

Post-void Residual Urinary Volume Is An Independent Predictor of Biopsy Results in Men at Risk for Prostate Cancer

LUIGI CORMIO¹, GIUSEPPE LUCARELLI¹, GIUSEPPE STEFANO NETTI², GIOVANNI STALLONE³, OSCAR SELVAGGIO¹, FRANCESCO TROIANO¹, GIUSEPPE DI FINO¹, FRANCESCA SANGUEDOLCE⁴, PANTALEO BUFO⁴, GIUSEPPE GRANDALIANO³ and GIUSEPPE CARRIERI¹.

Departments of ¹Urology and Renal Transplantation, ²Clinical Pathology, ³Nephrology Dialysis and Transplantation, and ⁴Pathology, University of Foggia, Foggia, Italy

Abstract. Aim: to determine whether peak flow rate (PFR) and post-void residual urinary volume (PVRUV) predict prostate biopsy outcome. Patients and Methods: The study population consisted of 1780 patients undergoing first prostate biopsy. Results: Patients with prostate cancer (PCa) had significantly greater prostate-specific antigen (PSA) and PFR but lower prostate volume (PVol) and PVRUV than those without PCa. Receiver operator characteristic curve analysis showed that PVol and PVRUV were the most accurate predictors of biopsy outcome. The addition of PVRUV to the multivariate logistic regression model based on standard clinical parameters (age, PSA, digital rectal examination, PVol) significantly increased the predictive accuracy of the model in both the population overall (79% vs. 77%; $p=0.001$) and patients with PSA levels up to 10 ng/ml (74.3% vs. 71.7%; $p=0.005$). Conclusion: PVRUV seems to be an accurate non-invasive test to predict biopsy outcome that can be used alone or in combination with PVol in the decision-making process for men potentially facing a prostate biopsy.

Prostate biopsy (PBx) is the standard method for diagnosing prostate cancer (PCa) but the diagnostic yield of this procedure remains low. As a matter of fact, in current clinical practice, the diagnostic yield of a first extended PBx prompted by an elevated serum prostate-specific antigen (PSA) level or an abnormal digital rectal examination (DRE) is in the range of 40% (1); such a cancer detection rate drops to approximately 25% in the setting of screening programs, *i.e.* in patients with serum PSA between 2.5 and 10 ng/ml (2).

Correspondence to: Luigi Cormio, MD, Ph.D., Department of Urology and Renal Transplantation, University of Foggia, Via Pinto 1, 71122 Foggia, Italy. Tel/Fax: +39 0881732111, e-mail: luigicormio@libero.it

Key Words: Prostate-specific antigen, prostate cancer, biopsy, prostate volume, residual urinary volume.

Efforts to improve the diagnostic yield of PBx have been oriented towards the construction of predictive models that combine PSA with other readily available clinical information such as age, DRE findings, and prostate volume (PVol), as well as towards the identification of novel diagnostic tools, including novel biomarkers (3-5), or imaging techniques such as transrectal elastosonography (6) and magnetic resonance imaging. The incorporation of such novel diagnostic tools into nomograms (7, 8) has further, but not dramatically, increased the accuracy of these predictive models. Moreover, novel diagnostic tools are expensive or may be invasive and thus not easily applicable to everyday clinical practice. The identification of cheap, non-invasive and readily available predictive tools that can be used either alone or in the context of a nomogram therefore remains a major clinical issue.

PSA is significantly associated with benign prostatic obstruction (BPO) as patients with BPO have higher serum PSA levels than those without BPO (9, 10). Nevertheless, to our knowledge, no attempt has been made to determine whether uroflowmetry (UFM) and post-void residual urinary volume (PVRUV), the standard tools for initial BPO diagnosis, correlate with PSA levels and the diagnosis of Pca.

In view of the association between BPO and increased PSA levels, in the present study, we tested whether UFM and ultrasound measurement of PVRUV predicts PBx outcome.

Patients and Methods

Data of patients scheduled for ultrasound-guided transrectal PBx because of increased serum PSA (≥ 4 ng/ml) or abnormal DRE were prospectively entered into our Institutional Review Board-approved database. All patients underwent PSA measurement before DRE and transrectal ultrasound (TRUS). UFM was carried out before PBx, waiting for the patient to report a strong sensation to void; PVRUV was measured immediately after UFM by abdominal scanning. Following local anesthesia (11, 12), TRUS was used to determine the prostate and transition zone volume, and to guide transrectal prostate sampling according to our systematic 18-core biopsy scheme (13).

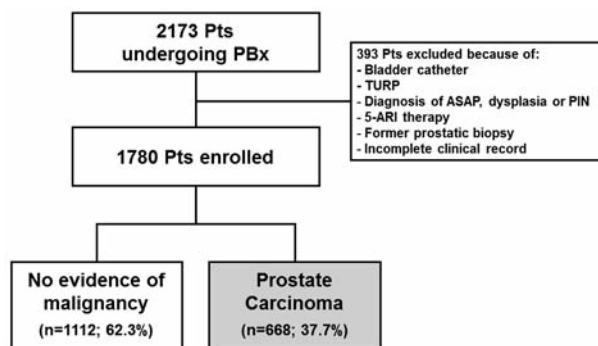


Figure 1. Algorithm showing patient selection and exclusion criteria for the present study. PBx, Prostate biopsy; TURP, transurethral resection of the prostate; PIN, prostatic intraepithelial neoplasia; ASAP, atypical small acinar proliferation; 5-ARI, 5-alpha-reductase inhibitor.

Men receiving medical therapy known to affect PSA levels, or who had previously undergone PBx or invasive treatment for benign prostatic hyperplasia, or with dwelling urethral catheters, or with a voided volume of less than 150 ml were excluded from the present case-control study.

Two senior uropathologists blind to UFM and PVRUV data evaluated the specimens according to contemporary diagnostic criteria for high-grade prostatic intraepithelial neoplasia, atypical small acinar proliferation of the prostate and PCa. Patients diagnosed with high-grade prostatic intraepithelial neoplasia or atypical small acinar proliferation of the prostate were excluded from the present analysis.

The protocol for the study was approved by University of Foggia Ethics Committee (n. 0125/14) and it conforms to the provisions of the Declaration of Helsinki. Written informed consent to take part was given by all participants.

Statistical analysis. The primary study endpoint was to determine the diagnostic accuracy of PFR and PVRUV in predicting PCa and to compare it with that of the commonly used predictive clinical factors such as age, PSA, DRE and PVol. The secondary endpoint was to look for cut-offs that would allow identification of patients in whom PBx could potentially be avoided.

Clinical characteristics were considered continuous variables and reported as means; those with normal distribution, according to the Skewness and Kurtosis test, were compared by Student's *t*-test for paired or unpaired data, whereas those with a non-parametric distribution were compared by the Mann-Whitney U-test for independent groups. Spearman's correlation was used to evaluate the association between two variables, whereas frequencies were compared by the χ^2 test. The combined predictive effect of the covariates was tested by logistic regression analysis, performing a backward selection procedure with a removal criterion of $p > 0.10$ based on the likelihood ratio test. Model calibration was measured by the Hosmer-Lemeshow goodness of fit test, with $p < 0.05$ considered statistically significant. Finally, receiver operator characteristic (ROC) curves analysis was used to test the diagnostic performance of the different clinical parameters, as well as the predictive accuracy of multivariate logistic regression models including only standard clinical parameters (age, PSA, DRE, PVol) or also the novel parameters (PVRUV and PFR). An operational

Table I. Patients' clinical and pathological characteristics.

Characteristic	PCa (n=668)	NEM (n=1112)	<i>p</i> -Value
Age (years)			
Mean	69	66	<0.001
Range	48-90	34-86	
PSA (ng/ml)			
Mean	19.0	7.8	<0.001
95% CI	15.6-22.4	7.5-8.1	
Prostate volume (ml)			
Mean	47.5	63.4	<0.001
95% CI	45.7-49.2	61.7-65.1	
Abnormal DRE	188 (28.1%)	255 (22.9%)	0.01
Peak flow rate (ml/min)			
Mean	13.3	12.6	<0.001
95% CI	12.9-13.8	12.2-12.9	
PVRUV (ml/min)			
Mean	36.7	58.3	<0.001
95% CI	34.2-39.3	55.5-61.1	
Gleason score			
<7	180 (27%)		
7	201 (30%)		
>7	287 (43%)		

PCa, Prostate cancer; NEM, no evidence of malignancy; PSA, prostate-specific antigen; DRE, digital rectal examination; PVRUV, post-void residual urinary volume; CI: confidence interval.

cut-off level was defined in order to differentiate the risk of PCa between the two groups. A two-sided value of $p < 0.05$ was considered statistically significant. Statistical calculations were carried out using MedCalc 9.2.0.1 (MedCalc Software, Ostend, Belgium) and PASW 18 (SPSS®, Chicago, IL, USA).

Results

Between January 2006 and December 2012, a total of 2173 patients underwent TRUS-guided PBx at our Institution; 1780 patients met the inclusion criteria and were enrolled in the present study (Figure 1). Their descriptive characteristics are summarized in Table I. PCa was found in 668 patients (37.7%), while the remaining 1112 (62.3%) had no evidence of malignancy; there was a statistically significant difference in all tested variables (age, PSA, DRE, PVol, PFR and PVRUV) between patients with and without PCa (Table I). As expected, PVRUV was directly related to PVol ($rs=0.346$, $p < 0.0001$) and inversely related to PFR ($rs=-0.495$, $p < 0.001$). Multivariate logistic regression analysis showed that age, PSA, PVol and PVRUV were the most significant predictors of PBx outcome, with the Hosmer-Lemeshow statistics showing adequate model calibration (Table III). ROC curve analysis (Figure 2) showed that PVol and PVRUV had the best predictive values [Area under the curve (AUC)=0.670, $p < 0.001$ and AUC=0.655, $p < 0.001$, respectively], outperforming both age and PSA (AUC =0.631, $p < 0.001$ and AUC=0.638, $p < 0.001$, respectively).

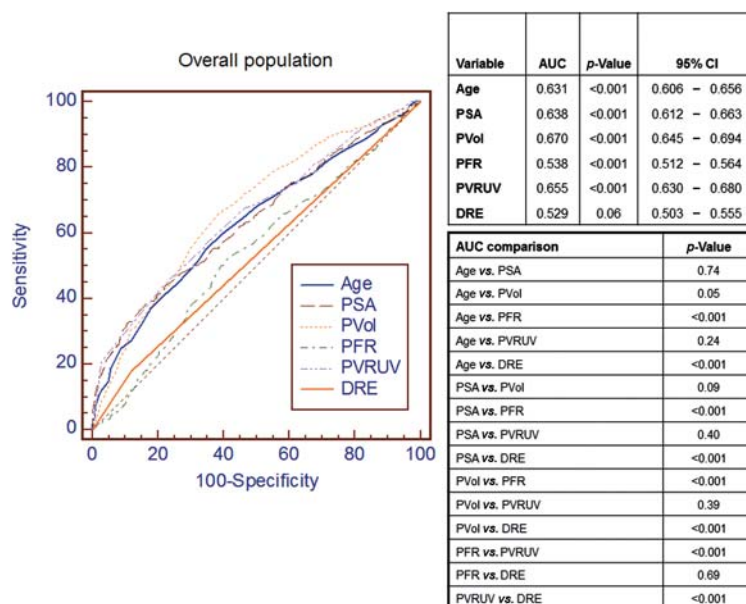


Figure 2. Receiver operating characteristic (ROC) curves for age, prostate-specific antigen (PSA), prostate volume (PVol), peak flow rate (PFR), postvoid residual urinary volume (PVRUV) and digital rectal examination (DRE), and the risk of prostate cancer (PCa) in differentiating between patients with PCa and those with no evidence of malignancy. AUC: Area under the ROC curve; CI: confidence interval.

The predictive value of the clinical variables was then tested in the subset of patients with PSA levels up to 10 ng/ml, as they are those who could potentially be spared from PB× if reliable predictors of procedure outcome were available. Interestingly, there was no difference in DRE status and mean PSA levels between patients with and those without PCa (6.2 vs 6.1 ng/ml; $p=0.2$); conversely, there was a statistically significant difference in all the other clinical variables (Table II). Multivariate logistic regression analysis showed that in this subset of patients, age, PVol and PVRUV were the only significant predictors of PB× outcome, with the Hosmer-Lemeshow statistics showing adequate model calibration (Table III). Again, ROC curve analysis showed that PVol and PVRUV had the best predictive values (AUC=0.671, $p<0.001$ and AUC=0.668, $p<0.001$, respectively), significantly outperforming all the other clinical variables (Figure 3a).

In patients with PSA>10 ng/ml, there was a statistically significant difference between those with and those without PCa in all variables but PFR (Table II). Multivariate logistic regression analysis showed that in this population, the most significant predictors of PB× outcome were age, PSA, PVol and PVRUV (Table III). ROC curve analysis (Figure 3b) showed that PVol, PSA and PVRUV had the best predictive values (AUC=0.717, $p<0.001$, AUC=0.682, $p<0.001$ and AUC=0.668, $p<0.001$, respectively); interestingly, the AUC for PVRUV was exactly the same (0.668) for patients with PSA up to 10 ng/ml and with PSA>10 ng/ml (Figure 3).

The addition of PVRUV to the multivariate logistic regression model based on standard clinical parameters (age,

PSA, DRE, PVol) significantly increased the predictive accuracy of the model in the overall patient population (79% vs. 77%; $p=0.001$; Figure 4a) as well as in the subset of patients with PSA levels up to 10 ng/ml (74.3% vs. 71.7%; $p=0.005$; Figure 4b); conversely, the addition of PFR failed to increase the predictive accuracy of the model based on standard parameters

Finally, since PVol and PVRUV were found to be the most reliable predictors of PB× outcome in patients with PSA levels up to 10 ng/ml, attempts were made to identify cut-offs for these parameters that could have allowed some of these patients to be spared from PB×. Using 80 ml as cut-off for PVol, 256 (19%) biopsies could have been avoided while missing 33 (7.9%) tumors, including only two cases of high-risk (Gleason >7) cancer; using 85 ml as cut-off for PVRUV, 215 (15.9%) biopsies could have been avoided while missing 35 (8.4%) tumors, including 10 high-risk cancer cases (Table IV). Interestingly, using the mean values of PVol and PVRUV as cut-offs in patients without PCa (60 ml for both of them *i.e.* “rule of 60”), 260 (19.2%) PB×s could have been avoided while missing 33 (7.9%) tumors, including six high-risk cases cancer (Table IV).

Discussion

The present study confirmed that patients with PCa were older, had higher PSA levels and smaller PVol than those without PCa; the novel finding of our study was that men with PCa had significantly greater PFR and lower PVRUV than those without PCa. When the combined predictive effect of the covariates

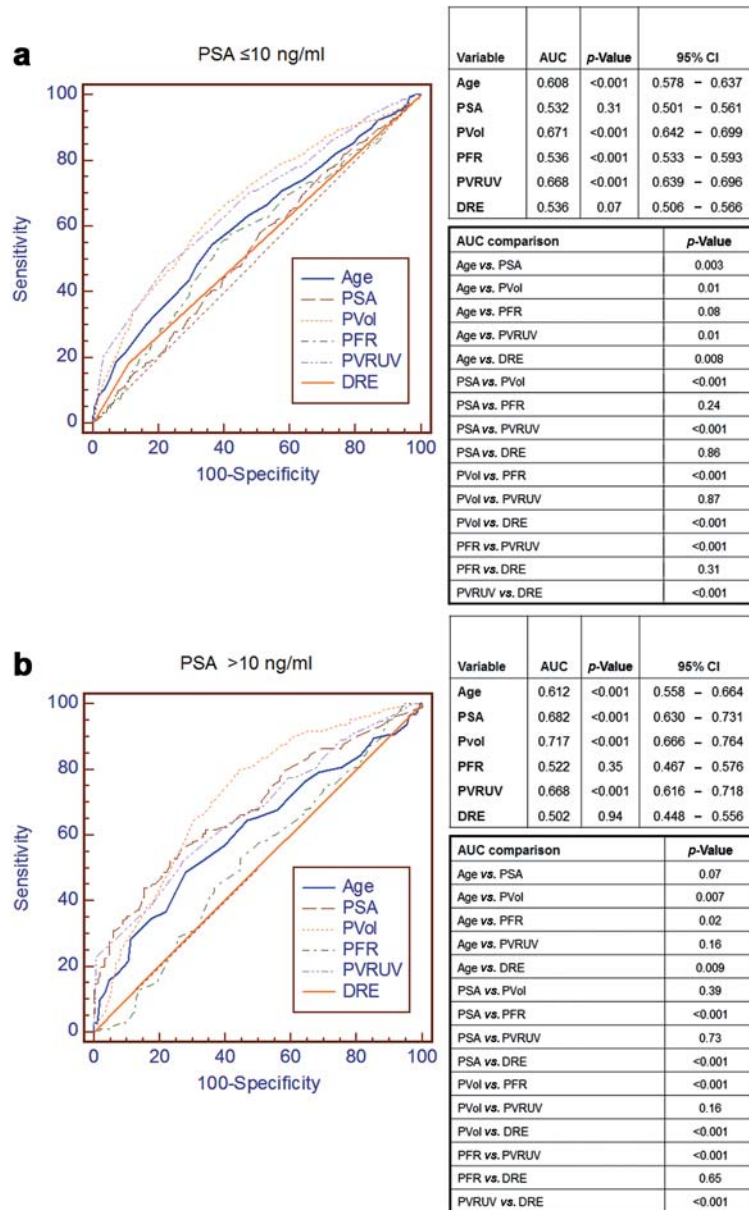


Figure 3. Receiver operating characteristic (ROC), prostate volume (PVol), peak flow rate (PFR), postvoid residual urinary volume (PVRUV) and digital rectal examination (DRE), in predicting prostate cancer in patients with total prostate-specific antigen (PSA) ≤ 10 ng/ml (a) and > 10 ng/ml (b). AUC: Area under the ROC curve; CI: confidence interval.

was tested by logistic regression analysis, it was found that age, PSA, PVol and PVRUV were the most significant predictors of PBx outcome; ROC curve analysis, however, showed that PVol and PVRUV had the best predictive value.

PVol has already been shown to be more accurate than age and PSA in predicting PBx outcome (14-16); the finding of PVRUV having almost the same predictive accuracy as PVol is novel and seems to us particularly interesting in view of the fact that differently from PVol, PVRUV measurement is

a non-invasive test. Moreover, the cancer detection rate of a standardized PBx scheme may be affected by PVol, as the greater the PVol, the greater the chances of a standard number of cores missing the focus of PCa (17-19); conversely, PVRUV does not have such potential bias.

Turning findings into clinical practice, all clinical parameters mentioned above are used to identify patients at risk of harboring PCa, who are thus candidates to PBx, but can also be used to identify those that because of their low risk of harboring PCa

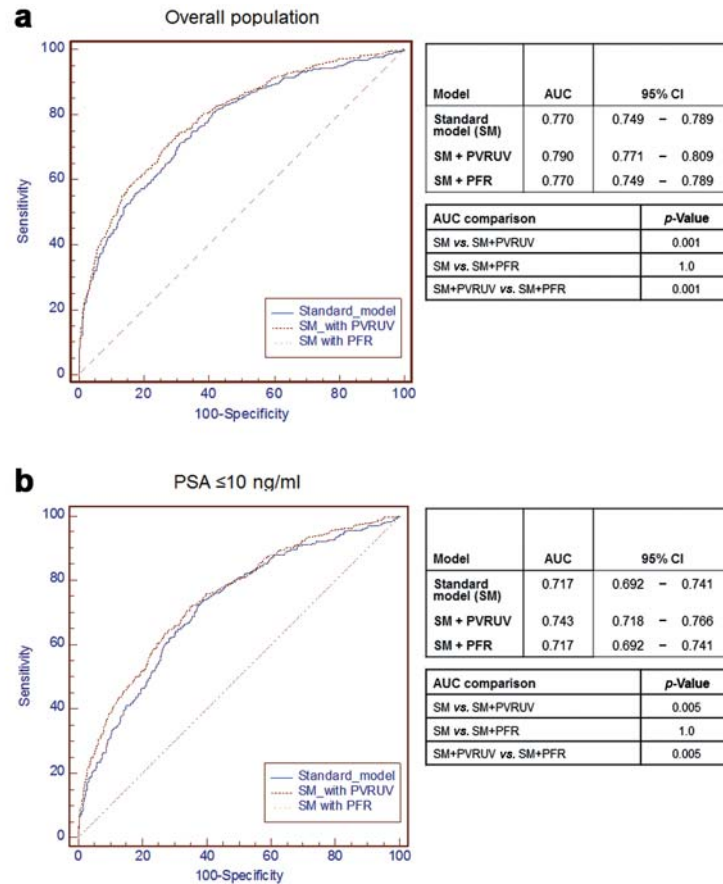


Figure 4. Receiver operating characteristic (ROC) curves comparing multivariate logistic regression models based on standard clinical parameters [‘standard’ model including age, prostate-specific antigen (PSA), and digital rectal examination (DRE) and prostate volume (PVol)] with models incorporating post-void residual urinary volume (PVRUV) or peak flow rate (PFR) for the entire patient cohort (a) and for patients with total PSA ≤ 10 ng/ml (b). AUC: Area under the ROC curve; CI: confidence interval.

could potentially be spared from a PB \times . Due to a lower cancer detection rate, patients with PSA levels up to 10 ng/ml are those who could potentially be spared from PB \times if reliable predictors of procedure outcome were available. The present study confirmed that in this patient population, there was no difference in mean PSA levels between those with and those without PCa. This finding is in agreement with previous studies (7, 20) and somewhat suggests that in men with PSA up to 10 ng/ml, there are clinical factors more relevant than PSA in determining PB \times outcome. According to multivariate logistic regression analysis, age, PVol and PVRUV were the most significant predictors of PB \times outcome; ROC curve analysis, however, showed that PVol and PVRUV had the best predictive value (AUC=0.671, $p<0.001$ and AUC=0.668, $p<0.001$, respectively), significantly outperforming all the other clinical variables.

PVol and PVRUV also kept their predictive value in the subset of patients with PSA >10 ng/ml, whereby PSA returned, as expected, as a significant predictor of PB \times

outcome in both multivariate logistic regression and ROC curve analysis. An interesting finding was that the AUC for PVRUV was exactly the same (0.668) for patients with PSA up to 10 ng/ml and those with PSA >10 ng/ml, somewhat confirming the predictive value of this parameter being independent on PSA level.

In the present study, we did not evaluate other non-invasive tests such as serum free PSA, serum PSA isoform [-2]proPSA (p2PSA), the gene-based urinary marker prostate cancer antigen 3 (PCA3), or their combination such as free-to-total PSA ratio and prostate health index (PHI), a mathematical combination of PSA, free PSA and p2PSA. Previous studies addressing this issue showed that PHI performed better than free PSA, free-to-total PSA ratio and PCA3 (AUC 0.70, 0.62, 0.60 and 0.59, respectively) (7, 21); interestingly, PVol had a similar AUC to that found in our study population (0.68 and 0.62 vs. 0.67), somewhat providing indirect external data validation.

Table II. Clinical and pathological characteristics according to total prostate-specific antigen (PSA).

Characteristic	PCa (n=417)	NEM (n=933)	p-Value
PSA ≤10 ng/ml			
Age (years)			
Mean	67	65	0.0001
Range	48-86	34-86	
PSA (ng/ml)			
Mean	6.2	6.1	0.2
95% CI	6.1-6.4	6.0-6.3	
Prostate volume (ml)			
Mean	45.9	60.1	0.0001
95% CI	43.7-48.2	59.8-63.2	
Abnormal DRE	121 (29%)	232 (24.8%)	0.1
Peak flow rate (ml/min)			
Mean	14.1	12.7	0.0001
95% CI	13.4-14.7	12.3-13.1	
PVRUV (ml/min)			
Mean	34.2	60.0	0.0001
95% CI	31.2-37.2	54.1-60.1	
Age (years)			
Mean	71	68	0.0001
Range	50 - 90	43-85	
PSA >10 ng/ml			
PSA (ng/ml)			
Mean	40.2	16.4	0.0001
95% CI	31.7-48.6	15.1-17.6	
Prostate volume (ml)			
Mean	50.0	73.1	0.0001
95% CI	47.2-52.8	68.2-78.1	
Abnormal DRE	67 (26.6%)	23 (12.8%)	0.0008
Peak flow rate (ml/min)			
Mean	12.2	11.9	0.3
95% CI	11.4-12.8	11.0-12.8	
PVRUV (ml/min)			
Mean	41.0	64.2	0.0001
95% CI	36.4-45.4	57.2-71.3	

PCa, Prostate cancer; NEM, no evidence of malignancy; PSA, prostate-specific antigen; DRE, digital rectal examination; PVRUV, post-void residual urinary volume; CI: confidence interval.

When a potential predictive or prognostic marker is analyzed for its efficacy, it is not sufficient to show that it is significantly linked to the outcome or even that it is the 'strongest' predictor of outcome (*i.e.* has the best AUC). To be useful in clinical practice, a novel marker should be proven to add information that significantly improves that provided by standard markers. The present study shows that the addition of PVRUV to the multivariate model based on standard clinical factors (age, PSA, DRE and PVol) significantly increased the predictive performance of the model in both the overall population and the subset of patients with total PSA ≤10 ng/ml.

As mentioned above, the secondary endpoint of our study was to determine whether simple cut-offs of the tested parameters could readily be used in clinical practice

Table III. Logistic regression model results.

Population	Variable	p-Value	OR	95% CI
Overall				
population	Age	<0.0001	1.067	1.049-1.085
	PSA	<0.0001	1.070	1.049-1.091
	PVol	<0.0001	0.975	0.970-0.981
	PVRUV	<0.0001	0.984	0.980-0.988
	PFR	0.01	0.973	0.952-0.995
	DRE	0.47		
Hosmer-Lemeshow test= 9.5 (p=0.1)				
PSA ≤10 ng/ml				
Age	Age	0.0001	1.065	1.044-1.087
	PSA	0.08		
	PVol	0.0001	0.981	0.974-0.987
	PVRUV	0.0001	0.985	0.980-0.990
	PFR	0.2		
	DRE	0.3		
Hosmer-Lemeshow test= 12.2 (p=0.1)				
PSA >10 ng/ml				
Age	Age	0.0001	1.078	1.039-1.117
	PSA	0.0001	1.061	1.032-1.090
	PVol	0.0001	0.960	0.948-0.973
	PVRUV	0.0001	0.984	0.976-0.986
	PFR	0.1		
	DRE	0.03	0.449	0.216-0.935
Hosmer-Lemeshow test= 13.7 (p=0.8)				

PSA, Prostate-specific antigen; PVol, prostate volume; PVRUV, post-void residual urinary volume; PFR, peak flow rate; DRE, digital rectal examination; OR: odds ratio; CI: confidence interval.

to identify patients in whom PB× could potentially be avoided; this analysis was carried out in patients with PSA levels up to 10 ng/ml, due to their lower risk of harboring PCa. In this subset, PVol outperformed PVRUV in terms of the ratio between number of PB× avoided and number of missed tumors, as well as in terms of missed high-grade tumors (Table IV). Interestingly, using the mean values of PVol and PVRUV as cut-offs in patients without PCa (60 ml for both), 260 (19.2%) PB×s could have been avoided while missing 33 (7.9%) tumors, including 6 high-risk ones. If confirmed in other large prospective studies, these findings would suggest that these simple clinical parameters (PVol ≥80 ml or the 'rule of 60') could readily be used in clinical practice to counsel patients about the possibility of being spared from PB× and simply scheduled for a strict follow-up.

The strengths of our study include its prospective nature, the use of a standardized extended PB× scheme, as well as a standardized protocol for UFM and PVRUV

Table IV. Diagnostic accuracy of different cut-offs for prostate volume (PVol) and post-void residual urinary volume (PVRUV) in patients with total PSA ≤ 10 ng/ml

Cut-off	Avoided biopsies, n (%)	Missed PCa, n (%)	No. of missed PCa with Gleason score >7
¹ PVol ≥ 80 ml	256/1350 (19%)	33/417 (7.9%)	2
¹ PVRUV ≥ 85 ml	215/1350 (15.9%)	35/417 (8.4%)	10
² PVol ≥ 60 ml and ² PVRUV ≥ 60 ml	260/1350 (19.2%)	33/417 (7.9%)	6

¹Cut-offs with >90% sensitivity; ²based on mean values of patients with no evidence of malignancy. PCa: Prostate cancer.

measurement and pathologists being blind to UFM and PVRUV data. A potential study limitation is not having attempted to construct a nomogram including PVRUV, but we felt this was beyond the scope of a study testing this parameter for the first time and exploring its performance in everyday clinical practice. Other potential limitations include single measurement of PVRUV, although this test is widely considered accurate (22), a study population consisting of white men only, thus limiting finding applicability to other ethnicities and lack of external pathological review.

In conclusion, the present study showed that PVRUV is a novel accurate non-invasive test for predicting PB \times outcome that can easily be used by clinicians, alone or in combination with PVol, in the decision-making process of men potentially facing a PB \times . It also provided grounds for this new parameter being externally validated in other populations, as well as being incorporated into more sophisticated prognostic models.

Conflicts of interest

The Authors declare that there is no conflict of interests regarding the publication of this article.

References

- Serag H, Banerjee S, Saeb-Parsy K, Irving S, Wright K, Stearn S, Doble A and Gnanapragasam VJ: Risk profiles of prostate cancers identified from UK primary care using national referral guidelines. *Br J Cancer* 106: 436-439, 2012.
- Bokhorst LP, Zhu X, Bul M, Bangma CH, Schröder FH and Roobol MJ: Positive predictive value of prostate biopsy indicated by prostate-specific-antigen-based prostate cancer screening: trends over time in a European randomized trial. *BJU Int* 110: 1654-1660, 2012.
- Lughezzani G, Lazzeri M, Larcher A, Lista G, Scattoni V, Cestari A, Buffi NM, Bini V and Guazzoni G: Development and internal validation of a Prostate Health Index based nomogram for predicting prostate cancer at extended biopsy. *J Urol* 188: 1144-1150, 2012.
- Lucarelli G, Fanelli M, Larocca AM, Germinario C, Rutigliano M, Vavallo A, Selvaggi FP, Bettocchi C, Battaglia M and Dittono P: Serum sarcosine increases the accuracy of prostate cancer detection in patients with total serum PSA less than 4.0 ng/ml. *Prostate* 72: 1611-1121, 2012.
- Lucarelli G, Rutigliano M, Bettocchi C, Palazzo S, Vavallo A, Galleggiante V, Trabucco S, Di Clemente D, Selvaggi FP, Battaglia M and Dittono P: Spondin-2, a secreted extracellular matrix protein, is a novel diagnostic biomarker for prostate cancer. *J Urol* 190: 2271-2277, 2013.
- Aboumarzouk OM, Ogston S, Huang Z, Evans A, Melzer A, Stolzenberg JU and Nabi G: Diagnostic accuracy of transrectal elastosonography (TRES) imaging for the diagnosis of prostate cancer: a systematic review and meta-analysis. *BJU Int* 110: 1414-1423, 2012.
- Auprich M, Haese A, Walz J, Pummer K, de la Taille A, Graefen M, de Reijke T, Fisch M, Kil P, Gontero P, Irani J and Chun FK: External validation of urinary PCA3-based nomograms to individually predict prostate biopsy outcome. *Eur Urol* 58: 727-732, 2010.
- Shukla-Dave A, Hricak H, Akin O, Yu C, Zakian KL, Udo K, Scardino PT, Eastham J, Kattan MW: Preoperative nomograms incorporating magnetic resonance imaging and spectroscopy for prediction of insignificant prostate cancer. *BJU Int* 109: 1315-1322, 2012.
- Laniado ME, Ockrim JL, Marronaro A, Tubaro A and Carter SS: Serum prostate-specific antigen to predict the presence of bladder outlet obstruction in men with urinary symptoms. *BJU Int* 94(9): 1283-1286, 2004.
- Kang MY, Ku JH and Oh SJ: Non-invasive parameters predicting bladder outlet obstruction in Korean men with lower urinary tract symptoms. *J Korean Med Sci* 25(2): 272-275, 2010.
- Cormio L, Lorusso F, Selvaggio O, Perrone A, Sanguedolce F, Pagliarulo V, Bufo P and Carrieri G: Noninfiltrative anesthesia for transrectal prostate biopsy: a randomized prospective study comparing lidocaine-prilocaine cream and lidocaine-ketorolac gel. *Urol Oncol* 31: 68-73, 2013.
- Cormio L, Pagliarulo V, Lorusso F, Selvaggio O, Perrone A, Sanguedolce F, Bufo P and Carrieri G: Combined perianal-intrarectal (PI) lidocaine-prilocaine (LP) cream and lidocaine-ketorolac gel provide better pain relief than combined PI LP cream and periprostatic nerve block during transrectal prostate biopsy. *BJU Int* 109: 1776-1780, 2012.
- Cormio L, Scattoni V, Lorusso F, Perrone A, Di Fino G, Selvaggio O, Sanguedolce F, Bufo P, Montorsi F and Carrieri G: Prostate cancer detection rates in different biopsy schemes. Which cores for which patients? *World J Urol* 32(2): 341-346, 2014.
- Al-Azab R, Toi A, Lockwood G, Kulkarni GS and Fleshner N: Prostate volume is strongest predictor of cancer diagnosis at transrectal ultrasound-guided prostate biopsy with prostate-specific antigen values between 2.0 and 9.0 ng/ml. *Urology* 69: 103-107, 2007.
- Kobayashi T, Mitsumori K, Kawahara T, Nishizawa K, Ogura K and Ide Y: Prostate gland volume is a strong predictor of biopsy results in men 70 years or older with prostate-specific antigen levels of 2.0-10.0 ng/ml. *Int J Urol* 12: 969-975, 2005.

- 16 Tang P, Jin XL, Uhlman M, Lin YR, Deng XR, Wang B and Xie KJ: Prostate volume as an independent predictor of prostate cancer in men with PSA of 10-50 ng ml-1. *Asian J Androl* 15: 409-412, 2013.
- 17 Uzzo RG , Wei JT , Waldbaum RS, Perlmutter AP, Byrne JC and Vaughan ED Jr.: The influence of prostate size on cancer detection. *Urology* 46: 831-836, 1995.
- 18 Karakiewicz PI , Bazinet M , Aprikian AG , Trudel C, Aronson S, Nachabé M, Pélouquin F, Dessureault J, Goyal MS, Bégin LR and Elhilali MM: Outcome of sextant biopsy according to gland volume. *Urology* 49: 55-59, 1997.
- 19 Letran JL , Meyer GE , Loberiza FR and Brawer MK: The effect of prostate gland volume on the yield of needle biopsy. *J Urol* 160: 1718-1721, 1998.
- 20 Lazzeri M, Briganti A, Scattoni V, Lughezzani G, Larcher A, Gadda GM, Lista G, Cestari A, Buffi N, Bini V, Freschi M, Rigatti P, Montorsi F and Guazzoni G: Serum index test %[-2]proPSA and Prostate Health Index are more accurate than prostate specific antigen and %fPSA in predicting a positive repeat prostate biopsy. *J Urol* 188: 1137-1143, 2012.
- 21 Scattoni V, Lazzeri M, Lughezzani G, De Luca S, Passera R, Bollito E, Randone D, Abdollah F, Capitanio U, Larcher A, Lista G, Gadda GM, Bini V, Montorsi F and Guazzoni G: Head-to-head comparison of prostate health index and urinary prostate cancer antigen 3 in predicting the presence of cancer at initial or repeat biopsy. *J Urol* 190: 496-501, 2013.
- 22 Madersbacher S, Alivizatos G, Nordling J, Sanz CR, Emberton M and de la Rosette JJ: EAU 2004 Guidelines on assessment, therapy and follow-up of men with lower urinary tract symptoms suggestive of benign prostatic obstruction (BPH Guidelines). *Eur Urol* 46: 547-554, 2004.

Received December 15, 2014
Revised January 23, 2015
Accepted January 27, 2015