Published in final edited form as:

Urology. 2012 October ; 80(4): 883–888. doi:10.1016/j.urology.2012.05.045.

Low Prostate-specific Antigen and No Gleason Score Upgrade Despite More Extensive Cancer During Active Surveillance Predicts Insignificant Prostate Cancer at Radical Prostatectomy

Jeong S. Han, Adam D. Toll, Ali Amin, H. Ballentine Carter, Patricia Landis, Stephen Lee, and Jonathan I. Epstein

Department of Pathology; Department of Urology; and Department of Oncology, The Johns Hopkins Medical Institutions, Baltimore, MD

Abstract

OBJECTIVE—To identify parameters that predict insignificant prostate cancer in 67 radical prostatectomies after biopsy reclassification to worse disease on active surveillance.

METHODS—Parameters evaluated at diagnosis and at biopsy reclassification included serum prostate-specific antigen, prostate-specific antigen density, number of positive cores, maximum percent involvement of cancer per core, and any interval negative biopsies. Gleason upgrading at biopsy reclassification was also assessed to predict insignificant cancer.

RESULTS—Mean time between diagnosis and radical prostatectomies was 30.3 months with a median of 3 biopsies (range 2–9). Nineteen of 67 (28.4%) had clinically insignificant cancer at radical prostatectomy. In the entire group, there were no variables significantly associated with insignificant cancer at radical prostatectomy. In a subgroup analysis of 37 patients without Gleason pattern 4/5 at biopsy reclassification, 16/37 (43.2%) showed insignificant cancer at radical prostatectomy. In this subgroup, prostate-specific antigen at diagnosis was significantly lower in men with insignificant cancer (3.7 ng/mL) vs significant cancer (5.4 ng/mL) ($P = .0005$). With prostate-specific antigen <4 ng/mL at diagnosis or at biopsy reclassification, 12/13 (92.3%) men showed insignificant cancer, whereas only 4/24 (16.7%) men with prostate-specific antigen >4 ng/mL both at diagnosis and at biopsy reclassification showed insignificant cancer.

CONCLUSION—Most men with biopsy reclassification while on active surveillance have significant disease at radical prostatectomy, justifying their treatment. Low prostate-specific antigen at diagnosis or at biopsy reclassification can predict a high probability of insignificant cancer in the absence of Gleason pattern 4/5 on biopsy. These men may be candidates for continuing active surveillance.

Overtreatment of well-differentiated, low-grade prostate cancer (Gleason score 6 tumors) is a recognized problem today, with systematic prostate gland sampling triggered by prostate-specific antigen (PSA) measurements.¹ Best evidence using endpoints from various sources, including competing risk analyses, surgical series, nonrandomized cohort studies, and randomized trials, all demonstrate the similarity of outcomes for men with Gleason score 6 tumors treated or not in the PSA era.^{2–6} Taken together, these data demonstrate that using a time horizon of 10–15 years, less than 3% of men diagnosed with well-differentiated tumors (Gleason score 6) and classified as *low risk* (based on a PSA <10 ng/mL and a stage of

T2a) will die of prostate cancer regardless of whether they are treated. The evidence calls into question the need for treating men with well differentiated or Gleason score 6 tumors who have a life expectancy of <10–15 years, especially if they are considered low risk.⁷

Because prostate cancer–specific death rate is much lower than the incidence rate, low-to-intermediate-risk patients may be candidates for active surveillance (AS) without immediate curative intervention. Since 1995, our institution has offered an option of AS with repeat annual biopsy to selected patients who are expected to have very-low-risk to low-risk prostate cancer based on PSA density and biopsy findings as described previously.⁸ Biopsy reclassification on AS is our trigger for intervention: (1) >2 cores are involved in 12–14 core biopsies, (2) >50% of a core is involved, or (3) when Gleason pattern 4 or 5 is present. Patients who are reclassified on a prostate biopsy while on AS are candidates for definitive treatments, such as radical prostatectomy (RP) or radiation therapy. We have previously shown that even when reclassification occurs on an annual biopsy in AS, some men on follow-up have clinically “insignificant” prostate cancer on subsequent RP,⁹ defined as: (1) organ-confined, (2) dominant tumor nodule <0.5 cm³, and (3) no Gleason pattern 4 or 5.¹⁰ The purpose of our study is to identify clinical and/or pathologic parameters that can predict insignificant prostate cancer on RP after biopsy reclassification in an AS program.

MATERIAL AND METHODS

Since 1995, >800 patients have enrolled in our AS program. Our AS protocol includes semiannual PSA measurements and annual 12–14 core biopsy.⁸

Surveillance biopsies and RP pathology from a consecutive series of AS patients who underwent surgery for biopsy reclassification were reviewed. All RP specimens were fixed in formalin, sliced at 3-mm intervals, and embedded in entirety. Tumor volume was determined using the grid method.¹¹ The following clinicopathological parameters were assessed and compared between insignificant cancer and significant cancer at initial diagnosis and at biopsy reclassification on AS: Gleason grade upgrading, PSA, PSA density, number of cores involved by cancer along with any interval negative biopsies, maximum percent involvement of cancer per core, number of cores with high-grade prostatic intraepithelial neoplasm (PIN), and presence of atypical glands. The outcome was to predict which men with biopsy reclassification to worse disease on AS had insignificant cancer in their RP, so that future patients with similar findings on biopsy reclassification may continue on AS.

Categorical data (eg, number of cases in each category) were compared with Fisher’s exact test and numerical data (eg, maximum percentage of core involved by cancer) were compared using unpaired *t*-test.

We identified 72 patients who met all 4 of our AS criteria (no more than 2 cores involved by cancer, no more than 50% of cancer involvement per core, no higher than Gleason score 6, and PSA density <0.15) at diagnosis and subsequently underwent RP because of reclassification on surveillance biopsy. Five cases were excluded (3 cases with unevaluable organ-confined status because of positive margin at intraprostatic incision and 2 cases where slides were not available for tumor volume analysis). The remaining 67 patients who underwent RP after biopsy reclassification on AS form the basis of the current study.

RESULTS

Overall Findings of RP During AS

Overall clinicopathological findings of RP from 67 patients with biopsy reclassification are summarized in Table 1. Median age at RP was 66.4 years (range 43.4–75.0). Mean AS time between the diagnostic biopsy and RP was 30.3 months, with a median number of 3 biopsies (range 2–9). Fifteen of 67 (22.4%) showed extraprostatic extension (EPE), 42/67 (62.7%) had Gleason pattern 4 or 5, and 41/67 (61.2%) had small tumor with dominant tumor nodule volume $<0.5 \text{ cm}^3$. There were 2 cases with positive margins and 1 case with seminal vesicle involvement. No lymph node involvement was seen. Nineteen (19) of 67 patients (28.4%) with biopsy reclassification on AS showed insignificant cancer at RP. Biopsy reclassification findings on surveillance biopsy are summarized in Table 2.

Clinicopathological Findings of Insignificant and Significant Cancer

Biopsy findings and PSA data were compared between insignificant and significant cancer and are summarized in Table 3A. For biopsy findings, comparison was done in terms of number of cases (categorical data) as well as average values (numerical data). At initial biopsy, number of cores involved by cancer, maximum percentage of cancer involvement, and PSA were not significantly different between the 2 groups. The presence of a negative interval biopsy that did not show cancer also failed to show significant difference between groups. At the time of biopsy reclassification (last biopsy before RP), number of cores involved by cancer, maximum percentage of cancer involvement, PSA, and PSA velocity were not significantly different when comparing groups. Number of cores involved by cancer and maximum percentage of cancer involvement were stratified with different cutoff values (2 and 3 for number of cores, 5% and 50% for maximum percentage). There was no significant difference between the groups in terms of presence of PIN, atypical glands suspicious for cancer, number of biopsies performed, PSA density, AS duration, and age (data not shown).

Clinicopathological Findings of Insignificant and Significant Cancer in a Subgroup with No Gleason Pattern 4 or 5 at Biopsy Reclassification

Because patients who have Gleason pattern 4 or 5 on biopsy should have significant cancer by definition, a subgroup of patients with Gleason score 6 at biopsy reclassification was analyzed separately. We identified 37 patients reclassified on biopsy without Gleason pattern 4 or 5 at the time of biopsy reclassification. Biopsy findings and PSA data were compared between insignificant and significant cancer similar to our prior analysis (Table 3B). At initial biopsy, number of cores involved by cancer and maximum percentage of cancer involvement were not significantly different between the 2 groups. PSA at diagnosis was significantly lower in patients with insignificant cancer ($P = .0005$). Presence of negative interval biopsy was similar between insignificant and significant cancer. At biopsy reclassification, the number of cores involved by cancer, maximum percentage of cancer involvement, PSA, and PSA velocity were not significantly different, although PSA showed a trend with $P = .054$. There was no significant difference between insignificant cancer and significant cancer in terms of presence of atypical glands, PIN, number of biopsy performed, PSA density, AS duration, and age (data not shown).

Predictors of Insignificant Cancer in Patients with Biopsy Reclassification

Combining all data, a flow chart was created to predict insignificant cancer based on biopsy finding and PSA (Fig. 1). Among 67 patients, 30 were reclassified on surveillance biopsy because of the presence of Gleason pattern 4/5. Twenty-seven of 30 (90%) had significant cancer at RP (in 3 men, RP grade was downgraded to Gleason score 6). In the group of 37

patients with reclassification on surveillance biopsy without Gleason pattern 4 or 5, subgroups were further divided by PSA value at 4 ng/mL, which empirically was the most discriminating cut-off value.

There were 13 patients who had PSA <4 at diagnosis or at the time of biopsy reclassification. Twelve of 13 (92.3%) of this subgroup had insignificant cancer. Of these 13 patients, 11 had PSA <4 ng/mL at diagnosis and 7 had PSA <4 ng/mL at surveillance biopsy reclassification. One patient who showed significant cancer had a PSA of 3.2 ng/mL at diagnosis and at surveillance biopsy reclassification, and showed a minute focus of focal extraprostatic extension with a small tumor nodule (0.2 cm³).

Twenty-four of 37 men reclassified on a surveillance biopsy without Gleason pattern 4 or 5 had PSA ≥ 4 both at diagnosis and at the time of biopsy reclassification. Four of those 24 (16.7%) had insignificant cancer on RP. Among 20 men (83.3%) who had significant cancer in this group, 12 men had Gleason score upgrade, 14 had dominant tumor nodule volume >0.5 cm³, and 8 had EPE.

COMMENT

The widespread adoption of PSA screening programs has resulted in an increasing incidence of prostate cancer, particularly very-low to low- to intermediate-risk cancer.^{12–14} AS programs have been recognized as a reasonable alternative to immediate curative intervention and its associated morbidity. The criteria for inclusion into AS has been supported by a prospective study of the AS program from our institution since 1995, which showed that 60% and 40% of men remain free of intervention at 5 and 10 years, respectively, without any prostate cancer–specific deaths reported to date.^{15–18}

Conversely, the present study shows that 72% of patients that are reclassified on a surveillance biopsy had significant cancer on RP, further validating the inclusion/exclusion criteria. Most of these patients showed relatively favorable pathologic findings, with a small portion of patients showing extraprostatic extension and positive margin without lymph node metastasis. Curative intervention was likely offered in time without losing a window of opportunity for complete cure. The proportion of patients with biopsy reclassification triggering curative intervention that had insignificant cancer at RP is in line with our previous report.⁹

In our model, presence of Gleason pattern 4/5 at the time of biopsy reclassification indicated a high likelihood for significant cancer (90%) at RP. This finding is expected because one of the criteria for significant cancer at RP is the presence of Gleason pattern 4. Gleason score has been recognized as the most important prognostic factor in prostate cancer. Prostate cancer with Gleason score 7 is significantly worse in prognosis, with a higher probability for adverse pathologic findings, biochemical recurrence, and long-term survival rate.^{19,20} Although EPE was seen in 22.4% of the RP specimens after biopsy reclassification, lymph node metastases were not seen, seminal vesicle invasion was seen in only 1 patient, and the mean tumor volume was small at 0.56 mL. Given the short time interval (mean 30 months) and the lack of increase in serum PSA levels between enrollment into the AS protocol and reclassification, the presence of extraprostatic extension at RP could already have been present in many of these cases at the time of enrollment.

A small portion of patients in the current study were downgraded to Gleason score 6 on RP. Although Gleason score upgrade on RP is a well-documented phenomenon that is mainly attributable to sampling issues,²¹ Gleason score downgrade likely represents overinterpretation on biopsy of tangentially sectioned glands of pattern 3 as poorly formed glands of Gleason pattern 4. In AS patients, follow-up biopsies in which the grade is

equivocal for Gleason pattern 4 should be graded as Gleason pattern 3. With the short interval between enrollment biopsy and biopsy reclassification, the presence of Gleason pattern 4 at reclassification probably represented undersampled higher-grade tumor, rather than tumor-grade progression. An alternative to better predict unsampled, more aggressive disease at the time of enrollment in the AS protocol is to perform a saturation biopsy before enrollment.

Clinicopathological comparison between insignificant and significant cancer did not show differences in number of positive cores, maximum involvement of cancer, and PSA. These parameters have been shown to be related with tumor volume previously.²² Because Gleason pattern 4/5 defines significant cancer regardless of tumor volume, failure to identify these parameters as predictors of insignificant cancer may not be surprising. A small tumor with Gleason pattern 4 at RP may not be associated with extensive cancer on biopsy or high serum PSA levels.

Our subgroup analysis with no Gleason pattern 4/5 on surveillance biopsy was performed to remove the confounding effect of Gleason grade. Number of positive cores and maximum involvement of cancer involvement did not appear to provide predictive value for insignificant cancer. The lack of sufficient strength of correlation and clear cutoff points may be to the result of a relatively small sample size or our highly selected patient population that is likely to have small tumor volume. The selected nature of our cohort, however, appears to increase the predictive value of PSA for insignificant cancer in patients with no Gleason pattern 4/5. PSA has been shown to be a nonspecific serum marker for prostate cancer,²³ but in our analysis with patients who had biopsy-proven cancer, low PSA at diagnosis or at biopsy reclassification was the best indicator for insignificant cancer in patients without Gleason score upgrade. Although it is conceivable to consider findings at biopsy reclassification more important than the data at diagnosis, our data suggest that PSA at diagnosis may add additional information in predicting insignificant cancer at the time of biopsy reclassification. PSA density, although one of our entry criteria to be a candidate for AS, was not as predictive as PSA for the distinction of insignificant vs significant cancer at RP at the time of biopsy reclassification.

Our study has limitations: (1) We studied a highly select population, thus findings may not be generalizable; (2) biopsy reclassification and pathology assessment may not correlate with important health outcomes, such as death from prostate cancer and freedom from metastatic disease in all cases; and (3) the results contain small numbers in subset analyses (although the present study presents the largest dataset to evaluate this issue to date).

CONCLUSIONS

Most patients who have biopsy reclassification while on AS during an annual biopsy have significant disease at RP, suggesting that treatment may be justified. At the time of biopsy reclassification, in the absence of biopsy grade progression, there are some men with only biopsy volume progression that still have insignificant cancer at RP. At the time of biopsy reclassification, patients with low PSA values either at the time of diagnosis or at the time of biopsy reclassification are unlikely to have significant cancer on RP. These men may be candidates to remain on AS, which can further reduce the number of patients requiring definitive treatment. Of the 67 men with biopsy reclassification who underwent RP in the current study, 13 (19.4%) would now be recommended to stay on AS. Only longer follow-up with less stringent criteria for AS will determine whether there is harm to patients in terms of death caused by prostate cancer.

References

1. Ganz PA, Barry JM, Burke W, et al. National Institutes of Health state-of-the-science conference: role of active surveillance in the management of men with localized prostate cancer. *Ann Intern Med.* 2012; 156:591–595. [PubMed: 22351514]
2. Parker C, Muston D, Melia J, et al. A model of the natural history of screen-detected prostate cancer, and the effect of radical treatment on overall survival. *Br J Cancer.* 2006; 94:1361–1368. [PubMed: 16641912]
3. Stattin P, Holmberg E, Johansson JE, et al. Outcomes in localized prostate cancer: national prostate cancer register of Sweden follow-up study. *J Natl Cancer Inst.* 2010; 102:950–958. [PubMed: 20562373]
4. Shappley WV 3rd, Kenfield SA, Kasperzyk JL, et al. Prospective study of determinants and outcomes of deferred treatment or watchful waiting among men with prostate cancer in a nationwide cohort. *J Clin Oncol.* 2009; 27:4980–4985. [PubMed: 19720918]
5. Eggener SE, Scardino PT, Walsh PC, et al. Predicting 15-year prostate cancer specific mortality after radical prostatectomy. *J Urol.* 2011; 185:869–875. [PubMed: 21239008]
6. Wilt TJ, Brawer MK, Barry MJ, et al. The prostate cancer intervention versus observation trial: VA/NCI/AHRQ cooperative studies program #407 (PIVOT): design and baseline results of a randomized controlled trial comparing radical prostatectomy to watchful waiting for men with clinically localized prostate cancer. *Contemp Clin Trials.* 2009; 30:81–87. [PubMed: 18783735]
7. Mohler JL. The 2010 NCCN clinical practice guidelines in oncology on prostate cancer. *J Natl Compr Cancer Netw.* 8:145.
8. Carter HB, Walsh PC, Landis P, et al. Expectant management of nonpalpable prostate cancer with curative intent: preliminary results. *J Urol.* 2002; 167:1231–1234. [PubMed: 11832703]
9. Duffield AS, Lee TK, Miyamoto H, et al. Radical prostatectomy findings in patients in whom active surveillance of prostate cancer fails. *J Urol.* 2009; 182:2274–2278. [PubMed: 19758635]
10. Ploussard G, Epstein JI, Montironi R, et al. The contemporary concept of significant versus insignificant prostate cancer. *Eur Urol.* 2011; 60:291–303. [PubMed: 21601982]
11. Graif T, Loeb S, Roehl KA, et al. Under diagnosis and over diagnosis of prostate cancer. *J Urol.* 2007; 178:88–92. [PubMed: 17499308]
12. DiGiuseppe JA, Sauvageot J, Epstein JI. Increasing incidence of minimal residual cancer in radical prostatectomy specimens. *Am J Surg Pathol.* 1997; 21:174–178. [PubMed: 9042283]
13. Weir HK, Thun MJ, Hankey BF, et al. Annual report to the nation on the status of cancer, 1975–2000, featuring the uses of surveillance data for cancer prevention and control. *J Natl Cancer Inst.* 2003; 95:1276–1299. [PubMed: 12953083]
14. Falzarano SM, Magi-Galluzzi C. Prostate cancer staging and grading at radical prostatectomy over time. *Adv Anat Pathol.* 2011; 18:159–164. [PubMed: 21326013]
15. Tosoian JJ, Trock BJ, Landis P, et al. Active surveillance program for prostate cancer: an update of the Johns Hopkins experience. *J Clin Oncol.* 2011; 29:2185–2190. [PubMed: 21464416]
16. van den Bergh RC, Vasarainen H, van der Poel HG, et al. Short-term outcomes of the prospective multicentre “prostate cancer research International: active surveillance” study. *BJU Int.* 2010; 105:956–962. [PubMed: 19817747]
17. Cooperberg MR, Cowan JE, Hilton JF, et al. Outcomes of active surveillance for men with intermediate-risk prostate cancer. *J Clin Oncol.* 2011; 29:228–234. [PubMed: 21115873]
18. Dall’Era MA, Konety BR. Active surveillance for low-risk prostate cancer: selection of patients and predictors of progression. *Nat Clin Pract Urol.* 2008; 5:277–283. [PubMed: 18285752]
19. Humphrey PA. Gleason grading and prognostic factors in carcinoma of the prostate. *Mod Pathol.* 2004; 17:292–306. [PubMed: 14976540]
20. Albertsen PC, Hanley JA, Gleason DF, et al. Competing risk analysis of men aged 55 to 74 years at diagnosis managed conservatively for clinically localized prostate cancer. *JAMA.* 1998; 280:975–980. [PubMed: 9749479]
21. Corcoran NM, Hovens CM, Hong MK, et al. Underestimation of Gleason score at prostate biopsy reflects sampling error in lower volume tumours. *BJU Int.* 2012; 109(5):660–664. [PubMed: 21895937]

22. Epstein JI, Walsh PC, Carmichael M, et al. Pathologic and clinical findings to predict tumor extent of nonpalpable (stage T1c) prostate cancer. JAMA. 1994; 271:368–374. [PubMed: 7506797]
23. Tosoian J, Loeb S. PSA and beyond: the past, present, and future of investigative biomarkers for prostate cancer. Scientific World-Journal. 2010; 10:1919–1931. [PubMed: 20890581]

Figure 1.

Number of insignificant and significant cancer in different categories classified by presence of Gleason pattern 4/5 and PSA at diagnosis and at time of reclassification on surveillance biopsy. (Color version available online.)

Table 1

Clinicopathological findings at RP in patients with reclassification on surveillance biopsy

Number of patients	67
Age (y) at RP	66.4 (43.4–75.0)
Mean ($\pm$ SEM) AS period (mo)	30.3 $\pm$ 3.2
Median number of biopsies during AS (range)	3 times (2–9)
Gleason score	
3 + 3 = 6	25 (37.3%)
3 + 3 with tertiary pattern 4	5 (7.5%)
3 + 4 = 7	22 (32.8%)
4 + 3 = 7	13 (19.4%)
4 + 5/5 + 4 = 9	2 (3%)
Extraprostatic extension	15 (22.4%)
Positive margins	2 (3.0%)
Lymph node involvement	0
Seminal vesicle involvement	1 (1.5%)
Mean ($\pm$ SEM) dominant tumor nodule volume (cm ³)	0.56 $\pm$ 0.09
Dominant nodule volume <0.5 cm ³	41/67 (61.2%)
Clinically insignificant cancer	19/67 (28.4%)

Table 2

Biopsy reclassification findings on surveillance biopsy

Biopsy Reclassification	Number of Cases (n = 67)	Number of Insignificant Cancer (n = 19)
Gleason grade upgrading only	15	2
>2 cores with cancer only	23	10
>50% of cancer involvement only	9	3
Gleason grade upgrading + >2 cores with cancer only	7	0
Gleason grade upgrading + >50% of cancer involvement only	4	0
>2 cores with cancer + >50% of cancer involvement only	5	3
Gleason grade upgrading + >2 cores with cancer + >50% of cancer involvement	4	1

Table 3

A. Comparison of pathologic findings and PSA between insignificant and significant cancer			
	Insignificant (n = 19)	Significant (n = 48)	P Value
Findings at initial biopsy			
Number of cores with cancer *	1.15 ± 0.085	1.23 ± 0.061	.53
1 core involved by cancer †	16/19 (84.2%)	37/48 (77.1%)	.74
2 cores involved by cancer †	3/19 (15.8%)	11/48 (22.9%)	
Maximum involvement of cancer (%) *	7.3 ± 1.8	10.6 ± 2.2	.37
PSA at diagnosis (ng/mL) * (range)	4.6 ± 0.95 (1.5–21.2)	4.9 ± 0.23 (0.7–10)	.65
Presence of negative interval biopsy	4/19 (21.1%)	14/48 (29.2%)	.56
Findings at reclassification on surveillance biopsy			
Gleason score upgrade †	3/19 (15.8%)	27/48 (56.3%)	.0029
Number of cores with cancer *	2.8 ± 0.28	2.6 ± 0.20	.51
Cores involved by cancer 2 †	5/19 (26.3%)	24/48 (50%)	.10
Cores involved by cancer 3 †	17/19 (89.5%)	37/48 (77.1%)	.32
Maximum involvement of cancer (%) *	39.1 ± 4.2	41.3 ± 7.4	.79
PSA at reclassification (ng/mL) * (range)	4.8 ± 0.59 (1.9–12.4)	5.7 ± 0.30 (1.5–14.1)	.13
PSA velocity (ng/mL/y) *	0.14 ± 0.89	0.57 ± 0.31	.57
B. Comparison of pathologic findings and PSA between insignificant and significant cancer in a subgroup with no Gleason pattern 4 or 5 at reclassification on surveillance biopsy			
	Insignificant (n = 16)	Significant (n = 21)	P Value
Findings at initial biopsy			
Number of cores with cancer *	1.19 ± 0.101	1.19 ± 0.088	1.0
1 core involved by cancer †	13/16 (81.3%)	17/21 (81%)	1.0
2 cores involved by cancer †	3/16 (18.7%)	4/21 (19%)	
Maximum involvement of cancer (%) *	5.8 ± 1.7	6.0 ± 1.0	.74
PSA at diagnosis (ng/mL) * (range)	3.7 ± 0.29 (1.5–5.9)	5.4 ± 0.32 (3.2–9.8)	.0005
Presence of negative interval biopsy	4/16 (25%)	4/21 (19.5%)	.69
Findings at reclassification on surveillance biopsy			
Number of cores with cancer *	2.9 ± 0.27	2.95 ± 0.30	.88
Cores involved by cancer 2 †	3/16 (18.8%)	7/21 (33.3%)	.46
Cores involved by cancer 3 †	15/16 (93.8%)	15/21 (71.4%)	.11
Maximum involvement of cancer (%) *	41.5 ± 7.9	39.7 ± 5.8	.98
PSA at reclassification (ng/mL) * (range)	4.7 ± 0.65 (1.9–12.4)	6.1 ± 0.36 (3.2–9.2)	.054
PSA velocity (ng/mL/y) *	0.92 ± 0.58	0.25 ± 0.22	.25

* Data shown as mean ± SEM (data analyzed by unpaired *t*-test).

† Categorical data analyzed by Fisher's exact test.