seram Sociedad Española de Radiología Médica
35 Congreso Nacional
Edición Virtual
19/26 MAYO 2021
17/18 MAYO 2021
CURSO PRECONGRESO
Symposium SERAM-RSNA

Outcomes and factors by risk group after prostate brachytherapy: Cohort study in 2316 patients

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PURPOSE

To evaluate the biochemical freedom from failure (bFFF) by risk group and treatment modality and the predictive factors of bFFF by risk group in patients with prostate cancer (PCa) undergoing permanent seed implantation (PI) with or without external beam radiation therapy (EBRT) in a nationwide prospective cohort study in Japan (J-POPS) during the first 2 years.

MATERIALS AND METHODS

- A total of 2,354 participants who were enrolled in the J-POPS study during the first 2 years (cohort 1)
- The median follow-up period: 60.0 months (interquartile range, 58.7–60.9 months)
- Loose I-125 seeds
- The recommended prescribed dose
  PI monotherapy:144 Gy
  EBRT combination therapy: PI 100–110 Gy + EBRT 40–50 Gy
- Risk groups

Low-risk group 1,028 cases	Intermediate-risk group 1,114 cases	High-risk group 133 cases	Locally advanced 2 cases
PSA <10 and GS ≦ 6 and T ≦ 2a	PSA 10–20 and/or GS = 7 and/or T2b–T2c	PSA >20 and/or GS 8 ~ 10 and/or T3a	T3b–T4

- Baseline characteristics of patients

Factors	n	Mean	SD	Minimum	Median	Maximum	Missing
Age (year)	2,316	68.1	6.4	45	69	89	0
Low-risk group	1,028	67.3	6.5	45	68	89	0
Intermediate-risk group	1,114	68.6	6.2	51	69	88	0
High-risk group	133	69.8	6.2	55	71	84	0
Pretreatment PSA (ng/ml)*	2,298	8.0	4.1	1.6	6.8	42.0	18
Low-risk group	1,028	6.2	1.7	1.6	6.0	9.98	0
Intermediate-risk group	1,114	8.8	3.7	1.9	8.1	20.0	0
High-risk group	132	14.6	9.0	3.7	11.4	42.0	1
Percent positive biopsies	2,196	27.5	19.1	3.9	21.4	100	120
Low-risk group	975	22.2	14.9	4.2	16.7	100	53
Intermediate-risk group	1,058	30.7	19.8	3.9	25	100	56
High-risk group	131	39.1	27.8	7.1	33.3	100	2
Prostate volume (ml)†	2,316	25.9	8.2	7.0	25.2	71.0	0
Low-risk group	1,028	26.9	8.1	7.3	26.2	60.9	0
Intermediate-risk group	1,114	25.4	8.3	8.6	24.8	71	0
High-risk group	133	22.9	7.8	7.0	22.2	45.8	0
Implanted seed number	2,316	68.3	16.6	25	69	120	0
Low-risk group	1,028	73.8	14.5	26	75	120	0
Intermediate-risk group	1,114	65.0	16.8	28	65	118	0
High-risk group	133	53.2	13.0	25	50	99	0
Total activity (MBq)	2,316	929.3	293.7	244.8	903.9	1,836	0
Low-risk group	1,028	1,000.9	267.9	254.5	982.5	1,836	0
Intermediate-risk group	1,114	868.8	225.0	334.0	915.4	1,545.8	0
High-risk group	133	707.6	236.0	265.5	640	1,514.7	0

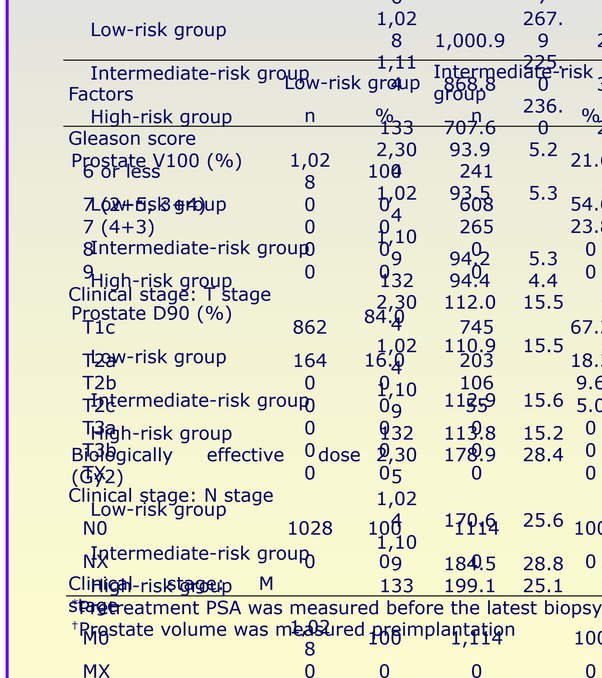
Factors	Low-risk group n	Low-risk group %	Intermediate-risk group n	Intermediate-risk group %	High-risk group n	High-risk group %	Total n	Total %
Gleason score								
6 or less	1,028	100	241	21.6	15	11.3	1,284	55.4
7 (3+4)	0	0	608	54.6	22	16.5	640	27.7
7 (4+3)	0	0	265	23.8	14	10.5	281	12.2
8	0	0	0	0	63	47.4	63	2.7
9	0	0	0	0	19	14.3	19	0.8
High-risk group	132	94.4	4.4	78.4	95.4	100.0	1	
Clinical stage: T stage								
Prostate D90 (%)	2,304	84.0	112.0	15.5	40.1	112.4	191.6	12
T1c	862	4	745	67.2	61	45.9	1,693	73.4
Low-risk group	164	16.0	203	18.3	31	23.3	403	17.5
T2a	0	0	106	9.6	15	11.3	121	5.3
T2b	0	0	55	5.0	10	7.5	66	2.9
T2c	0	0	1	0	16	12.0	16	0.7
T3a	0	0	0	0	2	1.5	2	0.1
T3b	0	0	5	0	0	0	5	0.2
(TX)								
Clinical stage: N stage								
Low-risk group	1,028	100	1114	100	133	100	2,299	99.4
N0	0	0	0	0	0	0	14	0.6
Intermediate-risk group	1,114	100	1,114	100	133	100	2,297	99.3
NX	0	0	0	0	0	0	16	0.7
Treatment modalities								
PI	1,011	98.3	701	62.9	23	17.3	1,774	76.6
PI + EBRT	17	1.7	413	37.1	110	82.7	542	23.4
Hormonal treatment								
Yes	495	48.1	607	54.5	107	80.5	1,209	52.2
No	533	51.9	507	45.5	26	19.5	1,107	47.8

- The Phoenix PSA failure definition (PSA nadir + 2.0 ng/mL) was used to define bFFF.
- The Kaplan-Meier method was used to estimate the bFFF. The Cox proportional hazards model was also used to identify the factors associated with the bFFF.
- A multivariate analysis was performed using the factors that were found to be significant in the univariate analysis.

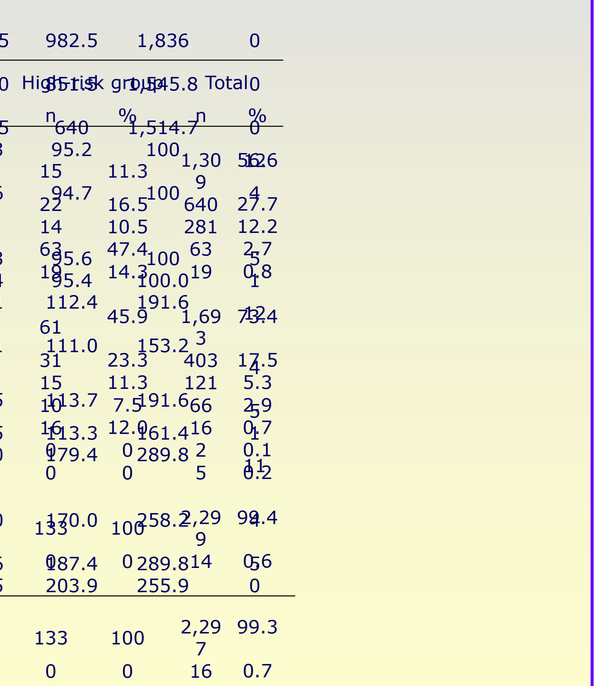
*Pretreatment PSA was measured before the latest biopsy
†Prostate volume was measured preimplantation

RESULTS

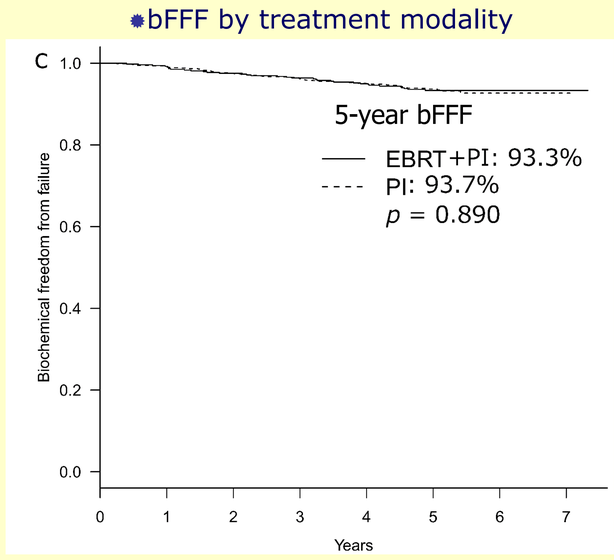
- bFFF in all patients



- bFFF by risk group



- bFFF by treatment modality



Analysis of factors associated with bFFF

Factors		Univariate analysis HR	95% CI	p	Multivariate analysis HR	95% CI	p
All cases							
Age		0.960	0.936–0.985	0.0016*	0.957	0.932–0.983	0.0012*
Pretreatment PSA		1.040	1.007–1.074	0.0161*	1.019	0.985–1.054	0.2830
Gleason score		–	–	<0.0001*	–	–	0.0030*
	6 or less		Reference			Reference	
	7 (3+4)	1.353	0.904–2.025	0.1412	1.261	0.826–1.925	0.2828
	7 (4+3), 8 to 10	2.460	1.649–3.670	<0.0001*	2.149	1.380–3.347	0.0007*
% Positive biopsies		1.016	1.009–1.024	<0.0001*	1.012	1.004–1.020	0.0026*
Prostate V100 (%)		0.968	0.943–0.995	0.0187	0.970	0.942–0.998	0.0368*
Low-risk group							
Age		0.928	0.891–0.967	0.0004*	0.926	0.889–0.964	0.0002*
Pretreatment PSA		1.219	1.044–1.423	0.0123*	1.246	1.069–1.452	0.0048*
Prostate D90 (%)#		0.983	0.967–0.999	0.0397*	–	–	–
Prostate V100 (%)		0.944	0.907–0.982	0.0044*	0.936	0.899–0.974	0.0012*
Intermediate-risk group							
Gleason score		–	–	0.0005*	–	–	0.0005*
	6 or less		Reference			Reference	
	7 (3+4)	2.149	0.958–4.821	0.0634	2.187	0.919–5.205	0.0769
	7 (4+3)	4.258	1.875–9.671	0.0005*	4.538	1.879–10.960	0.0008*
% Positive biopsies		1.014	1.003–1.024	0.0110*	1.014	1.003–1.025	0.0120*
Hormonal treatment	Yes	0.560	0.353–0.886	0.0133*	0.470	0.290–0.762	0.0022*
	No		Reference			Reference	
High-risk group							
Gleason score		–	–	0.0035*	–	–	0.0329*
	7 or less		Reference			Reference	
	8	0.503	0.084–3.010	0.4514	0.959	0.1455–6.317	0.9651
	9	5.544	1.386–22.170	0.0154*	5.553	1.201–25.670	0.0282*
% Positive biopsies		1.036	1.015–1.057	0.0007*	1.028	1.006–1.051	0.0120*
Prostate D90 (%)		1.041	1.003–1.081	0.0327*	1.047	0.9991–1.097	0.0545

*Significant risk factor
#Prostate D90 is the collinearity factor of prostate V100; therefore, prostate D90 is excluded in the multivariate analysis

DISCUSSION

- Our outcome in high-risk patients was relatively favorable as compared with the outcomes in the other studies [1-5].

  ↓

  We assume that this may be attributable to the higher rate of high-risk patients who received HT and the lower rate of patients with stage T3+ in all high-risk patients.

- The factor associated with bFFF: Younger age → Low-risk group
  - The relationship between younger age and more aggressive clinical behavior of PCa has been previously documented , and there is evidence that young-age PCa has several biological and genetic features, distinct from elderly-onset PCa [6, 7].

    ↓

    Because of the low BED and the low rate of patients who received HT in low-risk patients, aggressive PCa may not have been controlled.
- The factor associated with bFFF: Lower prostate V100 and D90 → Low-risk group
  - Because of the low rate of patients who received HT or EBRT in low-risk patients, the prostate dose of PI may have had a strong effect on the local control.
- The factor associated with bFFF:
  Higher percent positive biopsies → Intermediate-risk and high-risk group
  - Many studies reported that higher percent positive biopsies has been correlated with a higher likelihood of extracapsular extension [8-12].

    ↓

    Because of the lower percent positive biopsies, the probably low rate of extracapsular extension, and the low standard deviation of percent positive biopsies in low-risk patients, the percent positive biopsies may have not been a factor associated with biochemical failure.

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CONCLUSIONS

- PI with or without EBRT resulted in excellent short-term biochemical outcomes at all risk groups, especially at high-risk group in Japanese prostate cancer patients.
- Younger age, higher pretreatment PSA, and lower prostate V100 · D90 in low-risk patients; higher GS, higher percent positive biopsies, and no HT in intermediate-risk patients; and higher GS and higher percent positive biopsies in high-risk patients independently affected biochemical failure.