Title

Prostate Cancer Antigen 3 Score Does Not Predict for Adverse Pathologic Features at Radical Prostatectomy or for Progression-free Survival in Clinically Localized, Intermediate- and High-risk Prostate Cancer

Authors

Hegde, John V
Veruttipong, Darlene
Said, Jonathan W
et al.

Publication Date

2017-09-01

DOI

10.1016/j.urology.2017.05.028

Peer reviewed

HHS Public Access

Author manuscript

Urology. Author manuscript; available in PMC 2020 January 28.

Published in final edited form as:

Urology. 2017 September ; 107: 171–177. doi:10.1016/j.urology.2017.05.028.

Prostate Cancer Antigen 3 Score Does Not Predict for Adverse Pathologic Features at Radical Prostatectomy or for Progression-free Survival in Clinically Localized, Intermediate- and High-risk Prostate Cancer

John V. Hegde, **Darlene Veruttipong**, **Jonathan W. Said**, **Robert E. Reiter**, **Michael L. Steinberg**, **Christopher R. King**, **Amar U. Kishan**

Department of Radiation Oncology, UCLA Medical Center, University of California, Los Angeles, CA; the Department of Pathology, UCLA Medical Center, University of California, Los Angeles, CA; and the Department of Urology, UCLA Medical Center, University of California, Los Angeles, CA

Abstract

OBJECTIVE—To evaluate whether preoperative urinary prostate cancer antigen 3 (PCA3) scores predict for adverse pathologic features (APFs) or progression-free survival (PFS) in men with intermediate- or high-risk prostate cancer (PCa) undergoing radical prostatectomy (RP).

MATERIALS AND METHODS—One hundred nine men with intermediate- (n = 52) or high-risk (n = 57) PCa who underwent RP were retrospectively identified. Logistic regression analysis was performed to evaluate the association of PCA3 score with various APFs (eg, extracapsular extension, seminal vesicle invasion, etc.). Among 78 men with ≥1 year of follow-up, the association between PCA3 score and PFS was assessed using Cox regression analysis.

RESULTS—At RP, 52% of patients had at least 1 APF, and with median follow-up of 2.3 years, overall 3-year PFS was 70%. PCA3 was not a significant predictor of any APF on multivariate analysis (MVA), whereas canonical predictors (eg, biopsy Gleason score and initial prostate-specific antigen) remained predictive of various APFs. No significant predictors for PFS were found on MVA, although certain canonical predictors (eg, National Comprehensive Cancer Network risk group) were significant predictors of PFS on univariate analysis (UVA). PCA3 score was not a significant predictor of PFS on either UVA or MVA.

CONCLUSION—Unlike in lower risk cohorts, increasing PCA3 score was not associated with any APF in this higher risk cohort, despite enrichment for APFs, nor was it associated with PFS. Notably, multiple known preoperative predictors for APFs were significant on MVA, and multiple predictors were associated with PFS on UVA. Therefore, PCA3 may not be a useful adjunct predictive marker in men with intermediate- or high-risk PCa.

Address correspondence to: Amar U. Kishan, M.D., Department of Radiation Oncology, UCLA Medical Center, University of California, 200 UCLA Medical Plaza, Suite B265, Los Angeles, CA 90095. aukishan@mednet.ucla.edu.

Financial Disclosure: The authors declare that they have no relevant financial interests.

APPENDIX

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.urology.2017.05.028.

Prostate cancer gene 3 (PCA3) is highly overexpressed by prostate cancer (PCa) cells and is a validated biomarker that predicts the presence of PCa when prostate-specific antigen (PSA) levels are in an indeterminate range.[1–3] PCA3 scores, which are determined by calculating the ratio of PCA3 mRNA to PSA mRNA in the urine, also have particular utility for guiding repeat biopsy decisions in men with previous negative biopsies.[2] Furthermore, and of importance in upfront treatment discussions, PCA3 scores have been demonstrated to be predictive of high-grade PCa, significantly improving clinical models for diagnosing prostate cancer.[4]

In men with predominantly favorable-risk PCa (ie, predominantly low- or intermediate-risk PCa per the National Comprehensive Cancer Network stratification schema), PCA3 testing has also been investigated for its potential utility in predicting adverse pathologic features at radical prostatectomy (RP), with mixed results. Several studies found significant correlations with increasing PCA3 score and increased rates of higher risk disease, extracapsular extension, pathologic Gleason score (GS), tumor volume, tumor multifocality, and positive surgical margins (PSMs).[5–11] However, other studies found minimal, if any, association between PCA3 scores and adverse pathologic features or noted that PCA3 scores offered no incremental value to existing models for predicting adverse pathology.[12–15]

However, the potential associations of PCA3 score with adverse pathologic features have not been evaluated in a predominantly higher risk PCa population (ie, a population with more intermediate- and high-risk patients with PCa). Additionally, whether PCA3 scores can have prognostic utility with regard to progression-free survival (PFS) remains unknown. Therefore, we retrospectively evaluated the association between PCA3 scores and both adverse pathologic features and PFS in a cohort of men with higher risk PCa who underwent RP at a single institution.

MATERIALS AND METHODS

Patient Selection

The study cohort consisted of 109 men with clinically localized (cT1–T2), intermediate- or high-risk PCa who had PCA3 urine assay testing before treatment with RP between 2010 and 2015 at a single academic medical center. The criteria used for ordering PCA3 testing included evaluation for the probability of undiagnosed PCa in men with an elevated PSA (≥4 ng/mL) or for aiding in the management of men with one or multiple negative prostate biopsy procedures but a persistently elevated or rising PSA. This study was approved as part of an institutional review board-approved protocol evaluating a registry of men with higher risk PCa.

Urinary PCA3 Assay

Following digital prostatic massage, first-catch urine was collected from all patients as described in Groskopf et al.[16] The urine sample was analyzed to quantify PCA3-mRNA and PSA-mRNA concentrations. The PCA3 score was calculated by taking the ratio of PCA3 mRNA to PSA mRNA and multiplying this by 1000.

Pathologic Specimens

The pathologic specimens of the 109 men who underwent RP were step-sectioned and reviewed by an expert, academic genitourinary pathologist. Evidence of extracapsular extension (ECE), seminal vesicle invasion (SVI), lymph node involvement (pN+), pathologic Gleason scores (pGS), and presence of tertiary Gleason pattern 5 was recorded. Gleason histologic grading on the pathologic specimens was used based on the 2005 International Society of Urological Pathology Consensus Conference guidelines[17] for men treated through 2014 and based on the updated 2014 guidelines thereafter.[18]

Progression-free Survival

Disease progression was defined as biochemical recurrence, treatment with postoperative radiotherapy or androgen deprivation therapy, or the development of distant metastasis from PCa. No patients died during the period of this study. Biochemical recurrence was defined according to the American Urological Association guidelines (ie, an initial serum PSA ≥0.2 ng/mL with a subsequent confirmatory PSA[19]), or the initiation of salvage radiotherapy.

Statistical Methods

The distributions of clinical, biopsy, imaging, and pathologic characteristics of the entire study cohort (n = 109) and the subset with ≥1 year of follow-up (n =78) were calculated. For the entire cohort, univariate and multivariate logistic regression analyses were performed to assess the predictive value of PCA3 score (as a continuous variable) for adverse pathologic features, adjusting for known predictors, including age, initial PSA (iPSA), clinical T-stage, biopsy GS (bGS), percent positive biopsies (PPB), and magnetic resonance imaging (MRI) T-category. The adverse pathologic features evaluated included ECE, SVI, pN+, upgrading to pGS 8–10 or presence of tertiary Gleason pattern 5, upstaging to pathologic T3 (pT3) disease, PSMs, and a combined analysis for the presence of any adverse pathologic feature aside from PSMs and presence of any adverse pathologic feature including PSMs. Variables not found to be predictive on univariate analysis were not included in multivariate analysis. If no predictors were found on univariate analysis, then no multivariate analysis was performed.

In the subset of 78 men with at least 1 year of follow-up, univariate and multivariate Cox regression analyses were performed to evaluate the predictive value of PCA3 score to predict for PFS, adjusting for age, preoperative risk group, maximal tumor diameter, pGS, ECE, SVI, pN+, and PSMs. Kaplan-Meier survival analysis was performed to estimate PFS in this subset.

RESULTS

The Distribution of Characteristics of the Study Cohort

The distributions of clinical, biopsy, imaging, and pathologic characteristics of the entire cohort and the subset with ≥1 year of follow-up evaluated for PFS are reported in Table 1. The median age of the entire cohort was 65 years (interquartile range [IQR] 59–69). The median PCA3 score was 47 (IQR 23–73). Median PSA was 7.4 (IQR 5.3–11.7). All patients had clinically localized prostate cancer (86% T1c and 14% T2). Forty percent had bGS ≤3

+ 4, 14% had bGS 4 + 3, and 47% had bGS 8–10. Forty-eight percent had intermediate-risk prostate cancer and 52% had high-risk prostate cancer. Nine percent of patients had evidence of T3 disease on MRI.

At RP, 52% of patients had at least 1 adverse pathologic feature. Overall, 32% of patients had pT3a disease, 10% of patients had pT3b disease, and 10% of patients had pN+ disease. Twenty-one percent of patients experienced GS upgrading and 41% of patients were upstaged to pT3. The subset of patients with ≥1 year follow-up had similar distributions for all clinical, biopsy, imaging, and pathologic characteristics.

Univariate and Multivariate Logistic Regression Analysis: Adverse Pathologic Features

Univariate and multivariate analyses for the presence of ECE without SVI, SVI, and upstaging to pathological ≥T3a are presented in Table 2. There were no preoperative characteristics significantly predictive on univariate analysis for the presence of ECE without SVI, and multivariate analysis for this outcome was not performed. On multivariate analysis, only higher bGS (odds ratio [OR] 6.00, $P = .027$) was significantly associated with higher rates of SVI, whereas clinical T-category, PPBs, and MRI T-category were all significant on univariate analysis ($P < .05$). Higher bGS (OR 3.64, $P = .0062$), PSA (OR 1.08, $P = .023$), and PPBs (OR 1.03, $P = .025$) were all associated with upstaging on multivariate analysis, whereas higher clinical T-category (OR 4.85, $P = .011$) and MRI T-category (OR 6.67, $P = .020$) were associated only on univariate analysis. On multivariate analysis, increasing PSA (OR 1.12, $P = .0030$) and PPBs (OR 1.06, $P = .0026$) were both associated with pN+ (Table 2). Logistic regression analyses evaluating upgrading at RP to pGS 8–10 or to tertiary Gleason pattern 5 are reported in Table 3. bGS was the only variable associated with upgrading on univariate analysis ($P = .030$).

Similar regression analyses were also performed for predictors of PSMs (Table S1), any adverse pathologic feature (as a composite outcome) other than PSM (Table S2), and any adverse pathologic feature (as a composite outcome) including PSM (Table S3). No preoperative characteristic was significantly predictive of PSMs. Both increasing PSA (OR 1.11, $P = .0071$) and clinical T-category (OR 4.31, $P = .046$) were significant for predicting the composite outcome of any adverse pathologic feature aside from PSM on multivariate analysis, whereas only PSA was a significant predictor of adverse pathologic features including PSM, and only on univariate analysis (OR 1.1, $P = .015$).

Univariate and Multivariate Cox Regression Analyses: Progression-free Survival

The results for the univariate and multivariate Cox regression analyses evaluating predictors for PFS among men with ≥1 year follow-up are presented in Table 4. No potential predictors for PFS were significant on multivariate analysis. However, increasing pGS (hazard ratio [HR] 4.79, $P = .0006$), preoperative risk group (HR 4.17, $P = .022$), and maximal tumor diameter (HR 1.83, $P = .022$), as well as the presence of pN+ (HR 3.70, $P = .0034$), SVI (HR 3.04, $P = .021$), and ECE (HR 2.69, $P = .031$), were all positively associated with PFS on univariate analysis.

COMMENT

PCA3 scores have emerged as valid predictors of the presence of PCa in the presence of indeterminate PSA values or previously negative biopsies. However, whether PCA3 scores can have predictive value for the presence of adverse pathologic features at the time of RP or prognostic value for PFS following RP remains unknown. Previous evaluations of PCA3 scores as predictors of adverse pathology have generally focused on patients with low- or intermediate-risk disease and have reached conflicting conclusions. In the current study of patients with higher risk (ie, intermediate- and high-risk) PCa, we found that PCA3 scores did not predict for adverse pathologic features at RP, whereas canonical factors—including bGS, iPSA, PPB, and clinical T-category—did. Notably, adverse pathologic features were common in this cohort, and thus the lack of an association is unlikely to be confounded by low statistical power, particularly given the small confidence intervals for PCA3 score in every univariate analysis. Additionally, neither PCA3 scores nor canonical factors were significantly associated with PFS on multivariate analysis. These data suggest that PCA3 scores are unlikely to serve as a useful adjunct predictive marker for adverse pathology and further underscore the limitations of currently available prognostication tools for patients with higher risk PCa.

Although validated, robust preoperative stratification systems and nomograms for PCa risk are widely used in clinical practice to counsel patients, there remains significant heterogeneity in outcomes for men with intermediate- and high-risk disease.[20,21] Investigators have recently identified “favorable” and “unfavorable” subgroups of intermediate-risk PCa,[22] and similar strata within high-risk PCa, predominantly related to Gleason pattern 5 disease, have been proposed.[23–25] Nonetheless, further improvements to preoperative risk stratification in higher risk, but clinically localized, cohorts, remain essential for optimizing treatment selection.

For men with higher risk PCa who select RP for definitive treatment, improved stratification for the risk of adverse pathologic features or PFS using novel preoperative predictors may guide adjuvant or even neoadjuvant therapies. To our knowledge, this is the first study in a cohort of men with exclusively intermediate- or high-risk PCa to evaluate whether PCA3 score significantly predicts for adverse pathologic features, and the first study in men of any risk group evaluating the urinary PCA3 score’s potential predictive ability for PFS. Although multiple preoperative predictors for adverse pathologic features were found on multivariate analysis, including bGS, iPSA, and PPB, PCA3 score was not associated with any of these outcomes on univariate or multivariate analyses. Some previous studies, which focused exclusively on lower risk cohorts, have reported that increasing PCA3 score was associated with adverse pathologic features,[5–11] whereas others have not.[12–15] The present study cohort was enriched for adverse pathologic features; for example, 42% had ECE and 41% experienced pathologic upstaging. Therefore, the absence of an association in our study is unlikely to be related to an issue of statistical power and suggests limited, if any, utility of PCA3 as an adjunct predictive marker for adverse pathology. On the other hand, the lack of an association between PCA3 score and PFS may be ascribed to the short median follow-up of 2.3 years and 3-year progression rate of 30%. However, other canonical factors were at least predictive of PFS on univariate analyses, suggesting that an association between PCA3

and PFS, if present, is modest in strength at best. Still, the uncertain clinical significance of biochemical recurrence[26]—the most common form of progression seen in this cohort—renders conclusions about PCA3 scoring and ultimate clinical outcome premature.

Interestingly, a recently published study evaluating the Decipher Genomic Resource Information (GRID) PCa database found that *low* PCA3 expression was associated with higher grade disease and disease progression.[27] Although this study is different from ours as it evaluated PCA3 gene expression profiles in prostatic tissues rather than PCA3 score with the urine assay, the findings further suggest that the convention of using PCA3 to determine the risk of finding PCa at biopsy may be beneficial only in men with (as yet undiscovered) lower risk disease. These results contrast with an earlier evaluation of the addition of urinary PCA3 score to a clinical risk nomogram, which noted that a *higher* PCA3 score was associated with higher grade disease at biopsy and that a nomogram including PCA3 scores out-performed one without them for the identification of PCa.[4] However, other large series have suggested selecting the appropriate PCA3 score threshold is integral to avoid underdiagnosis of high-grade disease.[28] These limitations have led to proposals of combining PCA3 data with other biomarkers, including TMPRSS2:ERG fusion status.[29,30] Perhaps including these novel biomarker assays individually or in combination in the preoperative setting may improve the ability of existing preoperative risk models to predict adverse pathologic features at RP and disease progression.

This study has several limitations, including all limitations inherent to a retrospective study. This study only included patients who were definitively treated with RP, and thus the results are not generalizable to patients receiving other forms of definitive treatment. Furthermore, this study evaluated a small cohort of patients. Regardless, adverse pathologic features were common, and multiple known preoperative predictors of adverse pathologic features were significant on multivariate analysis. However, the small cohort size along with the short median follow-up translated to a disease progression rate of only 30% at 3 years. Even expected predictors of PFS failed to manifest on multivariate analysis (although they did manifest on univariate analyses), raising the possibility that our results might change with added patients or added follow-up. In addition, the PCA3 values in the study cohort are somewhat low (median 47, IQR 23–73). As some studies establishing associations between PCA3 and adverse features were performed in cohorts with higher median PCA3 values,[8,11,12,14] a study evaluating men at higher risk with higher PCA3 scores may yield different findings. Indeed, the study population may have PCA3 values below the threshold needed to predict adverse outcomes.

CONCLUSION

In conclusion, PCA3 score was not associated with any adverse pathologic features or with PFS in a cohort of patients with intermediate- and high-risk PCa, although canonical predictors were associated with adverse pathologic features on univariate and multivariate analyses, and with PFS on univariate analysis. Together, these results suggest that urine PCA3 testing may not be a useful adjunct predictor of outcomes in men with higher risk PCa and underscore the need for improved risk assessment and prognostication tools for these patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Marks LS, Fradet Y, Deras IL, et al. PCA3 molecular urine assay for prostate cancer in men undergoing repeat biopsy. Urology. 2007;69:532–535. [PubMed: 17382159]
2. Chun FK, de la Taille A, van Poppel H, et al. Prostate cancer gene 3 (PCA3): development and internal validation of a novel biopsy nomogram. Eur Urol. 2009;56:659–667. [PubMed: 19304372]
3. Vlaeminck-Guillem V, Ruffion A, Andre J, Devonec M, Paparel P. Urinary prostate cancer 3 test: toward the age of reason? Urology. 2010;75:447–453. [PubMed: 19586654]
4. Hansen J, Auprich M, Ahyai SA, et al. Initial prostate biopsy: development and internal validation of a biopsy-specific nomogram based on the prostate cancer antigen 3 assay. Eur Urol. 2013;63:201–209. [PubMed: 22854248]
5. Nakanishi H, Groskopf J, Fritsche HA, et al. PCA3 molecular urine assay correlates with prostate cancer tumor volume: implication in selecting candidates for active surveillance. J Urol. 2008;179:1804–1809, discussion 1809–1810. [PubMed: 18353398]
6. Whitman EJ, Groskopf J, Ali A, et al. PCA3 score before radical prostatectomy predicts extracapsular extension and tumor volume. J Urol. 2008;180:1975–1978, discussion 1978–1979. [PubMed: 18801539]
7. Ploussard G, Durand X, Xylinas E, et al. Prostate cancer antigen 3 score accurately predicts tumour volume and might help in selecting prostate cancer patients for active surveillance. Eur Urol. 2011;59:422–429. [PubMed: 21156337]
8. Vlaeminck-Guillem V, Devonec M, Colombel M, Rodriguez-Lafrasse C, Decaussin-Petrucci M, Ruffion A. Urinary PCA3 score predicts prostate cancer multifocality. J Urol. 2011;185:1234–1239. [PubMed: 21334023]
9. van Poppel H, Haese A, Graefen M, et al. The relationship between Prostate CAncer gene 3 (PCA3) and prostate cancer significance. BJU Int. 2012;109:360–366. [PubMed: 21883822]
10. Durand X, Xylinas E, Radulescu C, et al. The value of urinary prostate cancer gene 3 (PCA3) scores in predicting pathological features at radical prostatectomy. BJU Int. 2012;110:43–49. [PubMed: 22221521]
11. Ferro M, Lucarelli G, Bruzzese D, et al. Improving the prediction of pathologic outcomes in patients undergoing radical prostatectomy: the value of prostate cancer antigen 3 (PCA3), prostate health index (phi) and sarcosine. Anticancer Res. 2015;35:1017–1023. [PubMed: 25667489]
12. van Gils MP, Hessels D, Hulsbergen-van de Kaa CA, et al. Detailed analysis of histopathological parameters in radical prostatectomy specimens and PCA3 urine test results. Prostate. 2008;68: 1215–1222. [PubMed: 18500693]
13. Hessels D, van Gils MP, van Hooij O, et al. Predictive value of PCA3 in urinary sediments in determining clinico-pathological characteristics of prostate cancer. Prostate. 2010;70:10–16. [PubMed: 19708043]
14. Augustin H, Mayrhofer K, Pummer K, Mannweiler S. Relationship between prostate cancer gene 3 (PCA3) and characteristics of tumor aggressiveness. Prostate. 2013;73:203–210. [PubMed: 22782916]
15. Porpiglia F, Cantiello F, De Luca S, et al. In-parallel comparative evaluation between multiparametric magnetic resonance imaging, prostate cancer antigen 3 and the prostate health index in predicting pathologically confirmed significant prostate cancer in men eligible for active surveillance. BJU Int. 2016;118:527–534. [PubMed: 26350955]
16. Groskopf J, Aubin SM, Deras IL, et al. APTIMA PCA3 molecular urine test: development of a method to aid in the diagnosis of prostate cancer. Clin Chem. 2006;52:1089–1095. [PubMed: 16627561]
17. Epstein JI, Allsbrook WC Jr, Amin MB, Egevad LL. The 2005 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma. Am J Surg Pathol. 2005;29:1228–1242. [PubMed: 16096414]

18. Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, Humphrey PA. The 2014 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma: definition of grading patterns and proposal for a new grading system. Am J Surg Pathol. 2016;40:244–252. [PubMed: 26492179]
19. Cookson MS, Aus G, Burnett AL, et al. Variation in the definition of biochemical recurrence in patients treated for localized prostate cancer: the American Urological Association Prostate Guidelines for Localized Prostate Cancer Update Panel report and recommendations for a standard in the reporting of surgical outcomes. J Urol. 2007;177:540–545. [PubMed: 17222629]
20. Reese AC, Pierorazio PM, Han M, Partin AW. Contemporary evaluation of the National Comprehensive Cancer Network prostate cancer risk classification system. Urology. 2012;80:1075–1079. [PubMed: 22995570]
21. D'Amico AV, Whittington R, Malkowicz SB, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA. 1998;280:969–974. [PubMed: 9749478]
22. Zumsteg ZS, Spratt DE, Pei I, et al. A new risk classification system for therapeutic decision making with intermediate-risk prostate cancer patients undergoing dose-escalated external-beam radiation therapy. Eur Urol. 2013;64:895–902. [PubMed: 23541457]
23. Tendulkar RD, Reddy CA, Stephans KL, et al. Redefining high-risk prostate cancer based on distant metastases and mortality after high-dose radiotherapy with androgen deprivation therapy. Int J Radiat Oncol Biol Phys. 2012;82:1397–1404. [PubMed: 21665379]
24. Tsao CK, Gray KP, Nakabayashi M, et al. Patients with biopsy Gleason 9 and 10 prostate cancer have significantly worse outcomes compared to patients with Gleason 8 disease. J Urol. 2015;194:91–97. [PubMed: 25623747]
25. Jang WS, Yoon CY, Kim MS, et al. The prognostic role of tertiary Gleason pattern 5 in a contemporary grading system for prostate cancer. Prostate Cancer Prostatic Dis. 2017;20:93–98. [PubMed: 27845330]
26. Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC. Natural history of progression after PSA elevation following radical prostatectomy. JAMA. 1999;281:1591–1597. [PubMed: 10235151]
27. Alshalalfa M, Verhaegh GW, Gibb EA, et al. Low PCA3 expression is a marker of poor differentiation in localized prostate tumors: exploratory analysis from 12,076 patients. Oncotarget. 2017; doi:10.18632/oncotarget.15133.
28. Wei JT, Feng Z, Partin AW, et al. Can urinary PCA3 supplement PSA in the early detection of prostate cancer? J Clin Oncol. 2014; 32:4066–4072. [PubMed: 25385735]
29. Tomlins SA, Day JR, Lonigro RJ, et al. Urine TMPRSS2:ERG plus PCA3 for individualized prostate cancer Risk assessment. Eur Urol. 2016;70:45–53. [PubMed: 25985884]
30. Leyten GH, Hessels D, Jannink SA, et al. Prospective multicentre evaluation of PCA3 and TMPRSS2-ERG gene fusions as diagnostic and prognostic urinary biomarkers for prostate cancer. Eur Urol. 2014;65:534–542. [PubMed: 23201468]

Table 1.

Clinical, biopsy, imaging, and pathologic characteristics of the entire study cohort (N = 109) and the subset with ≥1 year follow-up

	Entire Cohort (N = 109)	Subset with ≥1 Year Follow-up (N = 78)
Age (y), median (IQR)	65.1 (58.5–69.0)	65.1 (58.5–69.0)
PCA3 score, median (IQR)	47 (23–73)	47 (23–73)
PSA (ng/mL), median (IqR)	7.4 (5.3–11.7)	10.8 (5.6–12.0)
Clinical T-category		
T1c	94 (86%)	67 (86%)
T2a-c	15 (14%)	11 (14%)
Biopsy Gleason score		
3 + 3	3 (3%)	2 (3%)
3 + 4	40 (37%)	26 (33%)
4 + 3	15 (14%)	8 (10%)
4 + 4	12 (11%)	11 (14%)
3 + 5/4 + 5/5 + 4	39 (36%)	31 (40%)
Percent positive biopsies (IQR)	30% (22%−44%)	36% (22%−46%)
Risk group		
Favorable intermediate	30 (28%)	20 (26%)
Unfavorable intermediate	22 (20%)	10 (13%)
High	57 (52%)	48 (62%)
MRI T-Category		
T1–T2	96 (88%)	68 (87%)
≥T3	10 (9%)	8 (10%)
N/A	3 (3%)	2 (3%)
RP T-Category		
pT2a-c	63 (58%)	40 (51%)
pT3a	35 (32%)	28 (36%)
pT3b	11 (10%)	10 (13%)
RP maximal tumor diameter (cm)	2.3 (1.8–3.0)	2.3 (1.8–3.0)
RP Gleason score		
3 + 4	55 (50%)	34 (44%)
4 + 3	27 (25%)	18 (23%)

	Entire Cohort (N = 109)	Subset with ≥1 Year Follow-up (N = 78)
8–10	27 (25%)	26 (33%)
Lymphovascular invasion		
Negative	102 (94%)	71 (91%)
Positive	7 (6%)	7 (9%)
Perineural invasion		
Negative	24 (22%)	17 (22%)
Positive	85 (78%)	61 (78%)
Lymph node involvement		
No	98 (90%)	67 (86%)
Yes	11 (10%)	11 (14%)
Positive surgical margins		
No	81 (74%)	54 (69%)
Yes	28 (26%)	24 (31%)

IQR, interquartile range; MRI, magnetic resonance imaging; PCA, prostate cancer antigen 3; PSA, prostate-specific antigen; RP, radical prostatectomy.

Table 2.

Predictors of adverse pathologic features: upstaging of disease

	Univariate Analysis		Multivariate Analysis	
Clinical Characteristic	**Odds Ratio (95% CI)**	***P* Value**	**Odds Ratio (95% CI)**	***P* Value**
ECE without SVI				
PCA3 score	1.00 (0.99–1.00)	.25	—	—
Age (y)	1.05 (0.98–1.12)	.17	—	—
PSA (ng/mL)	1.03 (0.98–1.08)	.19	—	—
Clinical T-Category				
T1	1.00 (ref)	—	—	—
T2	1.57 (0.51–4.83)	.43	—	—
Biopsy GS				
≤7	1.00 (ref)	—	—	—
8–10	2.03 (0.89–4.62)	.092	—	—
Percent positive biopsies	1.02 (1.00–1.04)	.13	—	—
MRI T-Category				
T1–T2	1.00 (ref)	—	—	—
T3–T4	1.54 (0.40–5.87)	.53	—	—
SVI				
PCA3 score	1.00 (0.98–1.01)	.47	—	—
Age (y)	1.00 (0.91–1.10)	.97	—	—
PSA (ng/mL)	1.06 (1.00–1.12)	.053	—	—
Clinical T-Category				
T1	1.00 (ref)	—	1.00 (ref)	—
T2	7.33 (1.89–28.43)	.0040	5.74 (0.95–34.79)	.057
Biopsy GS				
≤7	1.00 (ref)	—	1.00 (ref)	—
8–10	6.00 (1.23–29.23)	.027	6.80 (1.09–42.32)	.040
Percent positive biopsies	1.04 (1.01–1.08)	.015	1.03 (0.99–1.07)	.19
MRI T-Category				
T1–T2	1.00 (ref)	—	1.00 (ref)	—

	Univariate Analysis		Multivariate Analysis	
Clinical Characteristic	**Odds Ratio (95% CI)**	***P* Value**	**Odds Ratio (95% CI)**	***P* Value**
T3–T4	8.48 (1.93–37.26)	.0047	4.83 (0.89–26.23)	.068
Upstaging to ≥T3a				
PCA3 score	0.99 (0.99–1.00)	.14	—	—
Age (y)	1.04 (0.98–1.10)	.20	—	—
PSA (ng/mL)	1.08 (1.01–1.14)	.018	1.08 (1.01–1.15)	.023
Clinical T-Category				
T1	1.00 (ref)	—	1.00 (ref)	—
T2	4.85 (1.43–16.42)	.011	3.54 (0.80–15.66)	.096
Biopsy GS				
≤7	1.00 (ref)	—	1.00 (ref)	—
8–10	3.46 (1.56–7.69)	.0023	3.64 (1.44–9.20)	.0062
Percent positive biopsies	1.04 (1.01–1.06)	.0039	1.032 (1.004–1.06)	.025
MRI T-Category				
T1–T2	1.00 (ref)	—	1.00 (ref)	—
T3–T4	6.67 (1.34–33.14)	.020	3.86 (0.61–24.45)	.15
pN+ disease				
PCA3 score	0.98 (0.95–1.00)	.060	—	—
Age (y)	0.98 (0.89–1.08)	.73	—	—
PSA (ng/mL)	1.09 (1.03–1.17)	.0051	1.12 (1.04–1.21)	.0030
Clinical T-Category				
T1	1.00 (ref)	—	—	—
T2	3.85 (0.97–15.32)	.056	—	—
Biopsy GS				
≤7	1.00 (ref)	—	—	—
8–10	2.61 (0.65–10.49)	.18	—	—
Percent positive biopsies	1.05 (1.02–1.09)	.0045	1.06 (1.02–1.11)	.0026
MRI T-Category				
T1–T2	1.00 (ref)	—	—	—
T3–T4	4.02 (0.87–18.68)	.076	—	—

CI, confidence interval; GS, Gleason score; SVI, seminal vesicle invasion.

Table 3.

Predictors of Gleason score upgrading to pathologic Gleason score 8–10 or having tertiary Gleason pattern 5

	Univariate Analysis	
Clinical Characteristic	**Odds Ratio (95% CI)**	***P* Value**
PCA3 score	1.00 (0.99–1.01)	.59
Age (y)	1.02 (0.95–1.09)	.68
PSA (ng/mL)	1.045 (0.99–1.10)	.089
Clinical T-Category		
T1	1.00 (ref)	—
T2	2.11 (0.64–6.94)	.22
Biopsy GS		
≤7	1.00 (ref)	—
8–10	0.32 (0.12–0.89)	.030
Percent positive biopsies	1.00 (0.98–1.03)	.97
MRI T-Category		
T1–T2	1.00 (ref)	—
T3–T4	0.37 (0.045–3.11)	.36

Table 4.

Univariate and multivariate Cox regression analyses: progression-free survival

	Univariate Analysis		Multivariate Analysis	
Clinical Characteristic	**Odds Ratio (95% CI)**	***P* Value**	**Odds Ratio (95% CI)**	***P* Value**
PCA3 score	1.00 (0.99–1.01)	.35	—	—
Age (y)	1.01 (0.95–1.08)	.72	—	—
Preoperative risk group				
Intermediate	1.00 (ref)	—	1.00 (ref)	—
High	4.17 (1.23–14.11)	.022	1.00 (0.23–4.46)	1.00
Maximal tumor diameter	1.83 (1.09–3.05)	.022	1.20 (0.60–2.39)	.61
Pathologic GS				
≤4 + 3	1.00 (ref)	—	1.00 (ref)	—
≥4 + 4	4.79 (1.95–11.76)	.0006	1.98 (0.52–7.56)	.32
ECE				
No	1.00 (ref)	-	1.00 (ref)	—
Yes	2.69 (1.09–6.60)	.031	1.34 (0.31–5.80)	.69
SVI				
No	1.00 (ref)	—	1.00 (ref)	—
Yes	3.04 (1.18–7.78)	.021	1.36 (0.39–4.71)	.63
pN+				
No	1.00 (ref)	—	1.00 (ref)	—
Yes	3.70 (1.54–8.87)	.0034	1.77 (0.47–6.59)	.40
PSM				
No	1.00 (ref)	—	—	—
Yes	1.20 (0.48–2.97)	.69		

ECE, extracapsular extension; PSM, positive surgical margin.