

Title: Outcomes Of Active Surveillance For Men With Localized Prostate Cancer Stratified By AUA Risk Grouping

Authors: Andrew Gusev^{1,3}, Edouard H. Nicaise¹, Alice Yu¹, Timothy Baloda³, David Kuppermann¹, Keyan Salari¹, Carl Ceraolo¹, Michael L. Blute¹, Mark A. Preston², Douglas M. Dahl¹, Anthony I. Zietman², Adam S. Feldman¹

¹Massachusetts General Hospital, Boston, MA, USA

²Brigham and Women's Hospital, Boston, MA, USA

³University of Massachusetts Medical School, Worcester, MA, USA

Contact author email: Andrew.Gusev@umassmed.edu

Introduction:

Active surveillance (AS) is an accepted management strategy for very low risk, low risk, and some select cases of favorable intermediate risk localized prostate cancer (PCa).

Rationale:

Long term data, especially in the intermediate risk group, are critical for continued understanding of which patients are suitable for this strategy and when patients should transition to treatment.

Specific Aims:

We investigated our AS cohort to evaluate outcomes stratified by AUA risk groups with a focus on favorable intermediate risk.

Methods:

We reviewed our institutional database of men enrolled in AS for localized PCa from 1996-2016. Our AS protocol includes prostate specific antigen (PSA) and digital rectal exam (DRE) every 4-6 months for 3 years, then annually. Mandatory confirmatory 12 core biopsy is done at 12-18 months. Multiparametric magnetic resonance imaging (mpMRI) or additional systematic or MRI-fusion biopsies are done at the discretion of physician and patient. We evaluated freedom from treatment, freedom from metastasis, treatment type and indication. Survival analyses were conducted using Kaplan-Meier method, comparisons between risk group outcomes with the Wilcoxon rank sum test.

Results:

The cohort consisted of 1272 men: 637 very low risk (50.1%), 493 low risk (38.8%), 130 favorable intermediate risk (10.2%), and 12 unfavorable intermediate risk (0.9%). Unfavorable risk men were excluded from this analysis. Median follow-up time was 6.4 years (IQR 0.9-11.9). 1232 men (96.8%) had Grade Group (GG) 1 (Gleason 3+3) disease, 39 (3.1%) had GG 2 (Gleason 3+4), and one had GG 3 (Gleason 4+3). For the favorable intermediate risk group, 100 men (76.9%) were included due to PSA>10, while 30 (23.1%) were included either due to GG 2 or GG 1 with palpable (cT2) disease. 215 very low risk (33.8%), 190 low risk (38.5%), and 45 favorable intermediate risk (34.6%) men received treatment. Freedom from curative treatment at 5, 10, and 15 years was 67.9% (95% CI 65.1%, 70.1%), 56.0% (95% CI 52.4%, 59.3%), and 50.4% (95% CI 44.6%, 56.0%) respectively. Freedom from metastasis at 5, 10, and 15 years was 99.5% (95% CI 98.8%, 99.8%), 96.4% (95% CI 94.4%, 97.8%), 94.3% (95% CI 90.4%, 96.6%) respectively. Wilcoxon rank sum test indicated there was no significant difference in freedom from treatment nor freedom from metastasis between all three risk groups (Z=4.67, p = .097; Z=1.92, p = .383 respectively).

Conclusions:

Our results suggest that carefully selected men with favorable intermediate risk PCa may be reasonable candidates for active surveillance. Of note, PSA>10 was the primary driver for favorable intermediate risk classification in our cohort, as only a minority of these patients (20.1%) had GG 2. Overall, AS remains a safe and viable option for all three risk groups, with a 96.4% 10 year metastasis-free survival at our institution.

Table 1: Patient characteristics, treatment type, and indication

Baseline Characteristics	Very Low Risk N=637		Low Risk N=493		Favorable Intermediate Risk N=130	
	Median	IQR	Median	IQR	Median	IQR
Age at diagnosis, years	64.6	(59.1-69.8)	67.8	(62.2-73.1)	70.3	(66.5-75.7)
PSA, ng/mL	4.5	(3.3-5.46)	5.4	(4.2-7.04)	11.1	(10.0-13.6)
PSA density, ng/mL ²	0.09	(0.06-0.12)	0.18	(0.15-0.22)	0.18	(0.13-0.30)
% of positive cores	8.3	(8.3-16.6)	16.6	(8.3-24.3)	10	(8.3-16.7)
% max core positive	5	(5-15)	10	(5-30)	10	(5-25)
cT1 count	591	(92.8%)	454	(92.1%)	121	(93.1%)
cT2 count	46	(7.2%)	39	(7.9%)	9	(6.9%)

Treatment type	Very Low Risk N=215	Low Risk N=190	Favorable Intermediate Risk N=45
External beam radiotherapy	87 (40.5%)	93 (48.9%)	32 (71.1%)
Radical prostatectomy	103 (47.9%)	74 (38.9%)	11 (24.4%)
Brachytherapy	25 (11.6%)	23 (12.1%)	2 (4.4%)
Indication			
Grade progression	128 (59.5%)	124 (65.3%)	25 (55.6%)
Volume progression	41 (19.1%)	28 (14.7%)	4 (8.9%)
Patient driven	11 (5.1%)	9 (4.7%)	1 (2.2%)
PSA progression	29 (13.5%)	17 (8.9%)	10 (22.2%)
DRE progression	0 (0%)	0 (0%)	3 (6.7%)
Radiographic progression	5 (2.3%)	5 (2.6%)	2 (4.4%)
Unknown	1 (0.5%)	7 (3.7%)	0 (0%)

Figure 1: Kaplan-Meier freedom from curative treatment and freedom from PCa metastasis estimate

