Published in final edited form as:

Urology. 2014 July ; 84(1): 153–157. doi:10.1016/j.urology.2014.04.006.

Prostate Size and Adverse Pathologic Features in Men Undergoing Radical Prostatectomy

Sung Kyu Hong^{a,b,*}, Bing Ying Poon^c, Daniel D. Sjoberg^c, Peter T. Scardino^{a,d}, and James A. Eastham^{a,d}

^aUrology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

^bDepartment of Urology, Seoul National University Bundang Hospital, Seongnam, Korea

^cDepartment of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

^dDepartment of Urology, Weill Medical College of Cornell University, New York, NY, USA

Abstract

OBJECTIVE—To investigate the relationship between prostate volume measured from preoperative imaging and adverse pathologic features at the time of radical prostatectomy and evaluate the potential effect of clinical stage on such relationship.

METHODS—In 1756 men who underwent preoperative magnetic resonance imaging and radical prostatectomy from 2000 to 2010, we examined associations of magnetic resonance imaging-measured prostate volume with pathologic outcomes using univariate logistic regression and with postoperative biochemical recurrence using Cox proportional hazards models. We also analyzed the effects of clinical stage on the relationship between prostate volume and adverse pathologic features via interaction analyses.

RESULTS—In univariate analyses, smaller prostate volume was significantly associated with high pathologic Gleason score ($P < 0.0001$), extracapsular extension ($P < 0.0001$), and positive surgical margins ($P = 0.032$). No significant interaction between clinical stage and prostate volume was observed in predicting adverse pathologic features (all $P > 0.05$). The association between prostate volume and recurrence was significant in a multivariable adjusting for postoperative variables ($P = 0.031$), but missed statistical significance in the preoperative model ($P = 0.053$). Addition of prostate volume did not change C-Indices (0.78 and 0.83) of either model.

CONCLUSION—Although prostate size did not enhance the prediction of recurrence, it is associated with aggressiveness of prostate cancer. There is no evidence that this association differs

© 2014 Elsevier Inc. All rights reserved.

*Corresponding author: Sung Kyu Hong, Urology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10065, USA. Tel. +1 646 422 4338, Fax: +1 212 988 0759. skhong@snubh.org (S.K. Hong).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

There is no other conflict of interest.

depending on clinical stage. Prospective studies are warranted assessing the effect of initial method of detection on the relationship between volume and outcome.

Keywords

prostate; prostatic neoplasms; organ size; pathology

INTRODUCTION

Several radical prostatectomy (RP) series have shown an association between smaller prostate volume and adverse pathologic features including the presence of high-grade prostate cancer.^{1–4} Such observations have frequently been explained by the theory that the androgen-depleted milieu would select for more aggressive cancer in a smaller gland.^{5–9} However, others have raised the possibility of detection or ascertainment bias, suggesting that the observed association may simply be a consequence of the performance characteristics of prostate-specific antigen (PSA) rather than true tumor biology.^{10,11} As such no consensus has been reached regarding the relationship between prostate volume and adverse pathologic features of prostate cancer.

Published studies on the potential relationship between prostate size and adverse pathologic features, such as high Gleason score, in men who underwent RP have used different measures of prostate volume, making it difficult to compare the findings.^{1–4,10–12} These studies have used transrectal ultrasound (TRUS)-measured prostate volume or radical prostatectomy specimen weight as surrogates for prostate size. While TRUS volume is widely accepted as an adequate clinical surrogate for prostate size, it is also known to be somewhat user-dependent.¹³ Furthermore, RP specimens include bilateral seminal vesicles, vasa deferentia, and possibly large amounts of non-prostatic tissues such as bladder muscles in addition to the prostate, which may lead to inaccurate assessment of prostate size. However, the ability of magnetic resonance imaging (MRI) in analyzing the prostate and its dimensional volume precisely has been noted since the early 1980s.¹⁴ MRI has been increasingly utilized for staging prostate cancer, and it has been shown to be superior or similar to TRUS in accurately measuring prostate volume.^{15,16} Thus, we investigated the relationship between MRI-measured prostate volume and various adverse cancer features along with potential implication of clinical stage based on data from a large cohort of men treated with RP.

MATERIAL AND METHODS

With institutional review board approval, we reviewed the data of 2250 men who underwent both preoperative MRI and RP from January 2000 to December 2010 at Memorial Sloan-Kettering Cancer Center. Of these 2250 patients, we were missing preoperative data on age, preoperative PSA, or clinical stage for 51 patients. We were missing information on pathologic features, such as Gleason score, surgical margin, seminal vesicle invasion, extracapsular extension, and lymph node invasion for another 314 patients. Additionally, 183 patients had preoperatively received a transurethral resection of the prostate or were treated with 5 α -reductase inhibitor or neoadjuvant hormone therapy. After excluding

patients with missing data and/or preoperative treatment, a total of 1756 patients were eligible for our study.

Prostate volume was measured preoperatively by MRI using the widely recognized prolate ellipsoid formula.¹⁷ High tumor grade was defined as Gleason score ≥ 7 . For our study, biochemical recurrence (BCR) was defined as a PSA level > 0.1 ng/ml (confirmed on repeat testing), or secondary treatment for an elevated postoperative PSA.

We examined the associations of MRI-measured prostate volume with various outcomes of interest, including pathologic Gleason score, extracapsular extension, seminal vesicle invasion, margin status, lymph node involvement, and postoperative biochemical outcome. The relationships between prostate volume and pathologic outcomes were estimated via univariate logistic regression models. To assess whether the relationship between prostate volume and aggressive cancer was different by clinical stage (T1c vs T2a), we performed an interaction analysis between prostate volume and clinical stage in predicting each of the five adverse pathologic features, with and without adjusting for age and PSA. We also tested for nonlinearity in the relationship between prostate volume and each of the five adverse pathologic features using restricted cubic splines with knots at the tertiles. Because age at surgery, race, body mass index (BMI), PSA and clinical stage may be factors potentially confounding the relationship between prostate volume and adverse pathologic features, we repeated our analysis of the association between prostate volume and adverse pathologic features adjusting for these factors as a sensitivity analysis. The association of MRI-measured prostate volume with risk of BCR was evaluated using a multivariable preoperative Cox proportional hazards model, which included age, preoperative PSA, biopsy Gleason score, and clinical stage. We also used a postoperative model that included age, preoperative PSA, prostate volume, pathologic Gleason grade, seminal vesicle invasion, surgical margin, extracapsular extension and lymph node involvement. We calculated the concordance index of each of these models. All analyses were conducted using Stata 12.0 (Stata Corp., College Station, TX).

RESULTS

Patient characteristics are listed in Table 1. Median age was 59 years (interquartile range [IQR] 54–64) with a median preoperative PSA of 5 ng/ml (IQR 4.5–8.4) and median MRI-measured prostate volume of 31 cm³ (IQR 24–42). Among our subjects, there was a significant correlation between prostate volume measured on MRI and RP specimen weight (Pearson's $r = 0.82$; $P < 0.0001$). Clinical stage was T1c in 1072 (61.0%) patients, and biopsy Gleason score was ≥ 6 in 904 (51.5%) patients. High-grade disease at RP was observed in 1229 (70%) patients.

Univariate analyses showed that smaller MRI-measured prostate volume had a significant association with high pathologic Gleason score ($P < 0.0001$), extracapsular extension ($P < 0.0001$), and positive surgical margins ($P = 0.032$) (Table 2). Additionally, larger prostate volume was found to be associated with an increased risk of lymph node involvement ($P = 0.023$). Non-significant association was demonstrated between prostate volume and seminal vesicle invasion ($P = 0.200$). Similarly, after adjusting for clinical stage, age at surgery, race,

PSA, and BMI, multivariable analyses also showed smaller prostate volume to be associated with high pathologic Gleason score ($P < 0.0001$), extracapsular extension ($P < 0.0001$), and positive surgical margins ($P = 0.015$) (Table 2). Furthermore, smaller prostate volume was also observed to be associated with seminal vesicle invasion ($P = 0.019$).

Analyzing the effects of clinical stage on the potential association between prostate volume and cancer aggressiveness, we observed no significant interaction between clinical stage and MRI-measured prostate volume in predicting high pathologic Gleason score ($P = 0.11$), extracapsular extension ($P = 0.2$), seminal vesicle invasion ($P = 0.3$), positive surgical margins ($P = 1$), or lymph node involvement ($P = 1$). When adjusted for age and PSA, no significant interactions were observed between clinical stage and MRI-measured prostate volume in predicting high pathologic Gleason score ($P = 0.2$), extracapsular extension ($P = 0.2$), seminal vesicle invasion ($P = 0.2$), positive surgical margins ($P = 0.9$), or lymph node involvement ($P = 0.8$). Such results indicate that the association between prostate volume and each adverse pathologic feature did not differ significantly depending on a patient's clinical stage.

When introducing cubic splines into the models of relationship between MRI-measured prostate volume and adverse pathologic features, we observed a significant nonlinearity in the relationship between MRI-measured prostate volume and high pathologic Gleason score ($P = 0.003$). However, such significant nonlinearity was not maintained when 2 patients with extreme prostate volumes $> 250 \text{ cm}^3$, much higher than the 99th percentile of prostate volume at 111 cm^3 , were excluded from the analysis ($P = 0.3$). No evidence of significant nonlinearity was found in the relationship of MRI-measured prostate volume with extracapsular extension ($P = 0.3$), seminal vesicle invasion ($P = 0.6$), positive surgical margins ($P = 0.9$), or lymph node involvement ($P = 0.8$).

In our cohort of 1756 patients, 242 patients eventually developed BCR while 1514 remained BCR-free at median time to follow up of 5 years. The association between MRI-measured prostate volume and risk of postoperative BCR was not observed to be significant in the preoperative Cox proportional hazards model, which included preoperative variables of age, preoperative PSA, biopsy Gleason score, and clinical stage (hazard ratio [HR] 1.06 per 10 cm^3 , 95% CI, 1.00–1.12, $P = 0.053$). However in the postoperative model, larger prostate volume was observed to be significantly associated with lower risk of postoperative BCR (HR 1.07 per 10 cm^3 , 95% CI, 1.01–1.13, $P = 0.031$). The addition of prostate volume to these two models did not change the C-Index of 0.78 for the preoperative model or the C-Index of 0.83 for the postoperative model.

COMMENT

In this large cohort study, we observed that smaller prostate volume was significantly associated with adverse pathologic features, including high Gleason score, extracapsular extension, seminal vesicle invasion, and positive surgical margins in men undergoing RP. Moreover, we found no evidence indicating that these associations differed significantly depending on clinical stage. Such results suggest that prostate size may be associated with aggressiveness of prostate cancer on a biological level rather than as an artifact of diagnostic

methods, though there remains a possibility of systematic bias across clinical stages. Meanwhile, addition of prostate volume into multivariate models for predicting postoperative prognosis did not enhance predictive discrimination.

Published studies have offered conflicting results and theories on the potential relationship between prostate size and Gleason score. In analyzing patients who underwent sextant prostate biopsy, Karakiewicz et al reported that Gleason score was comparable throughout the range of gland-volume intervals among men with biopsy-proven cancer.¹⁸ Freedland et al analyzed TRUS volume and RP specimen weight of 1,602 men who were treated with RP and whose data were included in the Shared Equal Access Regional Cancer Hospital (SEARCH) Database.¹ They observed that men with smaller prostates had more adverse pathologic features and higher risk of tumor progression after RP. Despite using different surrogates for prostate size, our findings are similar in that smaller prostates were associated with more adverse pathologic features. Conversely, in an analysis of the association between prostate size and tumor grade in both the prostate biopsy and RP specimens, Kulkarni et al observed that larger prostates were more likely to have lower biopsy grade cancers, whereas there was no association between gland size and RP Gleason score.¹² Subsequently, they performed a follow-up study of men with low-risk cancer in which they found that TRUS volume was not associated with Gleason score upgrading after RP.¹⁹ Based upon their findings, Kulkarni et al argued that although smaller prostates increase the sensitivity of detecting high-grade tumors at biopsy, it does not predict high-grade tumors at RP. Meanwhile, Kassouf et al reported that patients with prostate size > 50 cc had a significantly higher incidence of well-differentiated tumors at RP and lower likelihood of tumor upgrading.³ They concluded that prostate size is a confounding variable in the relationship between PSA and prostate biopsy since PSA level is driven by both prostate size and by prostate cancer. In analyzing TRUS volume, a European group's study of an RP cohort of 3,412 men also demonstrated that tumors located in small glands are fundamentally more aggressive than those located within larger glands.² This group concluded that men with small prostates were predisposed to higher rates of high-grade cancer. Thus, while the association between prostate size and pathologic Gleason score has not been noted universally, the results from relatively larger series have indicated that the association between the two variables does exist, as observed in our findings.

For a given PSA level, smaller prostates have been suggested to be more likely to harbor high-grade disease than larger prostates.^{20,21} One may argue that the higher rate of high-grade disease for smaller prostates may simply be viewed as a consequence of the enhanced performance of PSA in smaller glands rather than a difference in cancer biology. A recent study that made this argument demonstrated that prostate size was associated with high-grade cancer in patients with clinical T1c prostate cancer but not in patients with T2 prostate cancer.¹⁰ The same group also reported that a smaller prostate only predicts high-grade cancer in men with T1c disease.¹¹ However, the approach of stratifying patients by clinical stage to analyze the size-grade relationship has been done by others with contrasting results. In the Freedland et al study, smaller prostate size, as assessed by RP specimen weight, remained significantly associated with high-grade disease even when they only included men with clinical stage T2 tumors.¹ It should also be reiterated that this method of stage stratification is not an accurate test of whether prostate size and adverse pathologic

features have a significantly different relationship in patients with T1c disease compared to those with T2a disease. For such a purpose, one would have to evaluate the interaction between prostate volume and clinical stage in predicting adverse pathologic features. We performed such an analysis and observed no evidence that the association of prostate volume and adverse pathologic features differed significantly according to clinical stage.

Notably, some physicians have previously reported that biphasic relationships existed between prostate volume and adverse pathologic features at RP.^{1,2} For example, increasing prostate volume was related to increased rates of high-grade disease at RP, extracapsular extension, seminal vesicle invasion, and tumor volume below a cutoff value of 45 cm³.² However, above the cutoff of 45 cm³, increasing prostate volume was inversely associated with all four pathologic features. In our study, we also observed evidence of nonlinearity in the relationship between prostate volume and pathologic Gleason score. However, such nonlinearity was not maintained when two patients with extreme prostate volume (> 250 cm³) were excluded. No evidence of significant nonlinearity in the relationship between MRI-measured prostate volume and other adverse pathologic features was observed in our study.

Currently, no exact underlying mechanism can be provided for the association between tumor grade and prostate size. Some have suggested that aggressive prostate tumors may suppress the production of testosterone resulting in smaller prostate size.^{22,23} Others proposed that low testosterone levels may affect the intraprostatic microenvironment, increasing both androgen receptor density and tumor microvessel formation to facilitate more aggressive prostate cancer.⁷ However, published data on the relationship between hormonal levels and prostate cancer aggressiveness have shown largely inconsistent findings, making it difficult to draw a conclusion.^{6,24–27} The fact that hormonal profiles assayed at the time of diagnosis of prostate cancer in a significant proportion of subjects studied may not have reflected long-term intraprostatic and/or systemic androgenicity, and therefore, may have played a large role in these inconsistent findings. Also, poor correlation between intraprostatic and systemic testosterone levels, as well as the time-dependent variation in serum testosterone complicates the issue further.²⁸

There are several potential limitations to our study, including its retrospective nature. Some patients were excluded due to missing data. We could not account for interobserver variation in the measurement of prostate volume via MRI. Not all men who had RP at our institution underwent MRI preoperatively. However, we found no significant evidence of difference in the prevalence of high-grade disease between patients who did and did not receive preoperative prostate MRI (data not shown). As lymph node dissection, not done in all cases, was not performed in the universally same manner in all of our subjects, the finding of increased rate of lymph node involvement with larger prostate size would be difficult to interpret and further evaluation would be necessary. Furthermore, while the association of prostate volume with postoperative biochemical outcome was not found to be significant in the preoperative model, the results may have been different if metastasis-free or prostate cancer-specific survival were assessed with longer postoperative follow-up.

CONCLUSION

Although prostate size did not enhance the prediction of prognosis in men who underwent RP, it is associated with aggressiveness of prostate cancer with no evidence that this association differs depending on clinical stage. Further studies, preferably prospective investigations, assessing the initial method of detection for prostate cancer to rule out possibility of ascertainment bias and on the relationship between in vivo androgenicity, prostate size, and aggressiveness of prostate cancer would be needed to elucidate the exact mechanism underlying the observed association.

Acknowledgments

This study has been supported in part by NIH/NCI Cancer Center Support Grant to MSKCC under award number P30 CA008748.

References

1. Freedland SJ, Isaacs WB, Platz EA, et al. Prostate size and risk of high-grade, advanced prostate cancer and biochemical progression after radical prostatectomy: a search database study. *J Clin Oncol.* 2005; 23:7546–7554. [PubMed: 16234520]
2. Briganti A, Chun FK, Suardi N, et al. Prostate volume and adverse prostate cancer features: fact not artifact. *Eur J Cancer.* 2007; 43:2669–2677. [PubMed: 17996442]
3. Kassouf W, Nakanishi H, Ochiai A, et al. Effect of prostate volume on tumor grade in patients undergoing radical prostatectomy in the era of extended prostatic biopsies. *J Urol.* 2007; 178:111–114. [PubMed: 17499289]
4. Newton MR, Phillips S, Chang SS, et al. Smaller prostate size predicts high grade prostate cancer at final pathology. *J Urol.* 2010; 184:930–937. [PubMed: 20643423]
5. Morgentaler A. Testosterone deficiency and prostate cancer: emerging recognition of an important and troubling relationship. *Eur Urol.* 2007; 52:623–625. [PubMed: 17433531]
6. Massengill JC, Sun L, Moul JW, et al. Pretreatment total testosterone level predicts pathological stage in patients with localized prostate cancer treated with radical prostatectomy. *J Urol.* 2003; 169:1670–1675. [PubMed: 12686805]
7. Schatzl G, Madersbacher S, Thurnidl T, et al. High-grade prostate cancer is associated with low serum testosterone levels. *Prostate.* 2001; 47:52–58. [PubMed: 11304729]
8. Yamamoto S, Yonese J, Kawakami S, et al. Preoperative serum testosterone level as an independent predictor of treatment failure following radical prostatectomy. *Eur Urol.* 2007; 52:696–701. [PubMed: 17412490]
9. Isbarn H, Pinthus JH, Marks LS, et al. Testosterone and prostate cancer: revisiting old paradigms. *Eur Urol.* 2009; 56:48–56. [PubMed: 19375844]
10. Liu JJ, Brooks JD, Ferrari M, et al. Small prostate size and high grade disease--biology or artifact? *J Urol.* 2011; 185:2108–2111. [PubMed: 21496855]
11. Ngo TC, Conti SL, Shinghal R, et al. Prostate size does not predict high grade cancer. *J Urol.* 2012; 187:477–480. [PubMed: 22177152]
12. Kulkarni GS, Al-Azab R, Lockwood G, et al. Evidence for a biopsy derived grade artifact among larger prostate glands. *J Urol.* 2006; 175:505–509. [PubMed: 16406982]
13. Tewari A, Indudhara R, Shinohara K, et al. Comparison of transrectal ultrasound prostatic volume estimation with magnetic resonance imaging volume estimation and surgical specimen weight in patients with benign prostatic hyperplasia. *J Clin Ultrasound.* 1996; 24:169–174. [PubMed: 8727414]
14. Hricak H, Williams RD, Spring DB, et al. Anatomy and pathology of the male pelvis by magnetic resonance imaging. *AJR Am J Roentgenol.* 1983; 141:1101–1110. [PubMed: 6196961]

15. al-Rimawi M, Griffiths DJ, Boake RC, et al. Transrectal ultrasound versus magnetic resonance imaging in the estimation of prostatic volume. *Br J Urol.* 1994; 74:596–600. [PubMed: 7530124]
16. Jeong CW, Park HK, Hong SK, et al. Comparison of prostate volume measured by transrectal ultrasonography and MRI with the actual prostate volume measured after radical prostatectomy. *Urol Int.* 2008; 81:179–185. [PubMed: 18758216]
17. Bianco FJ Jr, Mallah KN, Korets R, et al. Prostate volume measured preoperatively predicts for organ-confined disease in men with clinically localized prostate cancer. *Urology.* 2007; 69:343–346. [PubMed: 17320675]
18. Karakiewicz PI, Bazinet M, Aprikian AG, et al. Outcome of sextant biopsy according to gland volume. *Urology.* 1997; 49:55–59. [PubMed: 9000186]
19. Kulkarni GS, Lockwood G, Evans A, et al. Clinical predictors of Gleason score upgrading: implications for patients considering watchful waiting, active surveillance, or brachytherapy. *Cancer.* 2007; 109:2432–2438. [PubMed: 17497649]
20. Thompson IM, Ankerst DP, Chi C, et al. Operating characteristics of prostate-specific antigen in men with an initial PSA level of 3.0 ng/ml or lower. *JAMA.* 2005; 294:66–70. [PubMed: 15998892]
21. Elliott CS, Shinghal R, Presti JC Jr. The influence of prostate volume on prostate-specific antigen performance: implications for the prostate cancer prevention trial outcomes. *Clin Cancer Res.* 2009; 15:4694–4699. [PubMed: 19584168]
22. Risbridger GP. Recent progress in our understanding of inhibin in the prostate gland. *J Endocrinol.* 1998; 157:1–4. [PubMed: 9614351]
23. Miller LR, Partin AW, Chan DW, et al. Influence of radical prostatectomy on serum hormone levels. *J Urol.* 1998; 160:449–453. [PubMed: 9679896]
24. Chodak GW, Vogelzang NJ, Caplan RJ, et al. Independent prognostic factors in patients with metastatic (stage D2) prostate cancer. The Zoladex Study Group. *JAMA.* 1991; 265:618–621. [PubMed: 1824790]
25. Chen SS, Chen KK, Lin AT, et al. The correlation between pretreatment serum hormone levels and treatment outcome for patients with prostatic cancer and bony metastasis. *BJU Int.* 2002; 89:710–713. [PubMed: 11966629]
26. Iversen P, Rasmussen F, Christensen IJ. Serum testosterone as a prognostic factor in patients with advanced prostatic carcinoma. *Scand J Urol Nephrol Suppl.* 1994; 157:41–47. [PubMed: 7939452]
27. Zagars GK, Pollack A, von Eschenbach AC. Serum testosterone--a significant determinant of metastatic relapse for irradiated localized prostate cancer. *Urology.* 1997; 49:327–334. [PubMed: 9123693]
28. Mostaghel EA, Page ST, Lin DW, et al. Intraprostatic androgens and androgen-regulated gene expression persist after testosterone suppression: therapeutic implications for castration-resistant prostate cancer. *Cancer Res.* 2007; 67:5033–5041. [PubMed: 17510436]

Table 1

Patient characteristics

Variables	N =1756
Median age (IQR) (years)	59 (54–64)
Median body mass index (IQR) (kg/m ²)	28 (25–30)
No. race (%) (n = 1716)	
black	126 (7.3)
others	1590 (92.7)
Median MRI-measured prostate volume (IQR) (cm ³)	31 (24–42)
Median preoperative PSA (IQR) (ng/mL)	5.5 (4.0–7.9)
No. biopsy Gleason score (%)	
6	904 (51.5)
7	852 (48.5)
No. clinical stage (%)	
T1c	1072 (61.0)
T2	684 (39.0)
No. pathologic Gleason score (%)	
6	527 (30.0)
7	1229 (70.0)
No. extracapsular extension (%)	589 (33.5)
No. seminal vesicle invasion (%)	118 (6.7)
No. positive surgical margin (%)	235 (13.4)
No. lymph node involvement (%)	100 (5.7)

IQR = interquartile range; MRI = magnetic resonance imaging; PSA = prostate-specific antigen

Associations of magnetic resonance imaging (MRI)-measured prostate volume with adverse pathologic features at radical prostatectomy as assessed via univariate and multivariable logistic regression models

Table 2

Outcomes	MRI volume (per 10 cc) on univariate analysis			MRI volume (per 10 cc) on multivariable analysis		
	OR	95% CI	P	OR	95% CI	P
High pathologic Gleason score	0.85	0.81, 0.89	<0.0001	0.73	0.67, 0.79	<0.0001
Extracapsular extension	0.86	0.81, 0.92	<0.0001	0.78	0.72, 0.85	<0.0001
Seminal vesicle invasion	0.92	0.83, 1.03	0.2	0.82	0.69, 0.97	0.019
Positive margin	0.91	0.84, 0.99	0.032	0.88	0.79, 0.97	0.015
Lymph node involvement	1.09	1.01, 1.18	0.023	1.13	1.01, 1.25	0.026

Abbreviations: OR = odds ratio; CI = confidence interval