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Benign Prostatic Hyperplasia

Serum Prostate-Specific Antigen as a Predictor of Prostate Volume in the Community: The Krimpen Study

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Abstract

Objectives: Serum prostate-specific antigen (PSA) is considered a proxy for prostate volume (PV). This study investigates which range of PSA values has the best utility in the determination of PV (<30 cc, at 30, 40, and 50 cc), and whether PSA performs better than digital rectal examination (DRE) when estimating PV.

Methods: In a population-based follow-up study of 1688 men in Krimpen aan den IJssel, The Netherlands, at baseline we estimated PV by DRE and by transrectal planimetric ultrasound (TRUS), in addition to measuring PSA. Men who tested positive for prostate cancer (PCa) at baseline and at 2 and 4 yr of follow-up were excluded from the analyses (n = 142). Of the men without PCa, PSA and PV data were available in 1524 participants.

Results: Of all 1524 men analysed, 76.7% had a PSA of 0–2.0, 15.0% had a PSA of 2.1–4.0, and 8.3% a PSA > 4. Low PSA ranges (0–2 and 2.1–4.0) discriminate better for a PV of 30 cc (eg, in men with a PSA range of 2.1–2.5 ng/ml there was a 72% chance of having a PV > 30 cc). Higher ranges of PSA (>4.0) discriminate better for a PV > 40 or 50 cc. (eg, in men with a PSA in the range of 4.1–7.0 ng/ml there was a 69% chance of having a PV > 40 cc and in men with a PSA > 10 ng/ml there was a 75% chance of a PV > 50 cc). The receiver operating curve (ROC) for the performance of PSA in estimating a PV > 30 cc shows an area under the curve (AUC) of 0.79, denoting reasonable discrimination, and AUCs of 0.86 and 0.92, denoting good discrimination of PVs > 40 cc and >50 cc, respectively. PSA performed significantly better than DRE at estimating PV. Multiple regression analysis shows that both DRE and an interaction term for age and PSA provided minimal additional information beyond PSA in the prediction of PV; however, their contribution is numerically minimal/not clinically meaningful.

Conclusions: In men for whom a diagnosis of PCa has been ruled out, PSA can be used to detect an enlarged prostate (>30 cc and with more accuracy PV > 40 or 50 cc). More precision in estimating PV can be obtained when using a formula that contains PSA, age, DRE, and an interaction term between age and PSA; however, the clinical advantage of the formula over PSA alone is only modest as shown by the ROC curves. Thus, for clinicians looking for an easy and fast way to identify patients with an enlarged prostate, PSA is a good approximation for men without PCa.

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1. Introduction

Clinical benign prostatic hyperplasia (BPH), once established as a diagnosis by the occurrence of benign prostatic enlargement (BPE) in combination with lower urinary tract symptoms (LUTS) and benign outflow obstruction (BOO), has been considered to be a chronic and progressive disease by a panel of experts [1]. Baseline prostate volume has been linked to progression of BPH (eg, acute urinary retention and surgery for BPH) [2,3]. Furthermore, prostate volume (PV) has been shown to be a prognostic factor for treatment outcome with the two commonly used classes of agent for BPH: 5α-reductase inhibitors (5-ARIs) and α_1-blockers [4]. Current guidelines from the American Urological Association [5,6] on the short-term management of BPH recommend as an option α_1-blockers for men with symptoms secondary to BPH and 5-ARIs or combination therapy for men with symptoms and demonstrable prostate enlargement. Therefore, PV estimations are important both for an understanding of the natural history of the disease and to establish the most appropriate initial treatment for an individual patient. However, currently, guidelines for the initial evaluation of BPH for general practitioners, shared care clinics, and urology offices are generally not driven by PV, but they do use symptom severity and bother as criteria for further decisions in diagnostic work-up and therapy. The reason for this is the perceived lack of reliability of digital rectal examination (DRE) in general in estimating PV and the lack of expertise of some of these practitioners in the estimation of PV by DRE or transrectal ultrasound (TRUS). Furthermore, there is limited availability of TRUS for PV estimation. Therefore, a fast and accurate method for estimating PV is needed to facilitate treatment decisions and care of the patient with BPH in the community setting and in urology offices.

The planimetric method of PV assessment by TRUS is considered the gold standard due to its high accuracy and high reproducibility [7–12]. However, this method is too laborious to be used routinely in normal practice, even for those with access to TRUS. For most practitioners it is not practical to perform TRUS as an initial test in patients presenting with LUTS. Therefore, in everyday clinical practice, a quick, reliable, and reproducible alternative method for measuring PV is needed. For this reason, more rapid and convenient proxies such as DRE and serum prostate-specific antigen (PSA) have been recommended [13,14]. However, these studies examined PSA as a proxy for PV in a selected and largely clinical trial population. The actual performance of PSA as a proxy for PV in the general population is unknown. Our study assesses the utility of PSA as a proxy for PV in the general population because this population is most representative of the group of men initially diagnosed with BPH.

2. Patients, materials, and methods

2.1. Patients

The design of the Krimpen longitudinal community-based study has been described previously [15]. Briefly, all men aged 50–75 yr (age on reference date June 1995, $n = 3924$) in the Dutch municipality of Krimpen aan den IJssel were studied. Men with radical prostatectomy, a diagnosis of prostate or bladder cancer, neurogenic bladder disease, negative advice from their general practitioner, or who were unable to complete questionnaires and visit the health centre, were excluded. To ensure that patients who developed prostate cancer (PCa) during the study were excluded, prostate biopsies were performed according to a predefined protocol. At baseline all patients with a PSA $\geq$ 10.0 ng/ml underwent biopsy, those with a PSA of 2.0–10.0 ng/ml had a biopsy only if suspicious findings were noted on DRE or TRUS, and those with a PSA of 1.0–2.0 ng/ml underwent the procedure only if the DRE was suspicious. At the first and second follow-up visits, biopsies were performed in patients with a PSA $\geq$ 4.0 ng/ml or a PSA of 1.0–4.0 ng/ml with suspicious DRE. All men entering this cohort study provided written informed consent and ethical approval was gained from the Erasmus Medical Centre, Rotterdam, The Netherlands.

2.2. Measurements

At baseline, all participants ($n = 1688$, 50% of all eligible men) completed a 113-item self-administered questionnaire [15] and received a physical examination, including blood pressure, height and body weight measurement, and estimation of serum PSA, uroflowmetry, postvoid residual urine, DRE, and TRUS. Two follow-up visits were performed with an average follow-up time of 2.1 and 4.2 yr during which subjects completed the questionnaire and repeated assessments of PSA, uroflowmetry, postvoid residual volume, DRE, and TRUS.

Prostate volume was estimated by DRE in increments of 5 cc. After this in the same visit a TRUS of the prostate was performed with a 7-MHz Bruel and Kjaer multiplane sector-scanning probe. The planimetric technique of volume measurement is considered the gold standard [16]. This method involves measuring the surface area of transverse sections taken through the prostate at 5-mm intervals. The average of two intervals multiplied by 5 mm provides the volume for each step and the cumulative volume allows the total volume (in cc) to be derived [9].

2.3. Statistical analysis

Men were screened for PCa at baseline and at 2 and 4 yr of follow-up. All men with PCa were retroactively excluded from

the analyses ensuring that the population was PCa free with reasonable certainty. In men without PCa, we calculated the percentages of men with a PV above various volumes (30 cc, 40 cc, and 50 cc).

We used receiver operating characteristic (ROC) curves to examine how well DRE and PSA estimate/approximate PV as measured by TRUS. For this purpose the area under the ROC curves (AUC) was used. The discriminative value of a ROC AUC was assessed by the method described by Hanley and McNeill [17]: from 0.5 (no discrimination) to 1.0 (perfect discrimination, a value of 0.7–0.8 was considered "reasonable" and a value of ≥0.8 was designated as "good" discrimination by these authors).

We also ran a multiple regression model to estimate log PV from log PSA, age, DRE, and an interaction term for age and log PSA. This resulted in a predicted PV (referred to as Formula A). Leaving DRE out of the formula resulted in another formula for predicted PV (Formula B). PV and PSA were log-transformed to correct for non-normal distributions.

3. Results

Of all eligible men, 1688 (50%) participated in the Krimpen study. We excluded 142 men from the analyses who tested positive for PCa at baseline or during follow-up in addition to men without a PSA or PV measurement. Of all 1524 men analysed, 76.7% had a PSA of 0–2.0 ng/ml, 15.0% had a PSA of 2.1–4.0 ng/ml, and 8.3% a PSA > 4 ng/ml.

Table 1 shows the different PV cut-off values in relation to PSA ranges. Low PSA ranges (0–2 and 2.1–4.0) discriminate better for a PV of above or below 30 cc (eg, men with a PSA range of 2.1–2.5 ng/ml have a 72% chance of having a prostate volume >30 cc). Higher ranges of PSA (>4.0) discriminate better for a PV above or below 40 or 50 cc, respectively (eg, men with a PSA in the range of 4.1–7.0 ng/ml have a 69% chance of having a PV > 40 cc and men with a PSA > 10 ng/ml have a 75% chance of a prostate volume >50 cc; Table 1).

Table 2 shows the relationship between PV and age. Of the men aged 70–80 yr more than two thirds (68.5%) showed a PV > 30 cc. Of all men in the community >50 yr of age, approximately half (49.3%) had a PV above 30 cc.

Fig. 1 shows ROC curve (and standard error [SE]) for prediction of PV (>30, 40, and 50 cc) using serum PSA, by age group in community-based men without PCa. For a PV of >30 cc the ROC AUC was 0.782 (SE 0.012). For a PV of >40 cc and a PV > 50 cc the areas were 0.858 (SE 0.012) and 0.921 (SE 0.010), respectively. PSA performs better as a predictor of PV in the higher PV range (larger areas under the curve). The performance of PSA as an estimate of PV does not depend on age.

Table 3 shows the diagnostic performance in terms of predictive values and sensitivity for various

Table 1 – Percentage of men with a PV above a specific cut-off value according to various PSA ranges in community-based men without prostate cancer

PSA level	No. of patients	PV > 30 cc, %	PV > 40 cc, %	PV > 50 cc, %
0–0.5	243	14	1	0.0
0.6–1.0	469	34	5	0.4
1.1–1.5	297	52	12	2
1.6–2.0	160	65	25	8
2.1–2.5	96	72	40	12
2.6–3.0	56	79	57	27
3.1–4.0	77	84	48	27
4.1–7.0	85	98	69	48
7.1–10.0	29	90	76	66
>10.0	12	92	83	75
Total	1524	49.3	19.7	8.9

PV = prostate volume; PSA = prostate-specific antigen.

Table 2 – Frequency of prostate volumes (PV > 30, >40, >50 cc) by age group in community-based men without prostate cancer

Age group, yr	PV > 30 cc* *n* (%)	PV > 40 cc *n* (%)	PV > 50 cc *n* (%)	Total *n* (%)
50–59	279 (39.2)	76 (10.7)	21 (3.0)	711 (100)
60–69	359 (55.4)	157 (24.2)	71 (11.0)	658 (100)
70–80	113 (68.5)	67 (40.6)	44 (26.7)	165 (100)
All	751 (49.3)	300 (19.7)	136 (8.9)	1524 (100)

* Includes men with PV > 40 cc or >50 cc.

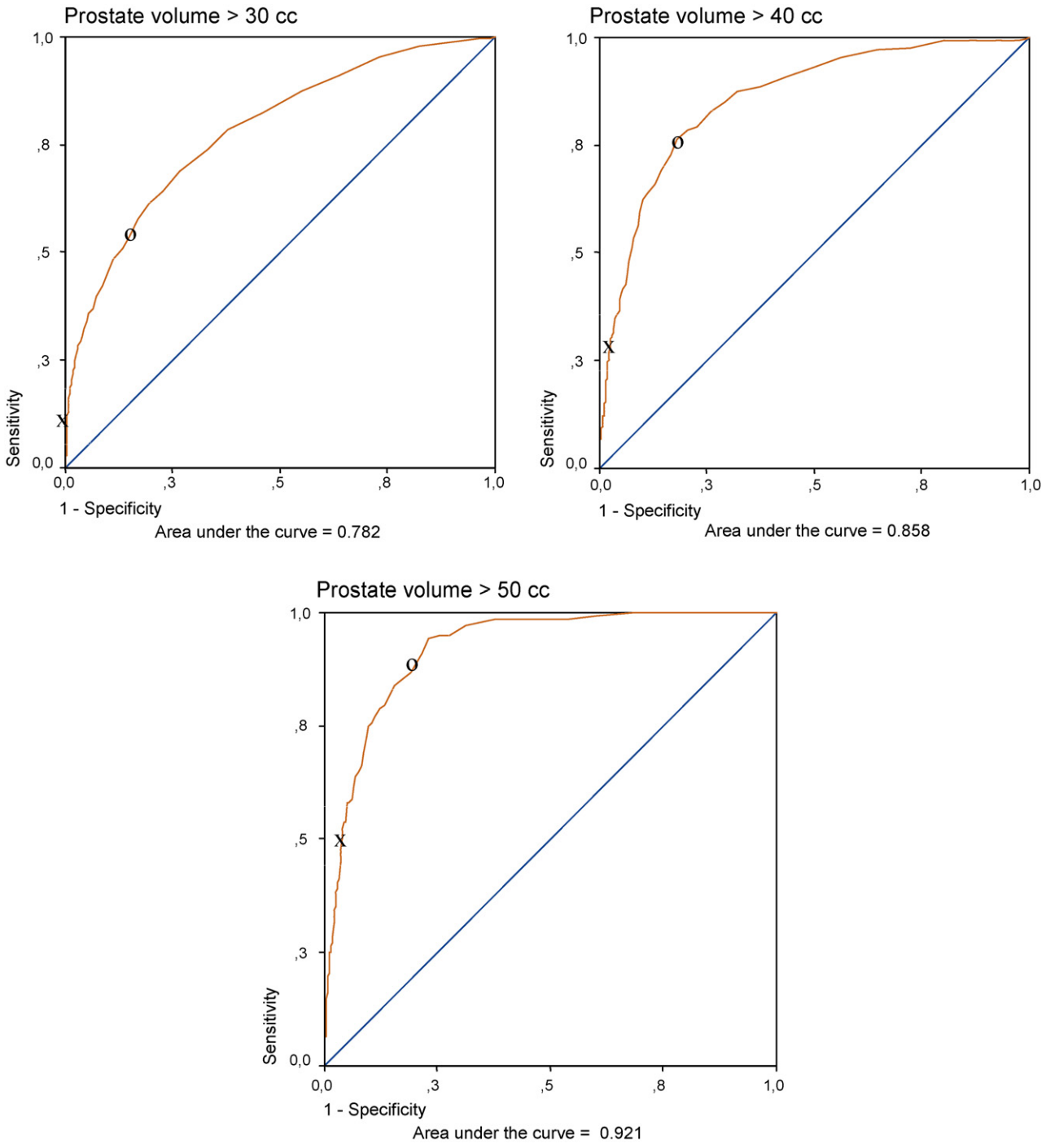

Fig. 1 – Receiver Operating Characteristic Curves, estimating various prostate volumes from PSA (PSA cutoff levels indicated as o = 1.5 ng/ml, x = 4 ng/ml).

age groups and cut-off values of PSA in predicting PV above and below 30 cc. Table 4 shows the diagnostic performance in terms of predictive values and sensitivity for various age groups and cut-off values of PSA in predicting PV above and below 40 cc. For example, in men aged 50–59 with a PSA > 1.5 ng/ml, 32% (a positive predictive value [PPV] of 0.32) had an actual PV > 40 cc. In the men aged 50–59 with a PV of 40 cc, 70% had a PSA level >1.5 ng/ml (sensitivity). In the men of the same age but with a PSA > 4 ng/ml the chance of a PV > 40 cc is 56% (PPV).

The percentage of correct estimations is highest (Pr cor = 0.84) in the PSA range 2.5–4.0 ng/ml. However, in this range the sensitivity is low (30–53%). A

Table 3 – Measures of diagnostic performance of various cut-off values of serum PSA to predict a prostate volume of ≥30 cc in community-based men without prostate cancer

Age		Upper limit of serum PSA interval, ng/ml							
		0.5	1.0	1.5	2	2.5	3	4	5
All	PPV	0.56	0.68	0.78	0.84	0.88	0.91	0.95	0.95
	NPV	0.86	0.73	0.65	0.61	0.59	0.57	0.55	0.53
	Pr cor	0.51	0.79	0.70	0.67	0.64	0.62	0.58	0.55
	FPR	0.73	0.33	0.14	0.07	0.04	0.02	0.01	0.01
	Sens	0.95	0.74	0.53	0.40	0.31	0.25	0.16	0.10
50–59	PPV	0.45	0.59	0.70	0.75	0.81	0.83	0.96	0.93
	NPV	0.84	0.76	0.70	0.68	0.66	0.65	0.63	0.62
	Pr cor	0.53	0.68	0.70	0.69	0.68	0.66	0.64	0.62
	FPR	0.72	0.29	0.12	0.06	0.04	0.02	0.00	0.00
	Sens	0.92	0.65	0.41	0.31	0.23	0.18	0.04	0.05
60–69	PPV	0.62	0.73	0.81	0.86	0.90	0.93	0.94	0.96
	NPV	0.87	0.70	0.62	0.56	0.53	0.52	0.49	0.48
	Pr cor	0.65	0.71	0.70	0.64	0.60	0.58	0.54	0.51
	FPR	0.74	0.36	0.17	0.09	0.05	0.02	0.01	0.01
	Sens	0.97	0.77	0.59	0.42	0.31	0.26	0.18	0.12
70–78	PPV	0.74	0.79	0.84	0.94	0.96	0.98	0.97	0.95
	NPV	0.93	0.61	0.51	0.49	0.46	0.42	0.38	0.65
	Pr cor	0.76	0.74	0.69	0.67	0.62	0.57	0.50	0.42
	FPR	0.75	0.50	0.27	0.08	0.04	0.02	0.02	0.02
	Sens	0.99	0.85	0.67	0.56	0.47	0.38	0.27	0.16

Indices indicating the diagnostic performance of PSA as a test for prostate volume.
PSA = prostate-specific antigen; PPV = positive predictive value; NPV = negative predictive value; PR cor = percentage of correctly predicted cases; FPR = false-positive rate; Sens = sensitivity.

Table 4 – Measures of diagnostic performance of various cut-off values of serum PSA to predict a prostate volume of ≥40 cc in community-based men without prostate cancer

Age		Upper limit of serum PSA interval, ng/ml							
		0.5	1.0	1.5	2	2.5	3	4	5
All	PPV	0.23	0.34	0.46	0.56	0.62	0.63	0.72	0.77
	NPV	0.99	0.96	0.94	0.91	0.89	0.87	0.85	0.84
	Pr cor	0.35	0.63	0.78	0.83	0.84	0.84	0.84	0.83
	FPR	0.80	0.44	0.23	0.13	0.08	0.06	0.03	0.02
	Sens	0.99	0.91	0.79	0.66	0.53	0.43	0.30	0.20
50–59	PPV	0.14	0.22	0.32	0.37	0.41	0.39	0.56	0.57
	NPV	1.00	0.98	0.96	0.94	0.93	0.92	0.91	0.90
	Pr cor	0.31	0.65	0.81	0.85	0.87	0.87	0.90	0.90
	FPR	0.77	0.38	0.18	0.11	0.07	0.06	0.02	0.01
	Sens	1.00	0.90	0.70	0.55	0.42	0.30	0.20	0.11
60–69	PPV	0.28	0.37	0.49	0.60	0.66	0.69	0.75	0.83
	NPV	0.98	0.95	0.92	0.89	0.86	0.84	0.82	0.80
	Pr cor	0.37	0.61	0.74	0.81	0.82	0.82	0.81	0.80
	FPR	0.83	0.49	0.27	0.14	0.09	0.06	0.04	0.02
	Sens	0.99	0.91	0.80	0.67	0.53	0.44	0.32	0.24
70–78	PPV	0.44	0.51	0.66	0.76	0.82	0.82	0.81	0.79
	NPV	1.00	0.88	0.89	0.84	0.80	0.74	0.69	0.64
	Pr cor	0.49	0.61	0.76	0.81	0.81	0.76	0.72	0.66
	FPR	0.86	0.61	0.32	0.16	0.10	0.08	0.06	0.04
	Sens	1.00	0.93	0.88	0.76	0.67	0.54	0.39	0.22

Indices indicating the diagnostic performance of PSA as a test for prostate volume.
PSA = prostate-specific antigen; PPV = positive predictive value; NPV = negative predictive value; PR cor = percentage of correctly predicted cases; FPR = false positive rate; Sens = sensitivity.

Table 5 – Areas under the ROC curve and 95%CIs for DRE and serum PSA as methods used to estimate prostate volume (compared with the planimetric TRUS method), by prostate volume cut-off points (30, 40, and 50 cc) in community-based men without prostate cancer

Method of volume estimation	AUC for volume cut-off of 30 cc (95%CI)	AUC for volume cut-off of 40 cc (95%CI)	AUC for volume cut-off of 50 cc (95%CI)
Serum PSA	0.79 (0.77–0.81)	0.86 (0.84–0.88)	0.92 (0.91–0.94)
DRE	0.69 (0.66–0.71)	0.74 (0.71–0.78)	0.82 (0.79–0.86)
Formula A*	0.81 (0.79–0.83)	0.88 (0.86–0.90)	0.95 (0.94–0.97)
Formula B†	0.79 (0.77–0.82)	0.86 (0.84–0.89)	0.94 (0.92–0.95)

ROC = receiver operator characteristic; CI = confidence interval; DRE = digital rectal examination; PSA = prostate-specific antigen; TRUS = transurethral ultrasound; AUC = area under the curve.

* Formula A predicts PV based on the results of a multiple regression to estimate log PV from log PSA, age, DRE, and an interaction term for age and log PSA.

† Formula B predicts PV based on the results of a multiple regression to estimate log PV from log PSA, age, and an interaction term for age and log PSA.

sensitivity of >79% is reached if a PSA cut-off of 1.5 ng/ml is used.

Because there were only 136 patients in the ≥50 cc group, we did not conduct separate analyses in this group.

We used ROC curves to determine the diagnostic performance of models that included PSA compared to PSA and DRE alone as proxies for PV. Table 5 shows the areas under the ROC curve (AUC). The confidence intervals of the AUC for serum PSA and DRE do not overlap. This indicates a significantly better performance of serum PSA over DRE in estimating PV (for all PV cut-off values of 30, 40, and 50 cc). Serum PSA preformed better in estimating a PV below or above 50 cc than in estimating a PV below or above 30 cc. Multivariate regression analyses demonstrated that age, PSA, DRE, and the interaction term for age and PSA all attributed statistically significantly to the prediction of PV. However, the model that included all other terms next to serum PSA (model A, $r = 0.71$, $p < 0.001$) did not result in significantly better estimation of PV than the estimation based on the model without DRE (model B, $r = 0.65$, $p < 0.001$) or the estimation based on PSA alone ($r = 0.63$, $p < 0.001$).

4. Discussion

We determined the utility of PSA as a proxy for PV in community-based men older than 50 yr in whom PCa has been ruled out with reasonable certainty. In these men, PSA performed better than DRE as a proxy for PV. Adding age or DRE to a formula based on PSA does not result in a numerically superior prediction. For the initial management of patients with LUTS or BPH it is important to use PSA as a proxy for PV with caution. According to current guidelines, PCa has to be ruled out first in men with a PSA > 4 ng/ml. In men with a PSA < 4 ng/ml, PSA can be safely used as a proxy for PV. In men with a PSA of ≥4 PCa has to be ruled out; in general, this means that TRUS-guided prostate biopsies will have to be performed. In that setting it is relative easy to additionally perform a TRUS-guided volume measurement.

Evidence from several clinical studies demonstrates that the risk of clinical progression in BPH is greatest in men with a prostate volume ≥30 ml and a PSA level of ≥1.5 ng/ml [18,19]. Our community data confirm that in men with a PSA < 1.5 the probability of an enlarged prostate (>30 cc) was low. PSA can be used as the basis for management of patients with BPH in those men who are bothered by their symptoms and have a PSA < 4 ng/ml.

Data from several epidemiologic studies have shown that DRE systematically underestimates prostate size compared to TRUS [13,20]. Bosch et al have shown that DRE overestimates the size of smaller prostates and underestimates the size of large prostates [16]. Roerhborn et al suggested that if the probability of predicting the outcome of DRE > 30 cc was 60% at least, DRE estimates may be useful as a preliminary assessment when prostate size is an important predictor of treatment outcome [20]. In the present study we have determined the PSA value above which at least 60% of men have an enlarged PV. We found that in the range of 1.1–1.5 ng/ml this percentage was 52% and in the range of 1.6–2.0, 65%. We have therefore concluded that a PSA > 1.5 ng/ml can be used as a reasonable cut-off to identify men with an enlarged prostate (>30 cc).

We chose 30 cc as a cut-off value for dichotomisation of the PV because in clinical practice ≥30 cc is commonly described as an ''enlarged'' PV [21]. However, when choosing another cut-off point for dichotomisation, for example, 40 or 50 cc, the ROC

curves demonstrated similar results to those of >30 cc (curves not shown).

Although TRUS and the planimetric method of PV determination are the most accurate methods for estimating PV, the use of these techniques is limited by their feasibility, relatively high costs, invasiveness, and lack of availability. Evidence of a relationship between PSA and PV provides a simple test that can be used in routine practice to evaluate the risk of BPH progression in men from the general population. Therefore, serum PSA measurement can provide a relatively inexpensive and straightforward surrogate marker of prostate size, helping to identify those patients most at risk of BPH progression. DRE can be used as a clinical adjunct to PSA and is used as part of the screening process for prostate malignancy but does not add to the prediction of PV, not even in the setting of our study where DRE was systematically performed by experienced investigators. TRUS measurement remains the gold standard where absolute accuracy is of paramount importance.

A prediction of PV based on a formula containing PSA, age, DRE, and an interaction term between age and PSA is statistically significantly better than a prediction based on PSA alone. However, the clinical advantage as shown by the numerically marginal increase in the area under the ROC curve is modest.

In men aged 50–59, for a PV > 30 cc the PPV of a PSA cut-off value of 1.5 ng/ml was 70% in our study, but 83% in the study by Mochtar et al [22], who studied PVs in a population of 1859 men attending a urology clinic. The frequency distribution of PVs of the men in Mochtar et al study is compatible with a distribution found in men who are on average >10 yr older than the men in our study. This emphasises the importance of conducting these analyses in a community population. Furthermore, to achieve a PPV of about 83% in our study the PSA cut-off value should be 3.0 ng/ml.

Roehrborn et al [14] reported on the utility of PSA as a proxy for PV in a group of men that was composed of participants in placebo-controlled studies in men with BPH (n = 4548) and from a safety study in normal young men (n = 179). In men aged 50–59 yr the authors found a PPV of 70% for PV > 40 cc if PSA was >1.5 ng/ml. In the community-based population of men in our study the PPV was 32% for the same age range. To achieve a PPV of 70% in these men we would have to choose a PSA cut-off of 5.0 ng/ml. Differences between these studies in clinical men and our community study may be due to the selection of men with more symptoms, larger prostates, and higher PSA values in the clinical studies.

A 78% PPV of a PSA of ≥1.5 ng/ml in men 55–78 yr old is good considering the fact that the men in our study were not selected based on symptoms, but can be considered part of a community sample. Our cut-off value for PSA of 1.5 ng/ml is also in line with the Proscar Long-term Efficacy and Safety Study (PLESS) by Roehrborn et al that showed that a PSA of ≥1.4 ng/ml (a quarter of all their participants) predicts the long-term response of finasteride treatment in men with clinical BPH [23].

5. Conclusion

We conclude that PSA can be used to detect enlarged prostates. The use of serum PSA provides a practical approach for estimating PV that can be used in everyday clinical practice. It is more accurate than DRE and can be easily measured when TRUS is not available or practical. However, it should be stressed that the current population is free from PCa. In daily practice, the use of PSA as a proxy for PV should be restricted to men with a PSA < 4 and to men with a PSA ≥ 4 in whom PCa has been excluded. Based on our analysis the use of PSA as a proxy for PV is meaningful in almost all men who present for initial management with at least moderate symptoms in combination with bother.

Conflicts of interest

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Editorial Comment on: Serum Prostate-Specific Antigen as a Predictor of Prostate Volume in the Community: The Krimpen Study

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The authors [1] report a strong relationship between prostate-specific antigen (PSA) and prostate volume in a large community cohort in which prostate cancer was ruled out by the simple and elegant expedient of time. It has three direct implications for urology practice.

First, PSA can be used as a simple estimator of benign prostatic enlargement. A prostate volume >30–40 ml is recognised in the European Association of Urology (EAU) 2004 guidelines as an indication for 5α-reductase inhibitor treatment in moderate/severe lower urinary tract symptoms (LUTS) [2] and is shown here to be best predicted by PSA values >1.5 ng/ml (Fig. 1). A similar threshold (1.4 ng/ml) was reported in the Proscar Long-term Efficacy and Safety Study (PLESS) to be associated with an increased risk of acute urinary retention or BPH-related surgery [3], as further confirmed in the placebo arm of the Medical Therapy of Prostatic Symptoms (MTOPS) study in which prostate volume and PSA both predicted progression [4]. PSA as a proxy for prostate volume assessment will simplify the diffusion of BPH current guidelines from the urologist community toward community medicine.

Second, we must reckon that high PSA values can be encountered in a significant minority of patients without cancer (PSA > 4 ng/ml, 126 of 1525, 8% in the present series). This was recently illustrated in the placebo arm of the Prostate Cancer Prevention Trial where only a large minority of subjects with elevated PSA (4–6 ng/ml, 49%; >6 ng/ml, 43%) was found with positive protocol biopsies [5], giving way in combination with other relevant predictors (digital rectal examination, age, and family history of cancer) to an externally validated prostate cancer risk calculator [6]. Breaking the infracortical link between PSA and prostate

cancer and refining the indications of prostate biopsies in view of an elevated PSA would be no minor improvement.

Third, only a weak improvement in the prediction of prostate volume was found when age was introduced in the model. On the reverse, it shows that PSA is essentially related to prostate volume and not to age, contrary to the concept age-specific ranges for PSA [7].

As a whole, the present paper, albeit its somewhat demanding reading, is of direct relevance to the practicing urologist and the authors should be congratulated for that.

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