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ORIGINAL ARTICLE

Serum prostate-specific antigen value adjusted for non-cancerous prostate tissue volume in patients undergoing radical prostatectomy: a new predictor of biochemical recurrence in localized or locally advanced prostate cancer

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The aim of this study was to investigate the significance of serum prostate-specific antigen (PSA) value adjusted for total tumor volume (PSA/tumor volume) and serum PSA value adjusted for non-cancerous prostate tissue volume (NCPV) (PSA/NCPV) as a predictor of pathological findings and clinical outcome after radical prostatectomy. Clinical and pathological data of 407 patients (median age: 66.5 years; range: 41.8–85.7 years) were reviewed retrospectively. The median follow-up period was 18.1 months (range: 1.0–107.8 months). Biochemical recurrence was defined as detectable PSA levels (greater than 0.2 ng ml^{-1}) and the time of biochemical recurrence was taken to be the first time PSA became detectable. In the multivariate model, PSA/NCPV was an independent predictor of extracapsular extension and positive surgical margin ($P<0.05$), but PSA/tumor volume was not. Kaplan–Meier curves revealed that PSA/NCPV correlated with biochemical recurrence-free survival ($P<0.001$; log-rank test) but PSA/tumor volume did not ($P=0.275$; log-rank test). PSA/NCPV was also a significant independent prognostic factor for biochemical recurrence-free survival on multivariate Cox proportional hazard analysis ($P=0.004$, relative risk=2.42). Our findings suggest that PSA/NCPV is associated independently with extracapsular extension and surgical margin status and may be an independent prognostic variable of PSA recurrence after radical prostatectomy.

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Keywords: prostatectomy; prostatic neoplasm; PSA; treatment outcome; tumor volume

INTRODUCTION

Treatment goals of prostate cancer are to potentially cure the disease, prolong biochemical recurrence-free or metastasis-free survival, and improve quality of life. The decision to use adjuvant therapeutic approaches is largely based on prognostic parameters that are known to independently predict tumor-free survival after radical prostatectomy. Some highly predictive prognostic parameters include histopathological feature of the cancer in radical prostatectomy specimens such as Gleason score, extraprostatic extension, positive surgical margin and tumor volume.[1] Other clinical factors such as prostate-specific antigen (PSA) levels and PSA half-life have also been shown to correlate with treatment failure.[2] However, there are limitations and no single method allows accurate estimation of the recurrence risk in an individual.

While PSA level correlated strongly with tumor stage, its ability to predict pathological stage for individuals is limited.[3] This may be due to the presence of benign prostatic hyperplasia (BPH) in the cancerous prostate, which may perturb the direct relationship between tumor volume and serum PSA value.[4] However, little attention has been paid to the relationships between PSA, tumor volume and non-cancerous prostate tissue volume (NCPV) when considering the adverse effect of BPH on serum PSA values. These considerations led us to investigate the significance of serum PSA value adjusted for total tumor volume and serum PSA value adjusted for NCPV as predictors of pathological findings and clinical outcome after radical prostatectomy.

Of the patients undergoing radical prostatectomy, 20–50% will suffer biochemical recurrence.[5] Prediction of biochemical recurrence after radical prostatectomy is imperative in counseling with patients on adjuvant therapy and prognosis. Therefore, the discovery of a new predictor of recurrence that strongly and independently predicts prostate cancer outcomes could provide complementary information, and aid patients and physicians in clinical decision making. In the present study, serum PSA value adjusted for NCPV provides significant prognostic information in addition to currently used parameters in patients undergoing radical prostatectomy.

METHODS

Patient population

Approval of the study was obtained from the Institutional Review Board of Seoul National University Hospital. Between 1996 and

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2005, 429 radical retropubic prostatectomies for the treatment of prostate cancer were performed at our single institution. The clinical and pathological data of the patients were obtained from our surgical database and reviewed retrospectively. Patients with positive lymph nodes and patients who had received neoadjuvant or immediate adjuvant androgen ablation or radiotherapy were excluded from the study. In total, 407 patients were included in the study. The median age at surgery was 66.5 years (range: 41.8–85.7 years). The median preoperative PSA level was 8.6 ng ml^{-1} (range: 0.7–142.0 ng ml^{-1}). None of the patients had evidence of nodal disease or distant metastasis on both either contrast-enhanced computed tomography or bone scans.

Histological analysis

The presence of carcinoma in needle biopsy tissue was assessed by a single pathologist (KCM). Gleason primary and secondary grades with sum scores were assigned and the number of core biopsy specimens containing carcinoma was quantified. The radical prostatectomy specimens were handled and processed in a standard manner, where all prostatic tissue was embedded as previously described.[6] The presence of extracapsular extension, seminal vesicle invasion, positive surgical margin and histological grade were also recorded. Total tumor volume and the tumor volume of each cancer focus were calculated by using the formula, 0.4×length×width×cross-section thickness, i.e., number of cross sections×section thickness.[7] NCPV was determined by the formula: NCPV=measured prostate volume–calculated total tumor volume. All specimens were scored according to the Gleason grading system. The pathological stages were recorded on the basis of the 2002 tumor-node metastasis classification and a positive surgical margin was defined as the presence of cancer cells in the inked surface of the prostate specimen.

Follow-up

Follow-up information was collected from the medical records. All patients were followed up by measuring their PSA levels every 3 months. The median follow-up period was 18.1 months (range: 1.0–107.8 months). Biochemical recurrence was defined as detectable PSA levels (greater than 0.2 ng ml^{-1}) and the time of biochemical recurrence was taken to be the first time PSA became detectable.

Statistical analysis

Pearson correlation coefficients for the relationships between PSA, tumor volume, NCPV, PSA/tumor volume and PSA/NCPV were generated. To identify the factors that could predict pathological findings, odds ratios (ORs) and *P* values for trends were estimated by univariate and multivariate logistic regression analyses. Several variables were used for these analyses, namely, age at surgery, body mass index, serum PSA level, number of positive biopsy cores, biopsy Gleason score, clinical stage, surgical Gleason score, tumor volume, PSA/tumor volume and PSA/NCPV. Only variables that had a *P* value less than 0.05 upon univariate analysis were included in the multivariate model.

The Kaplan–Meier method was used to assess the biochemical recurrence-free survival of the patients stratified according to the pathological findings. The differences were tested by using the log-rank test. Multivariate Cox proportional hazard analyses were then used to identify prognostic indicators of biochemical recurrence. Only variables that had *P* value less than 0.05 upon univariate analysis were included in the multivariate model. All *P* values were two-sided and $P<0.05$ was significant. All statistical analyses were performed by using the SPSS program (SPSS Inc., Chicago, IL, USA).

Table 1 Patient characteristics

	No. (%)	*Mean±s.e.m.*	*Median (range)*
Age (years)		65.9±0.3	66.5 (41.8–85.7)
Body mass index (kg cm^{-2})		23.9±0.1	24.1 (15.3–31.1)
Serum PSA (ng ml^{-1})		13.4±0.8	8.6 (0.7–142.0)
PSA density (ng ml^{-1} ml^{-1})		0.39±0.03	0.23 (0.01–5.07)
Biopsy Gleason score			
4	9 (2.2%)		
5	5 (1.2%)		
6	162 (39.8%)		
7	123 (30.2%)		
8	70 (17.2%)		
9	32 (7.9%)		
10	6 (1.5%)		
No. of positive biopsy cores		3.8±0.2	3.0 (1.0–12.0)
Clinical stage			
<cT3a	329 (80.8%)		
⩾cT3a	78 (19.2%)		
Surgical Gleason score			
4	2 (0.5%)		
5	4 (1.0%)		
6	97 (23.8%)		
7	236 (58.0%)		
8	31 (7.6%)		
9	35 (8.6%)		
10	2 (0.5%)		
Surgical margin			
Negative	258 (63.4%)		
Positive	149 (36.6%)		
Extracapsular extension			
Negative	273 (67.1%)		
Positive	134 (32.9%)		
Seminal vesicle invasion			
Negative	356 (87.5%)		
Positive	51 (12.5%)		
Tumor volume (ml)		7.3±0.4	3.9 (0.2–59.9)
NCPV (ml)		34.4±0.8	31.7 (2.8–120.7)
PSA/tumor volume (ng ml^{-1} ml^{-1})		4.1±0.3	2.2 (0.2–84.8)
PSA/NCPV (ng ml^{-1} ml^{-1})		0.67±0.10	0.25 (0.02–31.11)

Abbreviations: NCPV, non-cancerous prostate tissue volume; PSA, prostate-specific antigen.

RESULTS

Patient characteristics

The patient characteristics are listed in Table 1. Of the 407 patients, 329 (80.8%) had clinically localized prostate cancer (T1–T2, N0). However, 134 (32.9%) had extracapsular extension, 51 (12.5%) had seminal vesicle involvement and 149 (36.6%) had positive surgical margins.

Correlations between serum PSA level, tumor volume and NCPV

Correlation analysis of the relationships between serum PSA level, tumor volume and NCPV revealed that while correlation between serum PSA level and NCPV was low ($r=-0.179$, $P<0.001$), serum PSA level correlated better with tumor volume ($r=0.479$, $P<0.001$) and PSA/tumor volume ($r=0.346$, $P<0.001$). However, the highest correlation was found between serum PSA and PSA/NCPV ($r=0.626$, $P<0.001$). Tumor volume also correlated better with PSA/NCPV ($r=0.580$, $P<0.001$) than with PSA/tumor volume ($r=-0.267$, $P<0.001$). The results are shown in Figure 1.

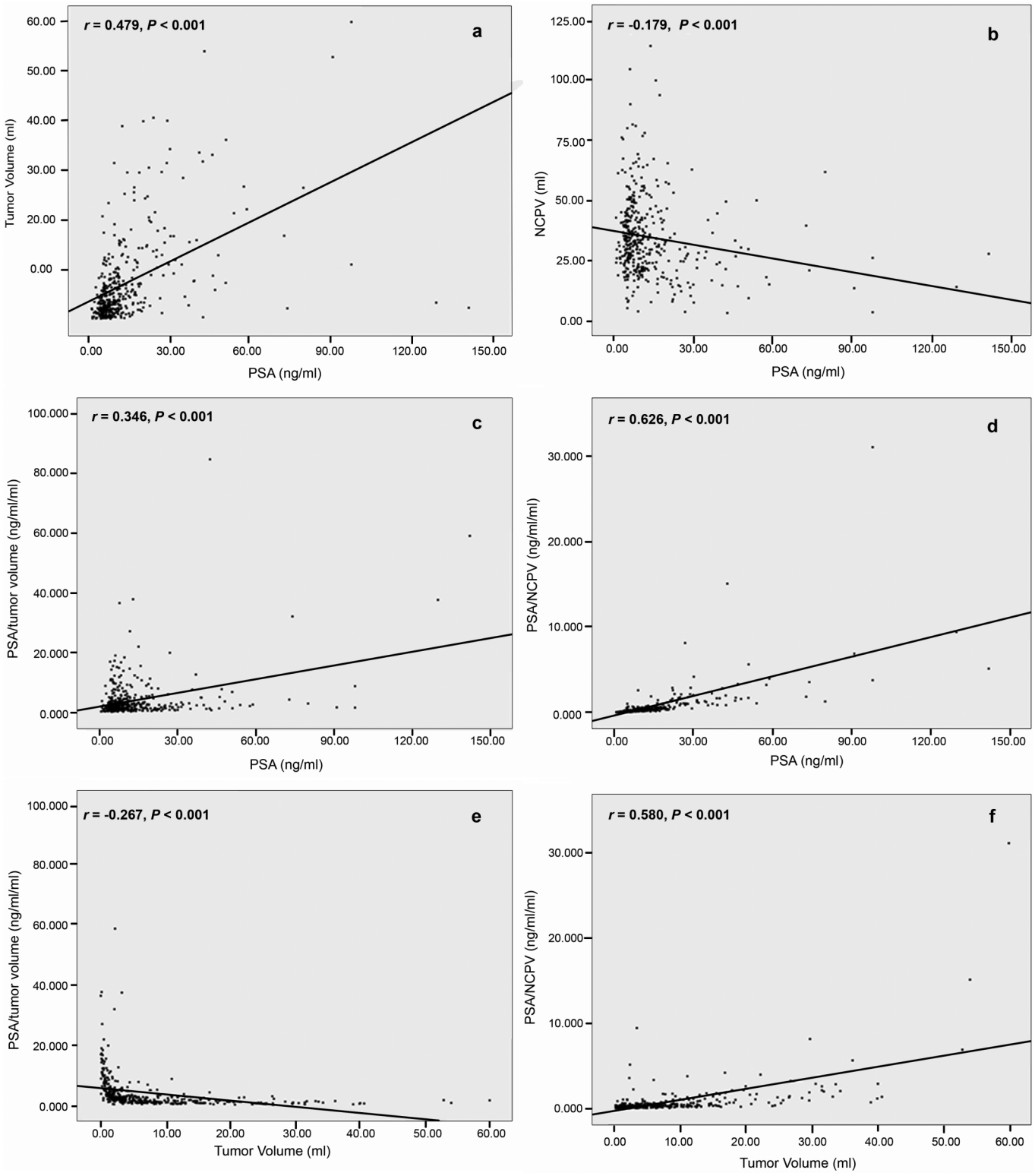

Figure 1 Regression model equations. (**a**) PSA versus tumor volume (r=0.479, P<0.001). (**b**) PSA versus NCPV (r=−0.179, P<0.001). (**c**) PSA versus PSA/tumor volume (r=0.346, P<0.001). (**d**) PSA versus PSA/NCPV (r=0.626, P<0.001). (**e**) Tumor volume versus PSA/tumor volume (r=−0.267, P<0.001). (**f**) Tumor volume versus PSA/NCPV (r=0.580, P<0.001). NCPV: non-cancerous prostate tissue volume; PSA: prostate-specific antigen.

Prediction of pathological findings

To identify factors that are predictive of pathological findings, we conducted logistic regression analyses. Univariate logistic regression analysis indicated that serum PSA levels, PSA density, number of positive biopsy cores, biopsy Gleason score, clinical stage, surgical Gleason score, tumor volume, PSA/tumor volume and PSA/NCPV

Table 2 Univariate and multivariate predictors of pathological findings

	Extracapsular extension		*Seminal vesicle invasion*		*Positive margin*	
	OR (95% CI) [Adjusted OR (95% CI)]	P *value [P value]*	*OR (95% CI) [Adjusted OR (95% CI)]*	P *value [P value]*	*OR (95% CI) [Adjusted OR (95% CI)]*	P *value [P value]*
Age (years)						
<65	1.000		1.000		1.000	
⩾65	1.087 (0.712–1.660)	0.699	0.948 (0.522–1.721)	0.861	0.797 (0.529–1.200)	0.277
Body mass index (kg cm^{-2})						
<25	1.000		1.000		1.000	
⩾25	1.206 (0.781–1.862)	0.398	1.111 (0.599–2.061)	0.739	1.330 (0.870–2.033)	0.188
Serum PSA (ng ml^{-1})						
<10	1.000		1.000		1.000	
⩾10	2.996 (1.953–4.595)	<0.001	3.929 (2.073–7.445)	<0.001	2.059 (1.365–3.105)	0.001
	[1.334 (0.522–3.406)]	[0.547]	[0.586 (0.129–2.657)]	[0.488]	[1.231 (0.492–3.083)]	[0.657]
PSA density (ng ml^{-1} ml^{-1})						
<0.25	1.000		1.000		1.000	
⩾0.25	2.977 (1.802–4.917)	<0.001	3.364 (1.565–7.228)	0.002	2.104 (1.299–3.408)	0.003
	[0.943 (0.342–2.596)]	[0.910]	[1.926 (0.382–9.707)]	[0.427]	[2.934 (1.070–8.048)]	[0.037]
No. of positive biopsy cores						
⩽3	1.000		1.000		1.000	
⩾4	3.557 (2.119–5.971)	<0.001	5.126 (2.230–11.783)	<0.001	3.319 (1.983–5.555)	<0.001
	[1.695 (0.815–3.528)]	[0.158]	[0.971 (0.298–3.171)]	[0.962]	[1.980 (0.956–4.102)]	[0.066]
Biopsy Gleason score						
⩽6	1.000		1.000		1.000	
7	2.537 (1.479–4.353)	0.001	4.400 (1.540–12.574)	0.006	2.198 (1.331–3.629)	0.002
	[0.855 (0.378–1.935)]	[0.706]	[1.357 (0.332–5.551)]	[0.671]	[1.779 (0.774–4.093)]	[0.175]
⩾8	5.342 (3.084–9.255)	<0.001	14.014 (5.239–37.486)	<0.001	2.235 (1.329–3.759)	0.002
	[0.699 (0.265–1.845)]	[0.470]	[1.425 (0.296–6.872)]	[0.659]	[1.280 (0.479–3.419)]	[0.622]
Clinical stage						
<cT3a	1.000		1.000		1.000	
⩾cT3a	2.147 (1.290–3.573)	0.003	3.687 (1.971–6.900)	<0.001	2.861 (1.721–4.756)	<0.001
	[1.463 (0.638–3.356)]	[0.369]	[2.164 (0.694–6.744)]	[0.183]	[2.824 (1.244–6.408)]	[0.013]
Surgical Gleason score						
⩽6	1.000		1.000		1.000	
7	4.199 (2.121–8.312)	<0.001	10.577 (1.406–79.585)	0.022	2.525 (1.446–4.408)	0.001
	[2.111 (0.811–5.498)]	[0.126]	[3.008 (0.300–30.155)]	[0.349]	[1.553 (0.602–4.006)]	[0.362]
⩾8	13.977 (6.258–31.217)	<0.001	65.000 (8.531–495.252)	<0.001	4.516 (2.269–8.989)	<0.001
	[6.672 (1.823–24.419)]	[0.004]	[17.076 (1.328–219.611)]	[0.029]	[1.439 (0.395–5.246)]	[0.581]
Tumor volume (ml)						
<4	1.000		1.000		1.000	
⩾4	3.326 (2.146–5.157)	<0.001	12.068 (4.684–31.092)	<0.001	2.789 (1.834–4.241)	<0.001
	[0.940 (0.365–2.419)]	[0.897]	[2.941 (0.560–15.453)]	[0.203]	[1.056 (0.401–2.782)]	[0.912]
PSA/tumor volume (ng ml^{-1} ml^{-1})						
<1.5	1.000		1.000		1.000	
1.5–2.9	0.748 (0.457–1.225)	0.249	0.412 (0.210–0.809)	0.010	0.732 (0.448–1.196)	0.213
	[0.825 (0.361–1.885)]	[0.648]	[0.515 (0.156–1.698)]	[0.276]	[0.692 (0.318–1.504)]	[0.352]
					[0.710 (0.304–1.658)]	[0.492]
⩾3	0.373 (0.220–0.632)	<0.001	0.073 (0.022–0.244)	<0.001	0.562 (0.343–0.919)	0.022
	[0.509 (0.187–1.385)]	[0.186]	[0.196 (0.031–1.225)]	[0.081]	[1.310 (0.487–4.523)]	[0.593]
PSA/NCPV (ng ml^{-1} ml^{-1})						
<0.2	1.000		1.000		1.000	
0.2–0.39	1.709 (0.951–3.068)	0.073	2.496 (0.813–7.661)	0.110	3.437 (1.970–5.996)	<0.001
	[1.255 (0.472–3.338)]	[0.649]	[1.205 (0.207–7.004)]	[0.836]	[4.132 (1.592–10.728)]	[0.004]
⩾0.4	5.585 (3.276–9.521)	<0.001	10.561 (4.015–27.783)	<0.001	5.121 (3.006–8.724)	<0.001
	[3.593 (1.025–12.602)]	[0.046]	[2.864 (0.383–21.407)]	[0.305]	[8.948 (2.444–32.764)]	[0.001]

Abbreviations: CI, confidence interval; OR, odds ratio; PSA, prostate-specific antigen; NCPV, non-cancerous prostate tissue volume.

were all possible risk factors for extracapsular extension, seminal vesicle invasion and surgical positive margin. In the multivariate model, surgical Gleason score and PSA/NCPV were the only independent predictors of extracapsular extension: a surgical Gleason score ⩾8 was associated with a 6.7-fold higher chance of extracapsular extension than a surgical Gleason score ⩽6 (OR: 6.672; 95% confidence interval (CI): 1.823–24.419; P=0.004), while a PSA/NCPV value of ⩾0.4 was associated with a 3.6-fold higher risk of extracapsular extension than a PSA/NCPV value of <0.2 (OR: 3.593; 95% CI: 1.025–12.602; P=0.046).

The multivariate analysis used in this study also showed that the OR (with a 95% CI representing the space between the high and low quartiles) for seminal vesicle invasion was increased for one factor only, namely, surgical Gleason score: a surgical Gleason score ⩾8 was associated with a 17.1-fold higher risk of seminal vesicle invasion

than a surgical Gleason score ⩽6 (OR: 17.076; 95% CI: 1.328–219.611; $P=0.029$).

Moreover, the multivariate logistic model indicated that PSA density, clinical stage and PSA/NCPV were dependent risk factors for a positive surgical margin. Patients with PSA density ⩾0.25 had a 2.9-fold greater risk of having a positive margin (OR: 2.934; 95% CI: 1.070–8.048, $P=0.037$). A clinical stage of ⩾cT3a was associated with a 2.8-fold higher likelihood of positive surgical margin (OR: 2.824; 95% CI: 1.244–6.408; $P=0.013$). Compared to a PSA/NCPV value of <0.2, a PSA/NCPV value of 0.2–0.39 was associated with a 4.1-fold higher risk (OR: 4.132; 95% CI: 1.592–10.728; $P=0.004$), while a PSA/NCPV value of ⩾0.4 (OR: 8.948; 95% CI: 2.444–32.764; $P=0.001$) was associated with a 8.9-fold higher risk. The results are shown in Table 2.

Biochemical recurrence after radical prostatectomy

At the median follow-up period of 18.1 months, biochemical recurrence was observed in 100 patients (24.6%). The median time to biochemical recurrence was 12.0 months (range: 0.5–107.8 months). The 1-, 3- and 5-year biochemical recurrence-free survival rates were 80.0, 59.9 and 52.3%, respectively. Kaplan–Meier curves revealed that surgical Gleason score ($P<0.001$; log-rank test), surgical margin status ($P<0.001$; log-rank test), extracapsular extension ($P<0.001$; log-rank test), seminal vesicle invasion ($P<0.001$; log-rank test), tumor volume ($P<0.001$; log-rank test) and PSA/NCPV ($P<0.001$; log-rank test) correlated with biochemical recurrence-free survival, whereas PSA/tumor volume did not correlate with biochemical recurrence-free survival ($P=0.275$; log-rank test).

Multivariate analysis

Multivariate Cox proportional hazard analysis revealed that surgical Gleason score ($P=0.049$, relative risk=2.33), surgical margin ($P<0.001$, relative risk=3.10), seminal vesicle invasion ($P=0.009$, relative risk=2.10) and PSA/NCPV ($P=0.004$, relative risk=2.42) were significant independent prognostic factors of biochemical recurrence-free survival, whereas tumor volume lost its statistical significance (Table 3).

DISCUSSION

Patients at a high risk of cancer progression should be identified as soon as possible because some of these patients may benefit from adjuvant therapeutic regimens. This highlights the importance of identifying parameters that can reliably predict the risk of cancer progression in individual patients who have been diagnosed with prostate cancer. While clinical and pathological stage, namely, PSA levels and Gleason score, respectively, are good and well-established prognosticators, there is a need to develop new tools by which patients can be further stratified with regard to disease status.

Table 3 Association of pathological findings with biochemical recurrence-free survival on multivariate Cox proportional hazards regression analysis

Variables	*HR*	*95% CI*	P *value*
Surgical Gleason score (⩽6 versus 7)	1.677	0.790–3.561	0.179
Surgical Gleason score (⩽6 versus ⩾8)	2.327	1.005–5.391	0.049
Surgical margin (negative versus positive)	3.101	1.945–4.944	<0.001
Extracapsular extension (negative versus positive)	1.245	0.748–2.073	0.399
Seminal vesicle invasion (negative versus positive)	2.096	1.208–3.637	0.009
Tumor volume (<4 ml versus ⩾4 ml)	0.760	0.464–1.246	0.277
PSA/NCPV (<0.2 versus 0.2–0.39)	1.112	0.580–2.134	0.749
PSA/NCPV (<0.2 versus ⩾0.4)	2.424	1.322–4.445	0.004

Abbreviations: CI, confidence interval; HR, hazard ratio; NCPV, non-cancerous prostate tissue volume; PSA, prostate-specific antigen.

At present, there is a great deal of debate about whether tumor volume should be recommended as a prognostic parameter for predicting disease-free survival in patients after radical prostatectomy. Stamey *et al.*[8] consider tumor volume to be an independent prognostic parameter that can also be used to differentiate significant from insignificant cancer. In contrast, Epstein *et al.*[9] have demonstrated that tumor volume does not provide additional information if the Gleason score and pathological stage are known. We also found in the present study that prostate cancer volume was not a significant predictor of biochemical failure after radical prostatectomy on multivariate analysis.

PSA is produced not only by prostate tumor but also by benign tissue, and its level increases with the size of the prostate. While it has been suggested that the serum PSA level reflects the size of the prostate, serum PSA alone predicts tumor size poorly.[10] This may be because of BPH, the volume of which can be significant: if a cancerous prostate gland also has BPH, the BPH may interfere with the direct relationship between tumor volume and serum PSA values.[4] This is supported by the findings in the present study: while tumor volume correlated reasonably well with serum PSA ($r=0.479$, $P<0.001$), there was also a weak inverse correlation between NCPV and serum PSA ($r=-0.179$, $P<0.001$).

There is a higher incidence of finding a well-differentiated tumor at prostatectomy in patients with a large prostate,[11] whereas men with a small prostate tend to have more advanced disease and to be at greater risk of progression after radical prostatectomy.[12] It has been shown that poorly differentiated cancers tend to produce less PSA per volume of tumor tissue.[4] Moreover, Hayashi *et al.*[13] reported recently that when PSA is adjusted for tumor volume, a low level is an independent predictor of biological failure. These findings suggest that prostate cancers that are associated with lower PSA secretion levels are associated with a higher risk of biochemical failure after surgery; they also suggest that the combination of a large tumor and low serum PSA level may reflect an aggressive phenotype, irrespective of the degree of BPH. However, the current study failed to find that tumor volume, or serum PSA level adjusted for tumor volume, was a significant predictor of PSA recurrence when adding serum PSA level adjusted for NCPV to the Cox proportional model. Furthermore, we observed that serum PSA value adjusted for NCPV was associated independently with extracapsular extension and surgical margin status and was an independent prognostic variable for PSA recurrence after radical prostatectomy. Indeed, radical prostatectomy specimens contain the index tumor (the largest tumor) and smaller satellite tumors.[14] Noguchi *et al.*[15] found that only index tumor volume, but not total tumor volume, was an independent predictor of biochemical recurrence. Wise *et al.*[16] also indicated that the importance of the index tumor rather than all tumors in radical prostatectomy specimens to predict prognosis. This would explain why tumor volume or serum PSA level adjusted for tumor volume was not a significant predictor of PSA recurrence in our study.

The influence of BPH on the serum PSA value depends on the volume of both the tumor and the non-cancerous prostatic tissue. We observed a significant inverse relationship between tumor volume and serum PSA value adjusted for tumor volume ($r=-0.267$, $P<0.001$). This reveals that the serum level of PSA does not increase in a proportional fashion with the volume of prostate cancer; rather, as tumor volume increases, the amount of serum PSA per cubic centimeter of tumor decreases. More interestingly, the present study showed that serum PSA value adjusted for NCPV correlated directly with both PSA ($r=0.626$, $P<0.001$) and tumor volume ($r=0.580$, $P<0.001$). Thus, the amount of serum PSA per cubic centimeter of

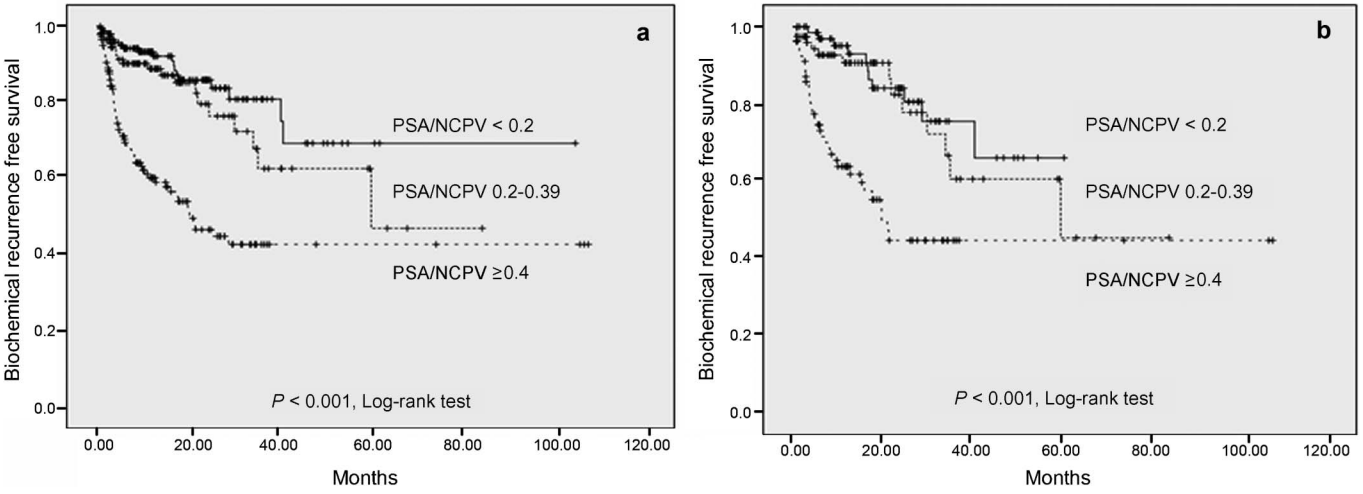

Figure 2 Biochemical recurrence-free survival in patients categorized according to serum prostate-specific antigen value adjusted for non-cancerous prostate tissue volume in total patients (**a**) and in patients with surgical Gleason score of 7 (**b**). NCPV: non-cancerous prostate tissue volume; PSA: prostate-specific antigen.

NCPV increases as the tumor volume or serum PSA level increases. These findings suggest that NCPV may contribute to the elevation of serum PSA in patients with large tumor volume.

Regarding PSA density, several investigators have suggested that a greater PSA density could reflect a greater tumor burden, adverse pathological findings and a worse prognosis.[17,18] However, others have found no additional benefit using this parameter.[19,20] In our series, PSA density correlated with PSA value adjusted for NCPV (r=0549, P<0.001; data not shown). However, in our multivariate regression analysis, although PSA density was an independent predictor of positive surgical margin, it was not associated with extracapsular extension or seminal vesicle invasion. These findings suggest that PSA value adjusted for NCPV might provide a more accurate measure of cancer aggressiveness since PSA level is related more closely to NCPV than prostate cancer.[21]

In the present study, serum PSA value adjusted for NCPV provides significant prognostic information in patients undergoing radical prostatectomy. In addition, this new predictor may provide complementary information. For example, we found that in patients with surgical Gleason score of 7, serum PSA value adjusted for NCPV correlated with biochemical recurrence-free survival (Figure 2). Therefore, further study with regard to this issue is needed.

AUTHOR CONTRIBUTIONS

Both Ja Hyeon Ku and Cheol Kwak worked on the concept and design, and drafting of the manuscript; Kyung Chul Moon worked on acquisition of data and critical revision; Sung Yong Cho worked on acquisition of data and statistical analysis; and Hyeon Hoe Kim worked on concept and design, and critical revision.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

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