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Tumor volume, tumor percentage involvement or prostate volume: Which is predictive of PSA recurrence?

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Abstract

Objective—To compare the effects of tumor volume (TV), tumor percentage involvement (TPI) and prostate volume (PV) on PSA recurrence (PSAR) following radical prostatectomy (RP).

Methods—A cohort of 3528 patients receiving RP between 1988 and 2008 was retrieved from the Duke Prostate Center. Patients were stratified by TV (<3cc, 3-6cc, >6cc), TPI (<10%, 10-20%, >20%) and PV (<35cc, 35-45cc, >45cc) and their effects on PSAR evaluated using Kaplan-Meier (KM) analysis. Clinico-pathological variables included in univariate analysis were age at surgery, race, year of surgery, PSA, pathological Gleason score, pathological tumor stage, margin status, extra capsular extension (ECE) and seminal vesicle invasion (SVI). The effects of TV, TPI and PV (as continuous and categorical variables) on PSAR were compared using Cox analysis.

Results—TPI, TV and PV were predictive of PSAR ($p < 0.05$) in KM. In multivariate analysis as continuous variables, TPI and PV were predictive of PSAR (Odds ratio (OR) = 1.16 and OR = 0.65, $p < 0.05$). As categorical variables, TPI > 20% and PV 10-35cc were predictive of PSAR (OR = 1.45 and OR = 1.25, $p < 0.05$). TV was not predictive of PSAR in either analysis. Pathological Gleason score 7, PSA, positive margins, SVI and tumor stage T3/4 were found to be predictors of PSAR ($p < 0.05$).

Conclusions—TV, TPI and PV were predictive of PSAR in univariate analysis, but only TPI and PV were predictive in multivariate analysis. TPI and PV should be considered when evaluating, assessing and counseling patients about PSAR risk.

Keywords

Prostate cancer; Tumor volume; Tumor percentage involvement; Prostate volume; PSA recurrence

INTRODUCTION

Tumor volume (TV), tumor percentage involvement (TPI) and prostate volume (PV) have all been implicated in PSA recurrence (PSAR), however, contention still exists as to which, if any, factors are clinically useful predictors.

TV has been shown to be an independent predictor of PSAR^{1,2}, positive surgical margins³ and overall survival.⁴ Conversely, others^{5,6} have shown that TV provides no individual

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CONFLICTS OF INTEREST None.

prognostic information when considered with Gleason score and pathological stage and Merrill et al⁷ showed that tumor volume is only predictive in patients with Gleason greater than or equal to 7.

The percentage of prostate occupied by tumor (TPI) is another variable of interest. It has been shown to be predictive of PSAR in both organ confined disease^{8,9} and all stages of disease.^{6,10} On the contrary, Epstein et al¹¹ showed that TPI offered no prognostic information for patients with stage pT2 prostate cancer.

Prostate volume has also been shown to be predictive of PSAR.^{12,13} Men with smaller prostates have been shown to have higher grade and more advanced disease¹⁴ and men with larger prostates have been shown to have lower rates of PSAR.^{15,16}

Currently there is no consensus on the utility of TV, TPI and PV in the prediction of PSAR. The goal of this study was to examine the effects of TV, TPI, and PV on PSAR following radical prostatectomy (RP) in a large patient population. To our knowledge, this was the first paper to examine all three variables in a single population.

MATERIAL AND METHODS

Patient Population

Following institutional review board approval, a cohort of 4562 patients receiving RP between 1988 and 2008 was retrieved from the Duke Prostate Center Database. Patients lacking information on TV, TPI and PV were excluded from the analysis. 3528 patients were included in the final analysis.

Specimen Collection

Prostate specimens were harvested in the operating room, prepared as previously described¹⁰ and submitted for microscopic evaluation. Tumor involvement of each slide was estimated by the percent of the slide containing tumor. Estimation of tumor percentage involvement for the entire prostate was completed by summing each individual slide and averaging the results from all slides analyzed.

Statistical Analysis

Patients were stratified by TV (< 3 cc, 3-6 cc, > 6 cc), TPI (< 10%, 10-20%, > 20%) and PV (< 35 cc, 35-45 cc, > 45 cc). Cut off points for the variables TV, TPI and PV were chosen to separate the patient populations, roughly into thirds. TPI was measured by pathologists at our institution as previously described.¹⁰ The prostate specimens were assessed and the percentage of tumor contained on each slide averaged. The clinical and pathologic variables age at surgery (<50, 50-60, 60-70, >70), race (African American (AA) or non-AA), year of surgery (pre-2000 or post-2000), PSA at diagnosis, pathological Gleason score (< 7, 7, > 7), pathological tumor stage (pT2 or pT3/4), surgical margin status (positive or negative), extra capsular extension (ECE) (positive or negative) and seminal vesicle invasion (SVI) (positive or negative) were included in univariate analysis. Chi-squared and Kruskal-Wallis tests were used where appropriate. PSA, PV and TPI were log transformed due to non-normal distribution. Individual effects of TV, TPI and PV on PSAR were evaluated using Kaplan-Meier (KM) analysis.

PSAR was defined as any increase in PSA greater than 0.2 ng/ml after the initial four week postoperative period.¹⁷ Variables entered into multivariate analysis were TV, TPI, PV, age at surgery, year of surgery, PSA, pathological Gleason score, pathological tumor stage, surgical margin status, ECE and SVI. TV, TPI, PV and PSA all exhibited non-normal

distributions and were log transformed for analysis. TV, TPI and PV were all analyzed as both continuous and categorical variables. Significant risk factors for PSAR were determined through Cox proportional hazards analysis using a backwards stepwise logistic regression method.

All statistical analyses were performed using SPSS® 15.0 (Cary, North Carolina).

RESULTS

Patient Demographics

The mean age at surgery for the 3528 patients was 62.3 years (35.0 to 83.1 years). 85.3% of patients were non-AA and 14.7% were AA. The median PSA for all men was 6.3 ng/ml. Statistics including Gleason score, pathologic stage and surgical margin status for all patients are shown in Table 1.

TV

In univariate analysis, age at surgery, race, pathological Gleason score, pathological tumor stage, year of surgery, PSA, SVI, ECE and positive surgical margins were all significantly different with regards to TV groups ($p < 0.05$). The higher TV, the higher the rate of PSAR was on Kaplan-Meier analysis ($p < 0.001$, Figure 1A).

In multivariate analysis, TV was analyzed as both a categorical and continuous variable. TV was not a significant predictor of PSAR in either analysis ($p > 0.05$). When TV was analyzed as a continuous variable pathological Gleason score > 7 , pathological Gleason score = 7, PSA, positive surgical margins, SVI and pathological tumor stage pT3/4 were significantly predictive of PSAR ($p < 0.05$). When TV was analyzed as a categorical variable pathological Gleason score > 7 , pathological Gleason score = 7, PSA, positive surgical margins, SVI and pathological tumor stage pT3/4 were significantly predictive of PSAR ($p < 0.05$). Hazard ratios (HR) and p-values are listed in Table 2.

TPI

In univariate analysis, age at surgery, race, pathological Gleason score, pathological tumor stage, year of surgery, PSA, SVI, ECE and positive surgical margins were all significantly different in regards to TPI groups ($p < 0.05$). For prostates with a higher TPI, a higher the rate of PSAR was identified on Kaplan-Meier analysis ($p < 0.001$, Figure 1B).

In multivariate analysis, TPI was analyzed as both a categorical and continuous variable. As a continuous variable, TPI was found to be a significant predictor (HR = 1.16, $p = 0.002$) of PSAR. Pathological Gleason score > 7 , pathological Gleason score = 7, PSA, positive surgical margins, SVI and pathological tumor stage pT3/4 were also found predictive of PSAR ($p < 0.05$). As a categorical variable, TPI $> 20\%$ was found to be a significant predictor of PSAR (HR = 1.45, $p = 0.001$). Pathological Gleason score > 7 , pathological Gleason score = 7, PSA, positive surgical margins, SVI and pathological tumor stage pT3/4 were also found predictive of PSAR ($p < 0.05$). HR and p-values are shown in Table 2.

PV

In univariate analysis, age at surgery, race, pathological Gleason score, pathological tumor stage, year of surgery, PSA, SVI, ECE and positive surgical margins were all significantly different in regards to PV groups ($p < 0.05$). The lower the PV the higher the rate of PSAR was on Kaplan-Meier analysis ($p = 0.012$, Figure 1C).

On multivariate analysis, PV was analyzed as both a categorical and continuous variable. As a continuous variable, PV was found to be a significant predictor of PSAR (HR = 0.65, $p < 0.001$). Pathological Gleason score > 7 , pathological Gleason score = 7, PSA, positive surgical margins, SVI and pathological tumor stage pT3/4 were also found predictive of PSAR ($p < 0.05$). As a categorical variable, PV < 35 cc was found to be a significant predictor of PSAR (HR = 1.25, $p = 0.015$). Pathological Gleason score > 7 , pathological Gleason score = 7, PSA, positive surgical margins, SVI and tumor stage T3/4 were also found predictive of PSAR ($p < 0.05$). HR and p-values are shown in Table 2.

TV, TPI and PV all considered as categorical variables

The final analysis performed included all three categorical variables. Continuous variables were not included in the analysis because TV was calculated using PV and TPI and was therefore linearly dependent. TPI $> 20\%$ and PV < 35 cc were found to be predictive of PSAR (HR = 1.32, $p = 0.03$, HR = 1.25, $p = 0.02$). TV was not found to be predictive of PSAR. Pathological Gleason score > 7 , pathological Gleason score = 7, PSA, positive surgical margins, SVI and pathological tumor stage pT3/4 were also found predictive of PSAR ($p < 0.05$). HR and p-values are shown in Table 2.

COMMENT

Previous studies have shown TV, TPI and PV to be predictive of PSA recurrence. However, for TV and TPI, conflicting studies exist.¹⁻¹¹ Though all three variables have been analyzed independently in the past, to our knowledge, this is the first study examining the variables within the same population in both univariate and multivariate analysis. Additionally, it is the largest cohort of patients analyzed in such a study.

TV

TV was found to be an independent predictor of PSAR in univariate analysis. However, when included in multivariate analysis it was not found to be a significant predictor of PSAR. These findings were in agreement with a number of previous studies.^{5,6,11}

There are two ways to measure TV. One is to use three dimensional reconstruction of radical prostatectomy specimens¹⁸ and the other is to use TPI and PV to calculate TV. The method of three dimensional reconstruction is accurate, but only about 12% of urologists have access to such processing and it is typically used for research purposes.¹⁹

This study used TPI and PV to calculate the TV. This process, while less exact than the process described previously, uses routinely reported pathologic variables. May et al⁶, using a similar technique for determining TPI (TV divided by PV) found that TPI $> 25\%$ was predictive of PSAR and that TV was not. These findings suggest that TPI and PV are the more important variables for determining PSAR risk and reveal that TV may only appear significant when conditions involving PV are suitable.

TPI

TPI was predictive of PSAR in both univariate and multivariate analysis. Previous studies with fewer patients (ranging from 528 to 2200) and comparable conditions obtained similar conclusions.^{6,9,8,10} This team and others had previously examined TPI as a categorical variable and found it predictive of PSAR in univariate analysis,^{8,10} however only a few have considered TPI as a categorical variable in multivariate analysis.

In one such study, Ramos et al⁹ categorized patients in TPI groups of $< 10\%$, 10- 20% and $> 20\%$ (1286, 465 and 99 patients respectively) and found that those with a TPI $> 20\%$ has a

relative risk (RR) of 2.1 for PSAR. This differed from our finding that patient with TPI > 20% had an HR of 1.45 times for PSAR. This difference is likely due to the higher number of patients and similar number of patients in each group (1159, 1461 and 831) in our cohort.

Our study showed that men with a TPI > 20% were at 1.45 times risk of PSAR relative to the TPI < 10% group, further demonstrating the utility in categorizing TPI. Interestingly, within our model, TPI > 20% was of higher predictive value of PSAR than Gleason = 7 (HR = 1.38) and pathological T3/T4 disease (HR = 1.22) and comparable to PSA (HR = 1.53), all of which are commonly used in nomograms predicting PSAR following treatment.^{20,21} These results were comparable to those of Ramos who found that men with a TPI > 20% had a relative risk of 2.1 of having PSAR. While further study is needed to confirm the utility, our findings suggest that TPI should be considered, along with other clinically useful variables, by clinicians in determining which patients are at the highest risk for recurrence and may benefit from adjuvant therapies.

PV

PV was shown to be a predictor of PSAR in both univariate and multivariate analysis. Previous studies from this team and others showed that men with small PV had higher risk of PSAR.^{2,12,14,15} The reason for this remains unknown, however a number of potential explanations exist. It has been suggested that men with smaller prostates may have lower levels of testosterone which has been shown to correlate with more aggressive prostate cancer.²² Another explanation is that a tumor within a small prostate has less distance to travel to get outside the prostatic capsule, demonstrated by Yadav et al. who showed that decreased PV is a predictor of ECE.²³ It is likely that a combination of these factors leads to a greater chance of PSAR following treatment for men with smaller PV.

Some of the most immediately applicable and important findings in our study came from the analysis of PV. As a categorical variable, our stratification and analysis of PV in sub-groups of < 35, 35-45, and > 45 cc, is one of only a few studies to analyze prostate volumes in a range that has immediate clinical relevance and, to our knowledge, included the largest cohort of patients. Our study showed that a prostate volume < 35 cc was a risk factor for PSAR compared to men with prostates > 45 cc. Many previous studies have analyzed prostate volume and while results were significant, they often focused on results from prostates in the 50-100 cm³ range.^{15,16,24} However, these larger prostate volumes are not consistently seen in routine practice. The size of a normal prostate is 20-30 cc^{25, 26} and reported medians in the literature set the median for diseased prostate volume around 35-45 cc.^{2, 12,13,15,24} In our study the median prostate volume was 38.4 cc, with only 25% of men having prostates larger than 50 cc and 10% larger than 64 cc. As a result, our finding that men with prostate volumes less than 35 cc have a 25% increased risk for PSAR compared to men with larger volume prostates provides clinicians with a clinically relevant value by which to assess patients risk for PSAR following RP. Additionally, the prognostic value was comparable to that of T3/T4 disease, a variable often considered when predicting risk for PSAR.^{27,28}

As a continuous variable, PSAR was significantly associated with PV (HR = 0.65, $p < 0.001$). The reduction in PSAR risk may initially seem unimpressive, however when considered in context with other variables, it becomes more significant. The prognostic value of PSA in this model was HR = 1.67, however, when the inverse is taken, an HR of 0.60 is found. Taking the reciprocal of PSA shows, as expected, that a decrease in PSA is predictive of decreased PSAR risk; interestingly, the predictive value is similar to that of PV. PSA is a major factor in the stratification of risk for PSAR^{20,21} and death^{29,30} for patients with prostate cancer. PV may offer additional information that should be considered when counseling patients about their risk of PSAR following RP.

TV, TPI and PV all considered as categorical variables

When TV, TPI and PV were all included in multivariate analysis as categorical variables, TPI > 20% and PV < 35 cc were found to be predictive of PSAR. Previous studies have examined the effects of two of the variables in a single population such as TPI and TV^{6, 9, 11} or TPI and PV¹⁰. To our knowledge, this is the first study to include TV, TPI and PV in multivariate analysis within a single population. The findings add strength to the argument that PV and TPI are of greater importance than TV with regards to PSAR risk.

PV and TPI are easily calculated pathological variables that give clinicians additional information regarding patient risk of PSAR following RP. While neither PV between 10-35 cc nor TPI > 20% was found to be as predictive as variables such as a Gleason score > 7, their prognostic abilities (HR = 1.24 and HR = 1.32 respectively) were comparable to that of a T3/T4 pathological stage (HR = 1.20), which is included in predictive nomograms²⁸ as well as considered when making decisions regarding treatment. The results of this study suggest that PV and TPI should be taken into consideration when counseling patients on their risk for PSAR following RP.

Limitations

Limitations of our study include potential population bias as Duke is a high volume and tertiary care center. This potentially limits the generalizability of the findings of the study. Additionally, this study was retrospective. Next, only 77% of our total patient population was included in the analysis due to missing data. While this represents a significant portion of the cohort, the excluded men were not found to be significantly different with respect to rates of PSAR than men included in the analysis. It should also be noted that as prostates get larger it may be more difficult to accurately characterize some pathological characteristics due to the increased work involved. Finally, within our analysis, TV was found by multiplying the TPI and PV rather than using the three dimensional reconstruction of radical prostatectomy specimens.

CONCLUSION

TV, TPI and PV were predictive of PSAR in univariate analysis, but only TPI and PV were predictive in multivariate analysis. Previous studies that considered only one or two of these variables may have failed to recognize important information related to PSAR risk. Considered individually, TPI > 20% and PV had PSAR predictive values comparable to or better than a pathological stage of T3/T4, Gleason score = 7 and PSA. When all variables were considered, patients with a PV less than 35 cc and patients with a TPI of greater than 20% were found to be at an increased risk of PSAR. TPI and PV should be considered when evaluating, assessing and counseling patients about the risks of PSAR.

Acknowledgments

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References

1. Nelson BA, Shappell SB, Chang SS, Wells N, Farnham SB, Smith JA Jr. Cookson MS. Tumour volume is an independent predictor of prostate-specific antigen recurrence in patients undergoing radical prostatectomy for clinically localized prostate cancer. *BJU Int.* 2006; 97:1169–72. [PubMed: 16686706]
2. Stamey TA, McNeal JE, Yemoto CM, Sigal BM, Johnstone IM. Biological determinants of cancer progression in men with prostate cancer. *JAMA.* 1999; 281:1395–400. [PubMed: 10217055]

3. Chun FK, Briganti A, Jeldres C, Gallina A, Erbersdobler A, Schlomm T, Walz J, Eichelberg C, Salomon G, Haese A, et al. Tumour volume and high grade tumour volume are the best predictors of pathologic stage and biochemical recurrence after radical prostatectomy. *Eur J Cancer*. 2007; 43:536–43. [PubMed: 17222546]
4. Vollmer RT. Percentage of tumor in prostatectomy specimens: a study of American Veterans. *Am J Clin Pathol*. 2009; 131:86–91. [PubMed: 19095570]
5. Kikuchi E, Scardino PT, Wheeler TM, Slawin KM, Ohori M. Is tumor volume an independent prognostic factor in clinically localized prostate cancer? *J Urol*. 2004; 172:508–11. [PubMed: 15247716]
6. May M, Siegsmund M, Hammermann F, Loy V, Gunia S. Visual estimation of the tumor volume in prostate cancer: a useful means for predicting biochemical-free survival after radical prostatectomy? *Prostate Cancer Prostatic Dis*. 2007; 10:66–71. [PubMed: 17189956]
7. Merrill MM, Lane BR, Reuther AM, Zhou M, Magi-Galluzzi C, Klein EA. Tumor volume does not predict for biochemical recurrence after radical prostatectomy in patients with surgical Gleason score 6 or less prostate cancer. *Urology*. 2007; 70:294–8. [PubMed: 17826492]
8. Carvalhal GF, Humphrey PA, Thorson P, Yan Y, Ramos CG, Catalona WJ. Visual estimate of the percentage of carcinoma is an independent predictor of prostate carcinoma recurrence after radical prostatectomy. *Cancer*. 2000; 89:1308–14. [PubMed: 11002227]
9. Ramos CG, Roehl KA, Antenor JA, Humphrey PA, Catalona WJ. Percent carcinoma in prostatectomy specimen is associated with risk of recurrence after radical prostatectomy in patients with pathologically organ confined prostate cancer. *J Urol*. 2004; 172:137–40. [PubMed: 15201754]
10. Rampersaud EN, Sun L, Moul JW, Madden J, Freedland SJ. Percent tumor involvement and risk of biochemical progression after radical prostatectomy. *J Urol*. 2008; 180:571–6. discussion 576. [PubMed: 18554662]
11. Epstein JI, Carmichael M, Partin AW, Walsh PC. Is tumor volume an independent predictor of progression following radical prostatectomy? A multivariate analysis of 185 clinical stage B adenocarcinomas of the prostate with 5 years of followup. *J Urol*. 1993; 149:1478–81. [PubMed: 8501792]
12. Schroeck FR, Sun L, Freedland SJ, Jayachandran J, Robertson CN, Moul JW. Race and prostate weight as independent predictors for biochemical recurrence after radical prostatectomy. *Prostate Cancer Prostatic Dis*. 2008
13. Stamey TA, Yemoto CM, McNeal JE, Sigal BM, Johnstone IM. Prostate cancer is highly predictable: a prognostic equation based on all morphological variables in radical prostatectomy specimens. *J Urol*. 2000; 163:1155–60. [PubMed: 10737486]
14. Freedland SJ, Isaacs WB, Platz EA, Terris MK, Aronson WJ, Amling CL, Presti JC Jr, Kane CJ. Prostate size and risk of high-grade, advanced prostate cancer and biochemical progression after radical prostatectomy: a search database study. *J Clin Oncol*. 2005; 23:7546–54. [PubMed: 16234520]
15. D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Tomaszewski JE, Wein A. A prostate gland volume of more than 75 cm³ predicts for a favorable outcome after radical prostatectomy for localized prostate cancer. *Urology*. 1998; 52:631–6. [PubMed: 9763083]
16. Foley CL, Bott SR, Thomas K, Parkinson MC, Kirby RS. A large prostate at radical retropubic prostatectomy does not adversely affect cancer control, continence or potency rates. *BJU Int*. 2003; 92:370–4. [PubMed: 12930421]
17. Cookson MS, Aus G, Burnett AL, Canby-Hagino ED, D'Amico AV, Dmochowski RR, Eton DT, Forman JD, Goldenberg SL, Hernandez J, 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; 177:540–5. [PubMed: 17222629]
18. Zeng J, Bauer J, Yao X, Zhang W, Sesterhenn I, Connelly R, Moul J, Mun SK. Building an accurate 3D map of prostate cancer using computerized models of 280 whole-mounted radical prostatectomy specimens. *Proc. of SPIE Medical Imaging Conference*. 2000; vol. 3976:466–477.
19. True LD. Surgical pathology examination of the prostate gland. Practice survey by American society of clinical pathologists. *Am J Clin Pathol*. 1994; 102:572–9. [PubMed: 7942619]

20. Kattan MW, Eastham JA, Stapleton AM, Wheeler TM, Scardino PT. A preoperative nomogram for disease recurrence following radical prostatectomy for prostate cancer. *J Natl Cancer Inst.* 1998; 90:766–71. [PubMed: 9605647]
21. Stephenson AJ, Scardino PT, Eastham JA, Bianco FJ Jr, Dotan ZA, DiBlasio CJ, Reuther A, Klein EA, Kattan MW. Postoperative nomogram predicting the 10-year probability of prostate cancer recurrence after radical prostatectomy. *J Clin Oncol.* 2005; 23:7005–12. [PubMed: 16192588]
22. Massengill JC, Sun L, Moul JW, Wu H, McLeod DG, Amling C, Lance R, Foley J, Sexton W, Kusuda L, et al. Pretreatment total testosterone level predicts pathological stage in patients with localized prostate cancer treated with radical prostatectomy. *J Urol.* 2003; 169:1670–5. [PubMed: 12686805]
23. Yadav R, Tu JJ, Jhaveri J, Leung RA, Rao S, Tewari AK. Prostate volume and the incidence of extraprostatic extension: is there a relation? *J Endourol.* 2009; 23:383–6. [PubMed: 19193138]
24. Descazeaud A, Zerbib M, Vieillefond A, Debre B, Peyromaure M. [The low weight of the prostate is an independent risk factor for positive surgical margins on radical prostatectomy specimens]. *Prog Urol.* 2007; 17:203–7. [PubMed: 17489319]
25. Tanagho, EA.; McAninch, JW. *Smith's General Urology.* Lange Medical Books/McGraw-Hill; New York: 2004. p. 758
26. Wein, A.; Kavoussi, L.; Novick, A.; Partin, AW.; Peters, C. *Campbell-Walsh Urology.* Vol. vol. 3. SAUNDERS ELSEVIER; Philadelphia, Pa: 2007.
27. Steuber T, Erbersdobler A, Graefen M, Haese A, Huland H, Karakiewicz PI. Comparative assessment of the 1992 and 2002 pathologic T3 substages for the prediction of biochemical recurrence after radical prostatectomy. *Cancer.* 2006; 106:775–82. [PubMed: 16400637]
28. Suardi N, Porter CR, Reuther AM, Walz J, Kodama K, Gibbons RP, Correa R, Montorsi F, Graefen M, Huland H, et al. A nomogram predicting long-term biochemical recurrence after radical prostatectomy. *Cancer.* 2008; 112:1254–63. [PubMed: 18286530]
29. Efstathiou JA, Chen MH, Catalona WJ, McLeod DG, Carroll PR, Moul JW, Roehl KA, D'Amico AV. Prostate-specific antigen-based serial screening may decrease prostate cancer-specific mortality. *Urology.* 2006; 68:342–7. [PubMed: 16904449]
30. Schroder FH, Hugosson J, Roobol MJ, Tammela TL, Ciatto S, Nelen V, Kwiatkowski M, Lujan M, Lilja H, Zappa M, et al. Screening and prostate-cancer mortality in a randomized European study. *N Engl J Med.* 2009; 360:1320–8. [PubMed: 19297566]

Figure 1A.
Increased PSA recurrence associated with increased tumor volume.

Figure 1B.
Increased PSA recurrence associated with increased tumor percent involvement.

Figure 1C.
Increased PSA recurrence associated with decreased prostate volume.

Table 1

Clinical and pathological characteristics of patients within cohort

<u>Age at Diagnosis (Years)</u>	n (%)
50	190 (5.5)
50.1-60	1100 (31.8)
60.1-70	1622 (46.9)
> 70	549 (15.9)
<u>Race</u>	
African American	517 (14.7)
Other	3004 (85.3)
<u>Body Mass Index</u>	
< 25	541 (22.7)
25-30	1192 (50.1)
> 30	647 (27.2)
<u>Pathological Gleason</u>	
< 7	1621 (45.9)
7	1484 (42.1)
> 7	423 (12.0)
<u>Tumor Stage</u>	
T1/T2	2115 (60.6)
T3/T4	1375 (39.4)
<u>Surgery Year</u>	
Before 2000	1817 (51.5)
After 2000	1711 (48.5)
<u>TV (cc)</u>	
< 3	1059 (34.3)
3-6	957 (31.0)
> 6	1074 (34.8)
<u>TPI (%)</u>	
< 10	1159 (33.6)
10-20	1461 (42.3)
> 20	831 (24.1)
<u>PV (g)</u>	
< 35	1267 (40.4)
35-45	843 (26.9)
> 45	1024 (32.7)
<u>PSA</u>	Median (IQR)
	6.3 (4.5-10.0)
<u>Seminal Vesicle Invasion</u>	409 (11.6)
<u>Extracapsular Extension</u>	1219 (34.6)
<u>Positive Margins</u>	1247 (35.3)
<u>PSA Recurrence</u>	988 (28.1)

IQR: Interquartile range

Table 2

Factors predicting PSA recurrence stratified by continuous and categorical consideration of tumor volume (TV), tumor percent involvement (TPI) and prostate volume (PV)

	Hazard Ratio	95% CI		p Value
Continuous variables considered individually				
<u>Continous TV</u>				
Pathological Gleason > 7	3.01	2.40	3.78	<0.001
Pathological Gleason = 7	1.60	1.32	1.92	<0.001
PSA	1.57	1.43	1.73	<0.001
Positive Margins	1.77	1.51	2.07	<0.001
Seminal Vesicle Invasion	1.77	1.46	2.15	<0.001
Pathological Tumor Stage T3/T4	1.29	1.07	1.54	0.006
TV	0.99	0.90	1.09	0.805
<u>Continuous TPI</u>				
Pathological Gleason > 7	2.48	2.02	3.04	<0.001
Pathological Gleason = 7	1.39	1.17	1.64	<0.001
PSA	1.53	1.41	1.66	<0.001
Positive Margins	1.59	1.38	1.84	<0.001
Seminal Vesicle Invasion	1.66	1.39	1.99	<0.001
Pathological Tumor Stage T3/T4	1.22	1.03	1.45	0.018
TPI	1.16	1.06	1.28	0.002
<u>Continous PV</u>				
Pathological Gleason > 7	2.90	2.33	3.60	<0.001
Pathological Gleason = 7	1.52	1.27	1.82	<0.001
PSA	1.67	1.53	1.83	<0.001
Positive Margins	1.66	1.42	1.93	<0.001
Seminal Vesicle Invasion	1.76	1.46	2.13	<0.001
Pathological Tumor Stage T3/T4	1.27	1.06	1.51	0.008
PV	0.65	0.54	0.78	<0.001
Categorical variables considered individually				
<u>Categorical TV</u>				
Pathological Gleason > 7	3.02	2.41	3.79	<0.001
Pathological Gleason = 7	1.60	1.32	1.92	<0.001
PSA	1.57	1.43	1.73	<0.001
Positive Margins	1.76	1.50	2.06	<0.001
Seminal Vesicle Invasion	1.78	1.47	2.16	<0.001
Pathological Tumor Stage T3/T4	1.29	1.07	1.54	0.006
TV > 6 cc	1.07	0.86	1.33	0.533
<u>Categorical TPI</u>				
Pathological Gleason > 7	2.45	2.00	3.01	<0.001
Pathological Gleason = 7	1.38	1.17	1.63	<0.001
PSA	1.53	1.41	1.66	<0.001

	Hazard Ratio	95% CI		p Value
Positive Margins	1.61	1.39	1.86	<0.001
Seminal Vesicle Invasion	1.67	1.40	2.00	<0.001
Pathological Tumor Stage T3/T4	1.22	1.03	1.44	0.019
TPI > 20%	1.45	1.16	1.81	0.001
<u>Categorical PV</u>				
Pathological Gleason > 7	2.86	2.30	3.57	<0.001
Pathological Gleason = 7	1.53	1.28	1.84	<0.001
PSA	1.66	1.51	1.82	<0.001
Positive Margins	1.70	1.46	1.99	<0.001
SV Invasion	1.75	1.45	2.12	<0.001
Pathological Tumor Stage T3/T4	1.30	1.09	1.55	0.004
PV 10-35 cc	1.25	1.05	1.49	0.010
All categorical variables considered together				
<u>TPI/TV/PV as Categorical Variables</u>				
Pathological Gleason > 7	2.87	2.28	3.62	<0.001
Pathological Gleason = 7	1.54	1.27	1.86	<0.001
PSA	1.57	1.43	1.74	<0.001
Positive Margins	1.72	1.47	2.03	<0.001
SV Invasion	1.68	1.38	2.05	<0.001
Pathological Tumor Stage T3/T4	1.20	1.00	1.45	0.05
TV > 6 g	0.94	0.67	1.31	0.71
TPI > 20%	1.32	1.02	1.69	0.031
PV 10-35 cc	1.24	1.04	1.49	0.018