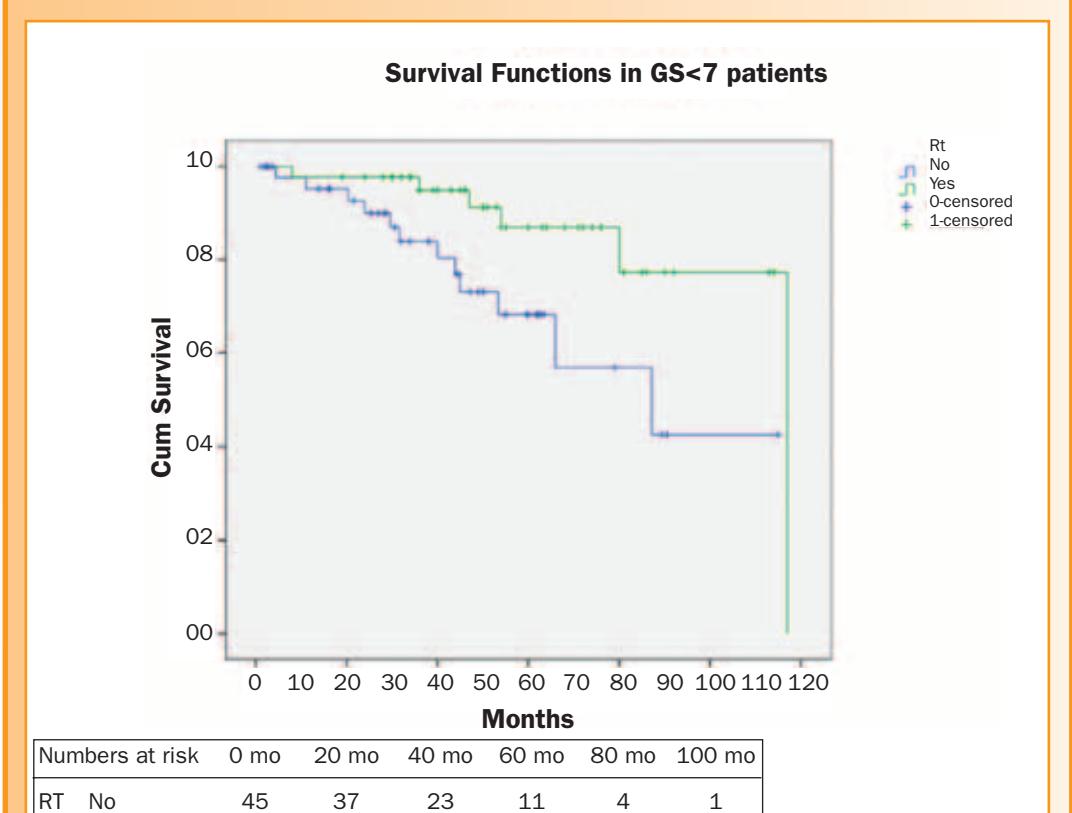
Case Processing Summary

Rt	Total N	N of Events	Censored N	Percent
No	70	21	49	69%
Yes	70	16	54	78%
Overall	140	37	103	73,60%

Medians for Survival Time

Rt	Estimate	Std. Error	Median 95% Confidence Interval	
			Lower Bound	Upper Bound
No	72,992	6,203	60,834	85,151
Yes	93,243	5,662	82,145	104,341
Overall	83,709	4,558	74,776	92,642

**Figure 4. PSA progression-free survival time in GS<7 patients
Log Rank (Mantel-Cox): Chi-Square 5.580, p=0.018**



**Figure 5. PSA progression-free survival time in multiple positive surgical margin patients
Log Rank (Mantel-Cox): Chi-Square 5.137, p=0.023**

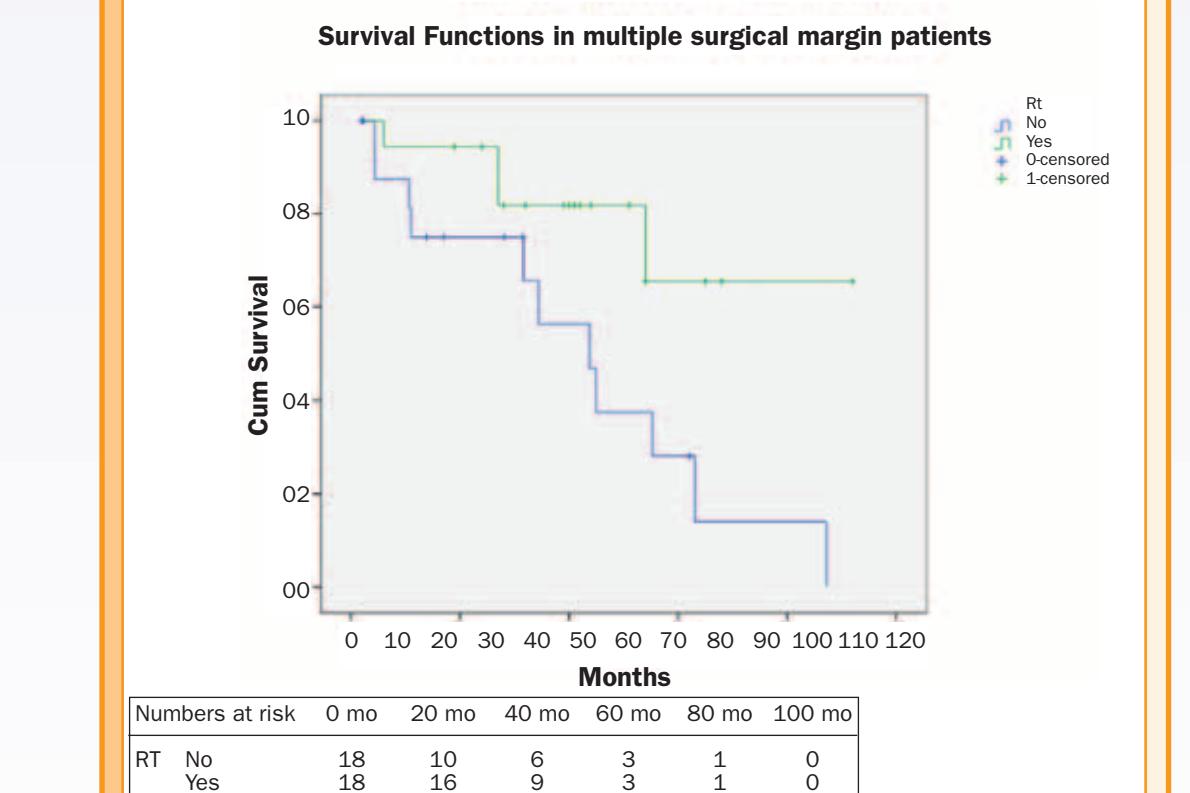


Table 2. Variables that did not show significant differences in univariate analysis

Variable	Chi-Square	p
PSA<10	3.220	0.085
PSA≥10	1.231	0.267
ct1	2.413	0.120
ct2	1.729	0.189
pT2	0.860	0.354
Focal margin	0.755	0.835
Apical	0.074	0.785
Basal	2.560	0.110
Postero-lateral	0.171	0.679

Table 3. Results of multivariate analysis

Variable	Hazard ratio	95% CI	p
Pathological stage	0.381	0.191-0.759	0.006
Gleason score	0.397	0.197-0.796	0.009
Multiple margin	0.383	0.191-0.767	0.007