Supplementary Online Content

Patel HD, Tosoian JJ, Carter HB, Epstein JI. Adverse pathologic findings for men electing immediate radical prostatectomy: defining a favorable intermediate-risk group. Published online July 13, 2017. *JAMA Oncol*. doi:10.1001/jamaoncol.2017.1879

This supplementary material has been provided by the authors to give readers additional information about their work.

Supplementary Material

Contents:

eTable 1. Clinical characteristics of favorable low-volume intermediate-risk patients by pathology at radical prostatectomy.

	No Adverse Pathology		Adverse RP Pathology		p-value
	Median/N	**(% or IQR)**	**Median/N**	**(% or IQR)**	
Total	458	(75%)	150	(25%)	-
Age	61	(56-65)	61	(56-66)	0.68
Year	2011	(2008-2014)	2010	(2008-2013)	0.02
PSA	4.8	(3.9-6.5)	6.1	(4.4-9.0)	<0.001
PSAD	0.10	0.07-0.14	0.13	(0.09-0.19)	<0.001
Two positive cores	265	(58%)	77	(51%)	0.16
Max % core inv.	30.0	(15-50)	37.5	(15-60)	0.35

RP = radical prostatectomy, PSA = prostate-specific antigen, PSAD = PSA density, IQR = interquartile range

eTable 2. Stratified risk of adverse pathology by PSA and PSAD for patients at favorable low-volume intermediate-risk.

	No Adverse Pathology		Adverse RP Pathology		RR	(95% CI)	p-value
	N	(%)	N	(%)			
PSA							
PSA ≥ 4.0	327	(72%)	128	(28%)	2.19	(1.40-3.41)	0.001
PSA < 4.0	129	(87%)	19	(13%)	-	-	
PSA ≥ 10.0	33	(50%)	33	(50%)	2.36	(1.76-3.15)	<0.001
PSA < 10.0	423	(79%)	114	(21%)	-	-	
PSAD							
PSAD ≥ 0.08	313	(73%)	118	(27%)	1.63	(1.13-2.37)	0.010
PSAD < 0.08	139	(83%)	28	(17%)	-	-	
PSAD ≥ 0.12	172	(67%)	85	(33%)	1.85	(1.39-2.46)	<0.001
PSAD < 0.12	280	(82%)	61	(18%)	-	-	
PSAD ≥ 0.15	101	(62%)	63	(38%)	2.01	(1.53-2.64)	<0.001
PSAD < 0.15	351	(81%)	83	(19%)	-	-	
PSAD ≥ 0.20	48	(59%)	33	(41%)	1.86	(1.37-2.54)	<0.001
PSAD < 0.20	404	(78%)	113	(22%)	-	-	

RR = relative risk; CI = confidence interval; PSA = prostate-specific antigen; PSAD = PSA density; RP = radical prostatectomy

eTable 3. Stratified risk of adverse pathology by maximum percent core involvement and number of cores with cancer for patients with favorable low-volume intermediate-risk.

	No Adverse Pathology		Adverse RP Pathology		p-value
	N	(%)	N	(%)	
Max % Core					0.59
<20%	113	(75%)	37	(25%)	
20-49%	182	(78%)	51	(22%)	
≥50%	148	(74%)	52	(26%)	
# Core & Max % Core					0.29
1 core, <20%	60	(71%)	24	(29%)	
1 core, 20-49%	84	(79%)	22	(21%)	
1 core, ≥ 50%	40	(66%)	21	(34%)	
2 cores, <20%	53	(80%)	13	(20%)	
2 cores, 20-49%	98	(77%)	29	(23%)	
2 cores, ≥ 50%	108	(78%)	31	(22%)	

RP = radical prostatectomy

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eMethods

Low risk (LR) prostate cancer is defined as Gleason 3+3 (Grade Group (GG) 1), T1-T2a, and prostate-specific antigen (PSA) <10 ng/ml. Very-low risk (VLR) prostate cancer is defined as Gleason 3+3 (GG1), T1c, ≤2 biopsy cores showing cancer, ≤50% cancer in any core, PSA<10 ng/ml, and PSA density (PSAD)<0.15 [1]. Notably, during the same time period of the present study which includes only men undergoing radical prostatectomy, a total of 1248 LR men with 803 meeting VLR criteria were followed on active surveillance at Johns Hopkins. Men with intermediate-risk prostate cancer were not eligible for active surveillance. The low-volume intermediate risk (LVIR) cohort of patients with prostate cancer before risk-stratification was defined as Gleason 3+4 (GG2), ≤2 biopsy cores showing cancer, and PSA<20 ng/ml. A total of 2.6% of patients had <10 biopsy cores, 6% had 10-11 cores, and the remainder (>90%) had 12 or more cores. Limited pelvic lymph node dissections with a standard template were performed for 4952 (90.7%) patients of the included cohort including 586/608 (96.4%) of LVIR patients, 4366/4849 (90.0%) of LR patients, and 1115/1264 (88.2%) of the VLR subgroup.

The proportions of men found to have Gleason ≥4+3=7 (GG≥3) disease and other adverse pathologic features were compared by risk group. The additional subgroup analyses of the LVIR population (Grade Group 2) included restriction to additional criteria for VLR (T1c, PSAD<0.15, ≤50% cancer in any core) and LR disease (≤T2a, PSA<10 ng/ml) as mentioned above and as suggested by NCCN guidelines for further risk-stratification of the LVIR population [2].

Patient-level variables included age, race, family history of prostate cancer, PSA, PSAD, and pathologic findings on biopsy. Among patients with two cores showing cancer, biopsy Grade Group data was only recorded for the core showing highest grade of cancer. Therefore, we could not separate patients with only one core showing Gleason 3+4 (GG2) from those with both cores showing Gleason 3+4 (GG2) disease, but detailed volume stratification was performed by both number of cores and maximum percent core involvement with cancer.

eReferences

1. Epstein JI, Walsh PC, Carmichael M, Brendler CB. Pathologic and clinical findings to predict tumor extent of nonpalpable (stage T1c) prostate cancer. JAMA. 1994 Feb 2;271(5):368-74.
2. Mohler JL, Armstrong AJ, Bahnson RR, et al. Prostate Cancer, Version 1.2016. J Natl Compr Canc Netw. 2016 Jan;14(1):19-30.