

# Nadir PSA and time to nadir PSA after radiotherapy ± androgen deprivation as predictor of prostate cancer outcome.

## PURPOSE

To determine whether nadir prostate-specific antigen (nPSA) < 1 ng/ml and the time to nPSA (TnPSA) are associated to biochemical or clinical failure after external beam radiotherapy for localised prostate cancer.

## PATIENTS AND METHODS

•From 1979 to 1999, **981 patients with T1b-T4 N0M0 stage prostate cancer** were treated with radical external beam radiotherapy (EBRT) ± androgen deprivation (AD). All medical records were reviewed.

•Clinical stage (according to the 1997 AJCC classification), Gleason, initial PSA and androgen deprivation distribution are shown in figs. 1-4).

•Initial PSA values (median PSA: 11.3 ng/ml) were available in 811 patients. In 651 of these, there were at least 4 PSA determinations at follow-up to study the biochemical failure (BF) incidence -according to ASTRO definition.

•**Radiotherapy treatment:** all patients were treated with megavoltage irradiation 1.8-2 Gy/day.

*Pelvic field* (907 p): conventional blocked four-field. *Mean dose:* 46 Gy (27-56 Gy).

*Prostate field:* conventional blocked four-field or 120° bilateral arc rotation. *Mean dose:* 70Gy (55-76.6 Gy).

•**Follow-up :** All patients were seen regularly every 6-12 months in the first 5 years and annually thereafter. Mean: 4.39 years (median: 3.9 y; min.0.15 y and max. 17.3 y).

•**Statistical analysis:**To identify the effect of potential prognostic factors on treatment outcome, univariate analysis was performed using the log-rank test. Multivariate analysis was performed using the Cox proportional hazards model. Chi-square test was performed to evaluate the relation of nPSA and TnPSA with biochemical failure. Estimates of BF and cause-specific survival were calculated using the Kaplan-Meier product-limit method. The log-rank test was used for comparisons between survival curves.

### Distribution of the pretreatment clinical characteristics.

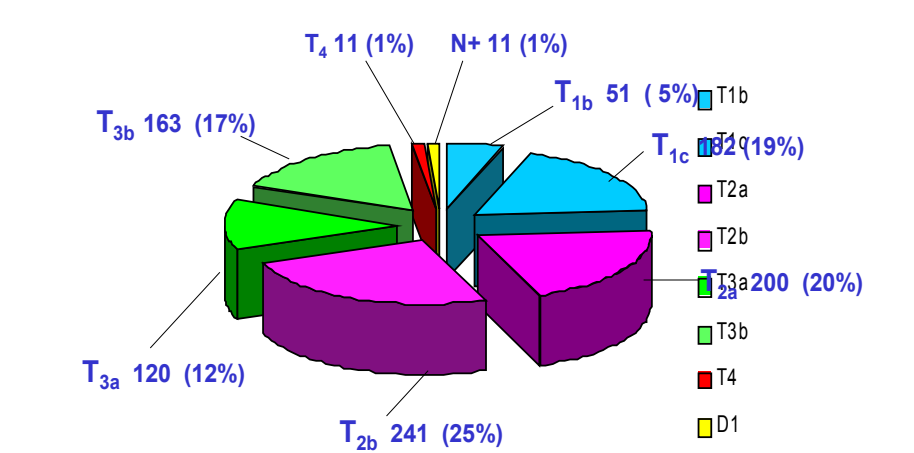


Fig.1 Staging distribution (TNM 1997)

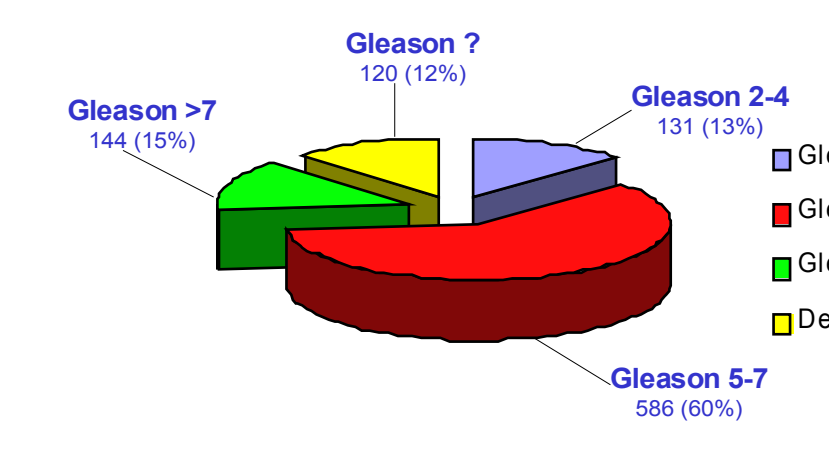


Fig.2 Gleason classification

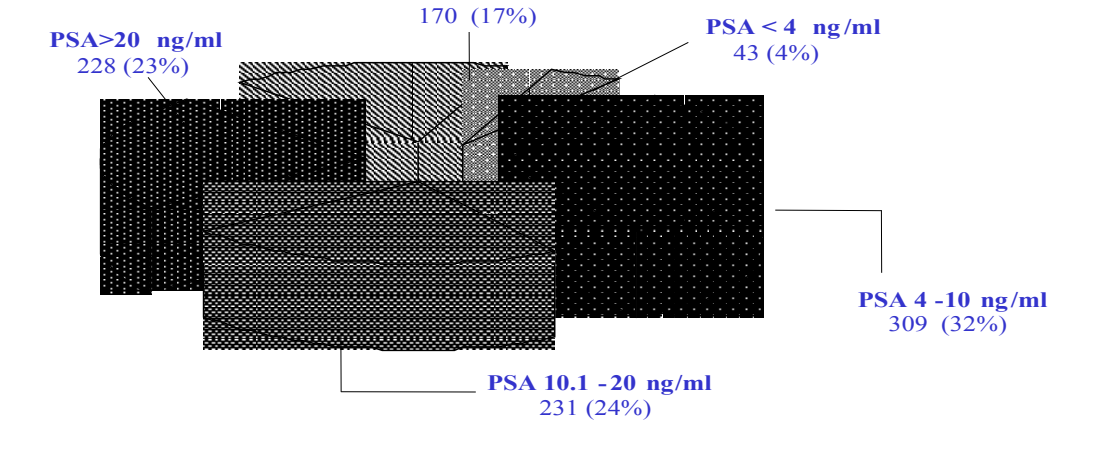


Fig.3 PSA classification

### Treatment characteristics

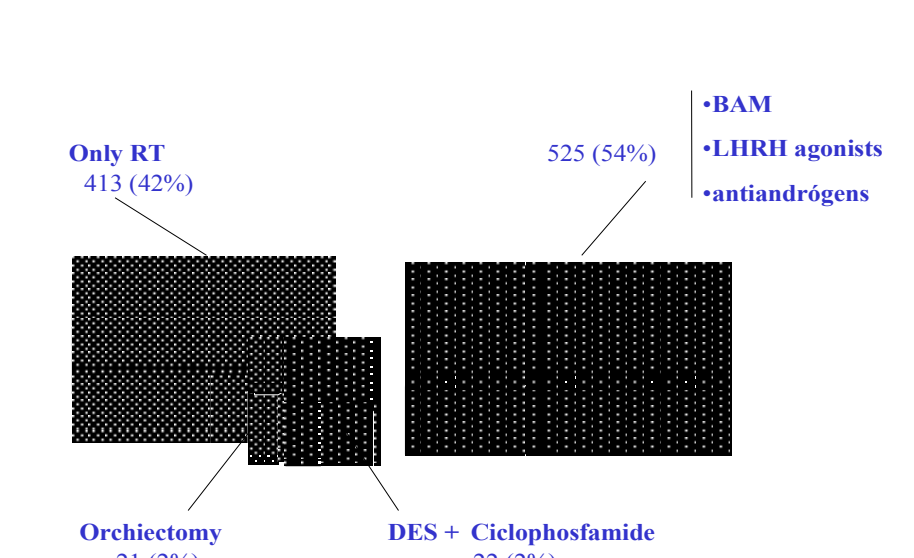


Fig.4 Hormonal treatment distribution.

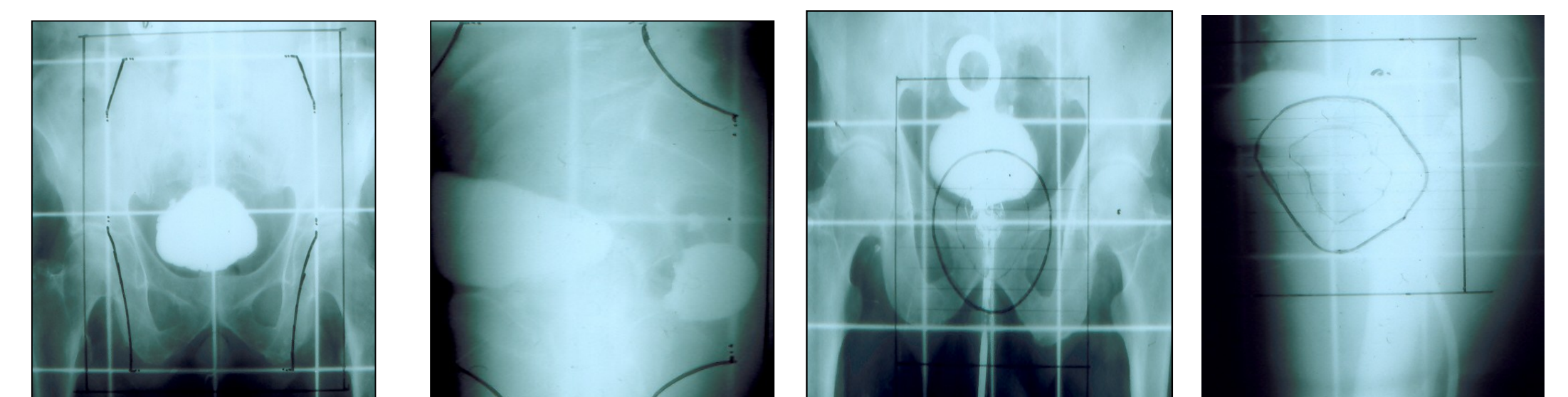
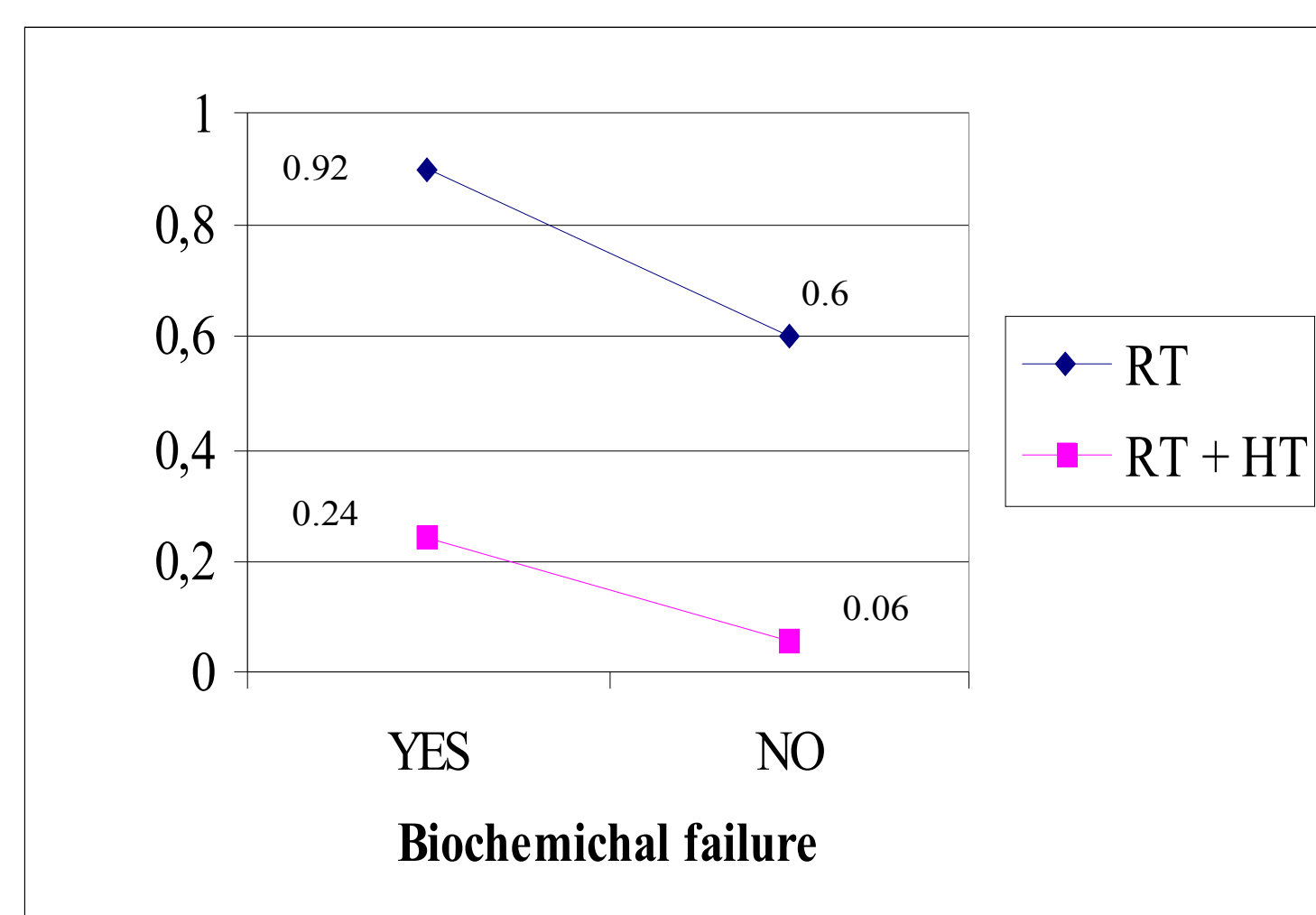


Fig.5 Simulation portals for four-field pelvic treatment.

Fig.6 Simulation portals for four-field prostate treatment.

## RESULTS

- BF was observed in 178/651 (27%) patients.
- The median nPSA was 0.20 ng/ml for BF-free patients and 0.49 ng/ml for the group with BF (p<0.001).
- For patients treated with RT alone the nPSA was 0.6 ng/ml and 0.92 ng/ml respectively (p<0.001), and for patients with RT and AD it was 0.06 and 0.24 ng/ml.



- For patients with nPSA ≥ 1 ng/ml the risk of BF was greater (44/122;36%) than for those with nPSA < 1 ng/ml 134/529; 25%). The difference was also significant for the group of patients treated with only RT.

Table 1. Nadir PSA and biochemical failure

Nadir PSA	Biochemical failure		Total
	No	Yes	
< 1 ng/ml	395 (75%)	134 (25%)	529
≥ 1 ng/ml	78 (64%)	44 (36%)	122
	473 (73%)	178 (27%)	651

$\chi^2$ : p = 0.013  
OR: 1.66 (IC: 1.07-2.57)

- Multivariate analysis confirmed that age, stage, Gleason score, pretreatment PSA, dose and nPSA < 1 ng/ml were all significantly associated with BF and clinical failure.

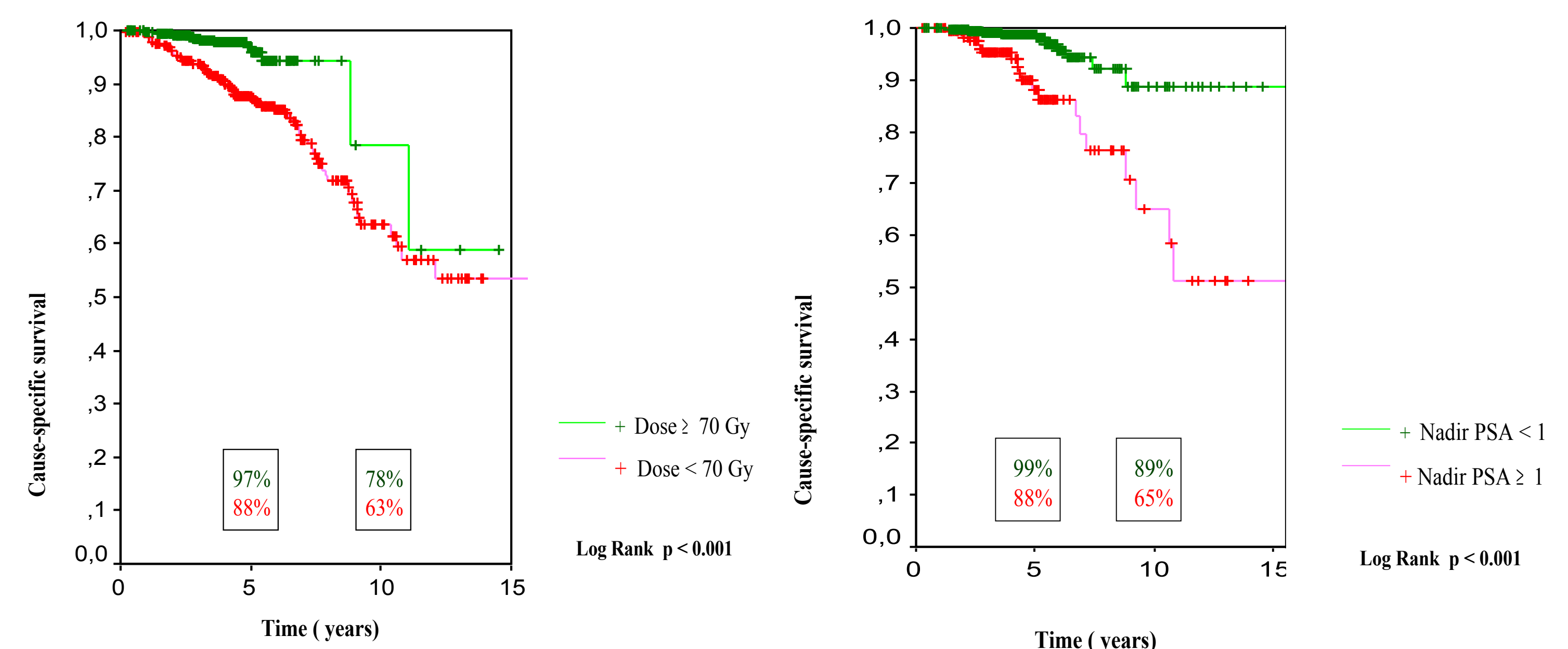
Table 3. Biochemical failure prognostic factors.. Multivariate analysis.

	$\beta$	p-Value	Exp(B)	C.I. 95% for Exp(B)
Age	-0.043	0.010	0.958	0.972-0.990
PSA	0.008	0.001	1.008	1.003-1.013
Gleason	0.197	0.003	1.218	1.072-1.385
T1-T2 stage	-0.936	0.001	0.923	0.224-0.687
Dose RT	-0.195	0.000	0.823	0.760-0.890
Androgen deprivation		NS		
Nadir PSA < 1 ng/ml	-0.533	0.033	0.587	0.359-0.959

- Multivariate cox regression showed stage and nPSA<1 ng/ml to be the only parameters associated with cause-specific survival.

Table 4. Cause-specific survival: multivariate analyses.

	$\beta$	p-Value	Exp(B)	C.I. 95% for Exp(B)
Age		NS		
PSA		NS		
Gleason		NS		
T1-T2 stage	-1.621	0.000	0.198	0.084-0.468
Dose RT (≥ 70 Gy)		NS		
Androgen Deprivation		NS		
Nadir PSA < 1 ng/ml	-1.607	0.001	0.200	0.079-0.509



- A TnPSA longer than 1 year was associated with less BF (52/284;18%) than TnPSA ≤ 1 year (126/367;34%) (p<0.001;OR: 2.15).

Table 5. Tnadir PSA and biochemical failure

Tnadir PSA	Biochemical failure		Total
	No	Yes	
≤ 1 year	241 (66%)	126 (34%)	367
> 1 year	232 (82%)	52 (18%)	284
	473 (73%)	178 (27%)	651

$\chi^2$ : p < 0.001  
OR: 2.15 (IC 95%: 1.46-3.19)

## CONCLUSION

A lower nPSA (< 1 ng/ml) and longer TnPSA (>1 year) are associated with improved outcome. There was a close relation between nadir PSA ≥ 1 ng/ml and subsequent development of biochemical and clinical failure.