RESEARCH ARTICLE

Age, prostate volume, prostate-specific antigen and prostate-specific antigen density as predictor factors in results of transrectal ultrasonography-guided prostate biopsy [version 1; peer review: 1 approved with reservations]

Prima Ciko Ade Putra , Rainy Umbas, Agus Rizal Ardy Hariandy Hamid ,
Chaidir Arif Mochtar

Department of Urology, Faculty of Medicine Universitas Indonesia, Jakarta, 10430, Indonesia

V1 First published: 17 Jun 2019, 8:875
<https://doi.org/10.12688/f1000research.18892.1>
Latest published: 17 Jun 2019, 8:875
<https://doi.org/10.12688/f1000research.18892.1>

Abstract

Background: To identify the predictor factors, such as prostate-specific antigen (PSA), age, prostate volume (PV), and PSA density (PSAD) as indications to perform transrectal ultrasonography (TRUS)-guided prostate biopsy in reducing unnecessary biopsies and improving detection rate.

Methods: A total of 1232 samples were obtained from the medical records of patients underwent prostate biopsy from January 2008 to December 2013 in Cipto Mangunkusumo Hospital Jakarta. Pre-biopsy data including age, PSA, prostate volume, and PSAD were obtained. The Mann-Whitney U-test and unpaired t-test were conducted on the quantitative variables; a chi-square test was used for qualitative variables. This study also conducted receiver operating characteristic (ROC) curve analysis to determine the cut-off point and the optimum specificity and sensitivity for each variable.

Results: Among 1232 patients, 33.5% had a positive biopsy result. The median age and PSA (68 years and 57.45 ng/ml) in the positive biopsy group was higher than in the negative group (65 years and 11.69 ng/ml), $p < 0.001$. PSAD in patients with PSA 4-10 ng/ml, 10-20 ng/ml, and 20 ng/ml (0.20, 0.35, 2.05) in positive group was higher than negative group (0.14, 0.24, 0.53), $p < 0.001$. Those with a positive biopsy result had a lower median PV (42 ml (range, 13.8-208)) compared to those with negative biopsies (55.4 ml) ($p < 0.001$). In ROC curve, PSAD had the highest sensitivity and specificity (81.4% and 82.0%) with a cut-off point of 0.43 ng/ml/ml ($p < 0.001$).

Conclusion: The incidence of PCa increased with higher PSA level, older age and lower PV. Utilization of PSAD 0.17 ng/ml/ml as a cut-off point in patients with PSA level between 4-10 ng/ml is recommended to improve PCa detection in Indonesian men.

Open Peer Review

Approval Status ?

	1
version 1	?
17 Jun 2019	view
1. Sebastiaan Remmers , Erasmus Medical Center, Rotterdam, The Netherlands	
Monique Roobol , Erasmus Medical Center, Rotterdam, The Netherlands	
Any reports and responses or comments on the article can be found at the end of the article.	

Keywords

Age, prostate volume, prostate specific antigen, PSA density, prostate biopsy, TRUS

Corresponding author: Rainy Umbas (rainy.umbas@gmail.com)

Author roles: **Putra PCA:** Conceptualization, Data Curation, Investigation, Methodology, Validation, Writing – Original Draft Preparation; **Umbas R:** Conceptualization, Investigation, Methodology, Resources, Supervision, Writing – Review & Editing; **Hamid ARAH:** Conceptualization, Project Administration, Supervision, Visualization, Writing – Review & Editing; **Mochtar CA:** Conceptualization, Data Curation, Formal Analysis, Investigation, Supervision, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2019 Putra PCA *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Putra PCA, Umbas R, Hamid ARAH and Mochtar CA. **Age, prostate volume, prostate-specific antigen and prostate-specific antigen density as predictor factors in results of transrectal ultrasonography-guided prostate biopsy [version 1; peer review: 1 approved with reservations]** F1000Research 2019, 8:875 <https://doi.org/10.12688/f1000research.18892.1>

First published: 17 Jun 2019, 8:875 <https://doi.org/10.12688/f1000research.18892.1>

Introduction

Prostate cancer (PCa) is an important health issue worldwide because of its increasing incidence; it was reported that there are 1.1 million PCa patients worldwide in 2012¹. The incidence of PCa among Indonesian men was estimated to be 14.8 per 100,000 population and the mortality rate was reported as high as 9.8 per 100,000 population in 2012¹.

Transrectal ultrasonography (TRUS) guided biopsy plays an important role for PCa detection and has become a standard diagnostic method for PCa detection. It is recommended for men with elevated prostate specific antigen (PSA) levels or abnormal digital rectal examination (DRE). In Indonesia, 66.5% of PCa was diagnosed with TRUS-guided biopsy during 1994–2005 and 66.7% of them were found in advanced stage during this period^{2,3}. An appropriate and early detection are needed to detect PCa in its early stages for better treatment results, survival rates, and quality of life⁴.

The detection rate of prostate biopsy in several Asian countries varied between 14.6% and 26.5% in patients with PSA levels ranging from 2–20 ng/ml⁵. This widely used procedure for PCa remains controversial as it may lead to over-diagnosis (23%–42%) and over-treatment⁵. Both are related to unnecessary risk of urinary, sexual, and bowel dysfunction, which can affect patients' quality of life^{4,6}. Although TRUS-guided prostate biopsy is a safe procedure, there are still complications causing significant morbidity. The most common complications are mild hematuria (62%), rectal bleeding (2%), urinary tract infections (1.7%–11.3%), acute urinary retention (0.3%–2.6%), hematospermia (45.3%–50.4%), vasovagal response (2.8%), and hospitalization due to infection (1%–4.1%)^{7,8}. Systematic screening for prostate cancer by determining other factors besides PSA may assist prevention of this circumstance⁵.

The aim of this study was to identify the predictor factors such as PSA, age, prostate volume (PV), and PSA density (PSAD) as indications to perform TRUS guided prostate biopsy. Those variables are thought to be important predictors to reduce unnecessary biopsies and improve detection rate.

Methods

Data source

This retrospective study was approved by FKUI Research Ethical Committee before data collection began. We collected data pre-biopsy data, including age, PSA, prostate volume, and PSAD. These data were obtained from the medical records of patients that underwent prostate biopsy from January 2008 to December 2013 in Cipto Mangunkusumo Hospital, Jakarta, Indonesia. The inclusion criteria were patients with LUTS, PSA level >4 ng/ml, abnormal DRE, IPSS score >7, and age >45 years old, while the exclusion criteria were patients who underwent transperineal prostate biopsy or had been biopsied previously. The indications for prostate biopsy in our hospital were PSA level >4 ng/ml or abnormal DRE. All patients underwent 6–12-core biopsy using an 18-gauge needle with a spring-loaded biopsy gun (Bard Magnum). PV was calculated by

measuring height (H), width (W), and length (L) of the prostate on TRUS and the formula would be: $V = 0.52 \times H \times W \times L$. Collected data were further analyzed. Although this study was conducted in a single institution, we believe it is representative of Indonesian men because the samples are recruited from several provinces in Indonesia, since Cipto Mangunkusumo Hospital is a national referral hospital in Indonesia.

Statistical analysis

The study analysis was performed with SPSS version 20.0. We calculated the statistical analysis using Mann-Whitney test and unpaired t-test for the quantitative variables (age, PV, PSA and PSAD). In addition, Chi-square was used for statistical significance for qualitative variables. $P < 0.05$ was considered as a significant result. Receiver operating characteristic (ROC) curve analysis was also conducted to determine the cut-off point and the optimum specificity and sensitivity for each variable.

Results

Baseline characteristics

A total of 1232 patients who underwent prostate biopsy were retrospectively analyzed. Among those patients, 413 patients had positive biopsy results (diagnosed with PCa) and 819 patients had negative biopsy result (diagnosed with benign prostate hyperplasia (BPH) or prostatitis). The characteristics of patients in this study can be viewed in [Table 1](#).

Comparison between biopsy groups

Compared to the negative biopsy group, the positive biopsy group had lower median PV, while serum PSA level and age in positive biopsy group was higher than negative biopsy group ([Table 1](#)). The mean PSAD in positive biopsy result group was higher than negative biopsy results, except PSAD in patients with PSA <4 ng/ml ([Table 1](#)).

Bivariate analysis using the Mann-Whitney U-test showed that age ($p < 0.001$), PSA ($p < 0.001$), PV ($p < 0.001$), and PSAD in patients with PSA 4–10 ng/ml ($p < 0.001$), 10–20 ng/ml ($p < 0.001$), and >20 ng/ml ($p < 0.001$) group had statistical significance differences. However, PSAD in patients with PSA <4 ng/ml ($p = 0.368$) showed no statistically significant difference using unpaired t-test.

According to the age groups, we classified them into three groups based on previous study⁹. As shown in [Table 2](#), those aged >70 years (43.4%) had the highest detection rate. In addition, the positive biopsy rate in patients with PSA >20 ng/ml was 57.2 %. Prostate volume <60 ml had higher detection rate (41.8%) compared to PV >60 ml which only has 18.2% ([Table 2](#)).

ROC analysis

The ROC curve demonstrated that PSAD was the best predictor factor among those variables (age, PSA, and PV) in TRUS-guided prostate biopsy ([Figure 1](#) and [Table 3](#)). The area under the curve (AUC) for PSAD (84.5%) and PSA (78.7%), while the AUC for PV and age were 62.4% and 61.2%, respectively. PSAD and PSA were thus considered better predictors for

Table 1. Patient characteristics and biopsy results. Negative biopsy results were diagnosed as benign prostate hyperplasia and/or prostatitis while positive biopsy results were diagnosed as prostate adenocarcinoma.

Variables	Total	Positive biopsy result	Negative biopsy result	P-value
Total patients, n (%)	1232	413 (33.5)	819 (66.5)	
Age (in years)	1232	68 (35-89) [#]	65 (40-83) [#]	<0.001
PSA (ng/ml)	1232	57.45 (0.8-7740) [#]	11.69 (0.82-126.08) [#]	<0.001
PV (ml)	1232	42 (13.8-208) [#]	55.4 (13.38-186) [#]	<0.001
PSAD of PSA < 4 ng/ml (ng/ml/ml)	24	0.06±0.05 [†]	0.07±0.03 [†]	0.368
PSAD of PSA 4–10 ng/ml (ng/ml/ml)	367	0.20 (0.08-0.64) [#]	0.14 (0.04-0.39) [#]	<0.001
PSAD of PSA 10–20 ng/ml (ng/ml/ml)	339	0.35 (0.09-1.22) [#]	0.24 (0.09-0.72) [#]	<0.001
PSAD of PSA > 20 ng/ml (ng/ml/ml)	502	2.05 (0.22-188.78) [#]	0.53 (0.13-4.61) [#]	<0.001

PSA, prostate-specific antigen; PV, prostate volume; PSAD, PSA density. [#]Values presented are median (range); [†]values presented are mean ± standard deviation.

Table 2. Bivariate analysis of factors associated with prostate cancer. Negative biopsy results were diagnosed as benign prostate hyperplasia and/or prostatitis while positive biopsy results were diagnosed as prostate adenocarcinoma.

Variables	Positive biopsy result, n (%)	Negative biopsy result, n (%)	P value
Age groups (years)			<0.001*
<60	178 (76.7)	54 (23.3%)	
60–70	430 (68.6)	197 (31.4%)	
>70	211 (56.6)	162 (43.4%)	
Prostate volume (ml)			<0.001*
<60	465 (58.2%)	334 (41.8%)	
≥60	354 (81.8%)	79 (18.2%)	
PSA groups (ng/ml)			<0.001*
<4	15 (62.5%)	9 (37.5%)	
4–10	319 (86.9%)	48 (13.1%)	
10–20	270 (79.6%)	69 (20.4%)	
>20	215 (42.8%)	287 (57.2%)	

PSA, prostate-specific antigen.

identifying PCa than PV and age. This study also conducted ROC curve analysis for PSAD in stratified PSA level (Table 3).

The optimal cut-off point of PSAD in the PSA group of 4–10 ng/ml was 0.17 ng/ml and its sensitivity and specificity were 75% and 66.5%, respectively. The cut-off point of PSA level was 32.5 ng/ml, giving a sensitivity and specificity for PSA of 62.0% and 87.1%, respectively. Prostate volume and age had lower optimum sensitivity and specificity compared to PSAD and PSA. (Table 3) This study divided PSAD variables into four groups based on PSA level (Table 3).

Discussion

Rashid *et al.* stated that TRUS-guided biopsy is recommended as the procedure of choice for early detection of PCa. Even though the elevation of PSA and the presence of an abnormal DRE are associated with PCa, those kind of examinations are not appropriate as a standard predictor⁹.

In our study, 33.5% of the 1,232 patients examined had prostate cancer based on the biopsy result of histopathology examination. The overall detection rate (33.5%) of PCa in this study was much lower than in Pakistan (50.3%)¹⁰. Na *et al.*

Figure 1. Receiver operating characteristic curve for (A) prostate-specific antigen (PSA), PSA density (PSAD), and age, and (B) prostate volume.

Table 3. Sensitivity, specificity, and cut-off point of each variable.

Variables	AUC	Cut-off point	Sensitivity (%)	Specificity (%)	P value	95% CI (%)	
						Lower	Upper
PSA	0.787	32.5 ng/ml	62.0	87.1	<0.001	75.7	81.7
PV	0.674	52.3 ml	55.2	75.5	<0.001	64.3	70.6
PSAD	0.845	0.43 ng/ml/ml	81.4	82.0	<0.001	82.0	87.0
Age	0.607	63.5 years	73.1	57.1	<0.001	57.4	64.0
PSAD of PSA group							
PSAD° of PSA <4 ng/ml	0.311	0.07 ng/ml/ml	33.0	67.0	0.128	5.0	57.2
PSAD° of PSA 4-10 ng/ml	0.737	0.17 ng/ml/ml	75.0	66.5	<0.001	65.8	81.5
PSAD° of PSA 10-20 ng/ml	0.741	0.33 ng/ml/ml	62.3	78.1	<0.001	67.2	81.0
PSAD° of PSA >20 ng/ml	0.881	1.00 ng/ml/ml	81.9	78.6	<0.001	85.2	91.0
PSA age specific							
PSA of age <60 years old	0.753	45.50 ng/ml	55.6	94.4	<0.001	66.8	83.7
PSA of age 60–70 years old	0.768	32.63 ng/ml	61.9	87.0	<0.001	74.5	83.0
PSA of age >70 years old	0.802	43.50 ng/ml	64.6	86.3	<0.001	76.6	83.7

AUC, area under the curve; PSA, prostate-specific antigen; PV, prostate volume; PSAD, PSA density.

and Presti *et al.* also showed differences compared to earlier Chinese and American studies; they reported that the detection rates were 47% and 42%, respectively^{11,12}.

The same results in positive biopsy rate are also found in other studies (Table 4). In Pakistan, Rashid *et al.* showed that 48.8%

of patients performing TRUS guided biopsy were detected as PCa⁹. In India, Prakash *et al.* found that 35.2% of PCa were diagnosed from prostate biopsy¹³. Tang *et al.* in China revealed that 36.4% of patients were positive for PCa after performing prostate biopsy, but this study only investigated PSA levels ranging from 10–50 ng/ml¹⁴. Study from Germany had a lower detection rate

Table 4. Comparison detection rate of positive prostate biopsy in other countries.

Study	Country	Total patient	PSA level	Number of cores	Detection rate
Rashid R, <i>et al.</i> (2013) ⁸	Pakistan	203	All PSA level	8 cores	48.8%
Kash P, <i>et al.</i> (2014) ⁹	Pakistan	300	All PSA level	8 cores	50.3%
Na R, <i>et al.</i> (2012) ¹⁰	China	1650	All PSA level	≥10 cores	47%
Presti JC, <i>et al.</i> (2000) ¹¹	USA	202	All PSA level	6–10 cores	42%
Prakash VS, <i>et al.</i> (2013) ¹²	India	96	All PSA level	10–16 cores	35.2%
Luboldt HJ, <i>et al.</i> (2001) ¹⁴	Germany	1115	All PSA level	< 6 and ≥6 cores	23.5%
This study	Indonesia	1232	All PSA level	6–12 cores	33.5%

PSA, prostate-specific antigen.

than current study, at only 23.5%¹⁵. The low detection rate in this study could be caused by inadequate sampling. In larger prostate volumes, the possibility of error sampling is higher than in smaller prostate volume. Hence, the number of cores should be adjusted based on the prostate volume.

In this study, the median age of PCa patients is 68 years old (range from 35–89 years) and those who were >70 years had the highest positive biopsy rate. This result is supported by other studies in Indonesia and Pakistan^{2,10,16}. Umbas *et al.* revealed that patients with PCa in Indonesia were predominantly those >70 years during 1995–2004². In addition, Ariani *et al.* also reported that the overall age of the PCa patients in their study was 67.12 years¹⁶. The previous two studies mentioned that the rate in Indonesia was not significantly different compared to studies conducted in Nepal Senegal, Pakistan and Taiwan (63.6, 65.5, 65.7, and 67.7 years, respectively)^{9,17–19}. However, other studies from China (Na *et al.* and Wu *et al.*) showed a slightly higher overall age compared to the current study, with mean ages of 71.24 and 73.4 years, respectively^{11,20}. In addition, the mean age of a group in Korea was found to be lower (63.8 years old) than that in the current study, but its result cannot be compared because the study use tPSA level less than 10 ng/ml²¹.

Age is one of many risk factors affecting PCa because the incidence of the disease increases along with aging. Prostate cancer is mostly (in about 75% of cases) diagnosed after 65 years of age. There only 2% of all PCa cases were diagnosed in males <50 years¹⁹.

The highest positive biopsy rate in PSA group within this study belongs to patients with PSA values >20 ng/ml. This result suggests that severe elevation of PSA will increase the probability of PCa. Prakash *et al.* and Rashid *et al.* showed that 73.8–74.6% of patients with PSA >20 ng/ml that underwent TRUS-guided biopsy were diagnosed with PCa^{10,13}. Another study by Barakazi *et al.* revealed a similar result to the current study²².

This study shows that patients with PSA level 4–10 ng/ml and 10–20 ng/ml had lower detection rate compared to those with PSA level below 4 ng/ml. Prakash *et al.* also generated similar results to those of our study, showing that PCa in patients

with PSA level <4 ng/ml was could be detected more easily compared to patients with PSA levels of 4–10 ng/ml and 10–20 ng/ml, with the addition of DRE examination¹³. These results suggested that DRE may still have an important role in assisting or predicting PCa in suspicious patients²³. Previous studies conducted in Taiwan and The Netherlands also revealed that DRE is an independent predictor of PCa^{19,24}.

In this study, the lowest detection rate of PCa is in those with a PSA level of 4–10 ng/ml. Therefore, PSA alone is not an effective screening method to diagnose PCa. PSA level alone could cause the high rate of false positive or negative biopsy rate in patients that underwent TRUS-guided prostate biopsy. PSA is a protein produced by the prostatic epithelium. It is organ-specific, but not cancer-specific. PSA can be manipulated by other disorders of the prostate, such as prostatitis, urinary retention, and BPH. Research into a large population regarding PSA screening in ERSPC revealed that PSA screening was able to reduce a number of 20% mortality in patients with PCa. Another study reported that PSA had no benefit in reducing mortality in PCa. PSA alone is not optimal to determine the risk of PCa¹¹. Other factors such as DRE, TRUS to asses PV, and PSAD must be considered when performing prostate biopsy²⁴.

The role of PV as a predictor factor is still being debated. In this study, the mean PV in patients with PCa is much lower than in those with negative biopsy results. A previous study in Indonesia conducted by Ariani *et al.* produced the same result as our study¹⁶. The study revealed that the incidence of PCa increased with decreasing PV¹⁶. Wu *et al.* reported that lower PV was able to indicate a higher risk of PCa detection²⁰. Tang *et al.* reported that decreasing PV was associated with higher risk of PCa in patient undergoing TRUS biopsy¹⁴. The high rate of negative biopsies resulting due to larger PV might be due to more sampling errors in TRUS biopsy. Therefore, assessing more cores from larger prostates could increase detection rate and reduce bias^{5,14,25}. Pietzak *et al.* revealed that patients with larger PV (50 ml) who had prior negative biopsy require multiple biopsies to increase the chance of gaining a positive biopsy²⁶.

This study revealed that PSAD had the best predictor in detecting PCa. A study from China showed a similar ROC cut-off

point (0.2 ng/ml/ml) and AUC (0.664) in intermediate PSA level (4–10 ng/ml) to this study²⁷. The previous study in Indonesia also reported that the optimum cut-off point was 0.19 in patients with an intermediate PSA level²⁸. The cut-off point of PSAD is similar in our study and is higher compared to the reference values of Western countries (0.15 ng/ml/ml) for prostate biopsy²⁹. This examination could be used to reduce unnecessary biopsy because the specificity of PSAD was much higher than specificity of PSA level 4 ng/ml (as indicated for prostate biopsy) in this study.

The limitation of our study is that the TRUS-guided biopsy is of limited value. It can only show small number of malignancies. The use of contrast agent combined with TRUS-guided prostate biopsy can increase the accuracy of prostate cancer diagnosis²⁹. We also noticed that according to Prakash *et al.*, the number of core biopsies have to be increased up to 16 cores in order to significantly increase the rate of prostate cancer detection¹³.

Another limitation of this study is that it is a retrospective study conducted in a single institution. In this study, PSA level was not defined adequately, therefore the cut-off point and

mean variables were difficult to obtain. Although this study is conducted in a single institution, it can represent the races from Indonesian men because the samples are recruited from several provinces in Indonesia.

Conclusion

In conclusion, the overall detection rate of PCa by biopsy in our study is 33.5%, much lower than other countries in Asia. The incidence of PCa increased with higher PSA level, older age and lower PV. Utilization of PSAD 0.17 ng/ml/ml as a cut-off point in patients with PSA level between 4–10 ng/ml is recommended to improve PCa detection in Indonesian men.

Data availability

Underlying data

Harvard Dataverse Repository: Final Data Biopsy RSCM 2008–2013. <https://doi.org/10.7910/DVN/JNNECM30>.

Grant information

The author(s) declared that no grants were involved in supporting this work.

References

1. Ferlay J, Soerjomataram I, Ervik M, *et al.*: **Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11**. [Internet] Lyon, France: International Agency for Research on Cancer; 2012; [cited 2013 1Sept 2014]. [Reference Source](#)
2. Umbas R: **Characteristics and management of prostate cancer in Jakarta over ten years period**. *Ind J Surgery*. 2005; 33(4): 107–14.
3. Umbas R, Mochtar C, Rahardjo H: **Current Status of Prostate Cancer in Asia**. *Indonesian Journal of Cancer*. 2011; 5(1): 21–4. [Reference Source](#)
4. Hoffman RM: **Clinical practice. Screening for prostate cancer**. *N Engl J Med*. 2011; 365(21): 2013–9. [PubMed Abstract](#) | [Publisher Full Text](#)
5. Teo JK, Poh BK, Ng FC, *et al.*: **Detection rate of prostate cancer on the basis of the vienna nomogram: a singapore study**. *Korean J Urol*. 2014; 55(4): 245–8. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
6. Draisma G, Etzioni R, Tsodikov A, *et al.*: **Lead time and overdiagnosis in prostate-specific antigen screening: importance of methods and context**. *J Natl Cancer Inst*. 2009; 101(6): 374–83. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
7. Lundström KJ, Drevin L, Carlsson S, *et al.*: **Nationwide population based study of infections after transrectal ultrasound guided prostate biopsy**. *J Urol*. 2014; 192(4): 1116–22. [PubMed Abstract](#) | [Publisher Full Text](#)
8. Anastasiadis A, Zapala L, Cordeiro E, *et al.*: **Complications of prostate biopsy**. *Expert Rev Anticancer Ther*. 2013; 13(7): 829–37. [PubMed Abstract](#) | [Publisher Full Text](#)
9. Rashid R, Mubarak M, Kazi J: **Frequency of Adenocarcinoma in Transrectal Ultrasound-guided Prostate Needle Biopsies in Men with clinical suspicion of Prostate Cancer and Raised Serum Prostate Specific Antigen**. *Middle East J Cancer*. 2013; 4(2): 73–8. [Reference Source](#)
10. Kash DP, Lal M, Hashmi AH, *et al.*: **Utility of digital rectal examination, serum prostate specific antigen, and transrectal ultrasound in the detection of prostate cancer: a developing country perspective**. *Asian Pac J Cancer Prev*. 2014; 15(7): 3087–91. [PubMed Abstract](#) | [Publisher Full Text](#)
11. Na R, Jiang H, Kim ST, *et al.*: **Outcomes and trends of prostate biopsy for prostate cancer in Chinese men from 2003 to 2011**. *PLoS One*. 2012; 7(11): e49914. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
12. Presti JC Jr, Chang JJ, Bhargava V, *et al.*: **The optimal systematic prostate biopsy scheme should include 8 rather than 6 biopsies: results of a prospective clinical trial**. *J Urol*. 2000; 163(1): 163–6; discussion 166–7. [PubMed Abstract](#) | [Publisher Full Text](#)
13. Prakash VS, Mohan GC, Krishnaiah SV, *et al.*: **Ten-core versus 16-core transrectal ultrasonography guided prostate biopsy for detection of prostatic carcinoma: a prospective comparative study in Indian population**. *Prostate Int*. 2013; 1(4): 163–168. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
14. Tang P, Jin XL, Uhlman M, *et al.*: **Prostate volume as an independent predictor of prostate cancer in men with PSA of 10-50 ng ml⁻¹**. *Asian J Androl*. 2013; 15(3): 409–12. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
15. Luboldt HJ, Bex A, Swoboda A, *et al.*: **Early detection of prostate cancer in Germany: a study using digital rectal examination and 4.0 ng/ml prostate-specific antigen as cutoff**. *Eur Urol*. 2001; 39(2): 131–7. [PubMed Abstract](#) | [Publisher Full Text](#)
16. Ariani D, Umbas R: **The Role of Prostate Volume and Serum PSA for Detecting Prostate Cancer in LUTS Patients with Normal DRE**. *Indonesian Journal of Cancer*. 2011; 5(2): 88–93.
17. Belbase NP, Agrawal CS, Pokharel PK, *et al.*: **Prostate cancer screening in a healthy population cohort in eastern Nepal: an explanatory trial study**. *Asian Pac J Cancer Prev*. 2013; 14(5): 2835–8. [PubMed Abstract](#) | [Publisher Full Text](#)
18. Niang L, Kouka CN, Jalloh M, *et al.*: **Screening for Prostate Cancer by Digital Rectal Examination and PSA Determination in Senegal**. *ISRN Oncol*. 2011; 2011: 943704. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
19. Wang JC, Huan SK, Kuo JR, *et al.*: **A multivariable logistic regression equation to evaluate prostate cancer**. *J Formos Med Assoc*. 2011; 110(11): 695–700. [PubMed Abstract](#) | [Publisher Full Text](#)
20. Wu YS, Na R, Xu JF, *et al.*: **The influence of prostate volume on cancer detection in the Chinese population**. *Asian J Androl*. 2014; 16(3): 482–6. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
21. Ahn JH, Lee JZ, Chung MK, *et al.*: **Nomogram for prediction of prostate cancer with serum prostate specific antigen less than 10 ng/mL**. *J Korean Med Sci*. 2014; 29(3): 338–42. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
22. Barakzai M, Mubarak M, Kazi J: **Histopathological lesions in transrectal ultrasound guided biopsies of prostate in patients with raised serum prostate**

specific antigen: A preliminary report. *Nephro-Urol Mon.* 2011; 3(3): 186–90.
Reference Source

23. Gosselaar C, Roobol MJ, Roemeling S, *et al.*: **The role of the digital rectal examination in subsequent screening visits in the European randomized study of screening for prostate cancer (ERSPC), Rotterdam.** *Eur Urol.* 2008; 54(3): 581–8.
PubMed Abstract | Publisher Full Text
24. Roobol MJ, van Vugt HA, Loeb S, *et al.*: **Prediction of prostate cancer risk: the role of prostate volume and digital rectal examination in the ERSPC risk calculators.** *Eur Urol.* 2012; 61(3): 577–83.
PubMed Abstract | Publisher Full Text
25. Basillote JB, Armenakas NA, Hochberg DA, *et al.*: **Influence of prostate volume in the detection of prostate cancer.** *Urology.* 2003; 61(1): 167–71.
PubMed Abstract | Publisher Full Text
26. Pietzak EJ 3rd, Kabarriti AE, Mucksavage P, *et al.*: **The presence of high-grade prostatic intraepithelial neoplasia or atypia on prostate biopsy does not adversely affect prostatectomy outcomes for patients otherwise eligible for active surveillance.** *Urology.* 2014; 84(6): 1442–7.
PubMed Abstract | Publisher Full Text
27. Zhao R, Huang Y, Cheng G, *et al.*: **Developing a follow-up strategy for patients with PSA ranging from 4 to 10 ng/ml via a new model to reduce unnecessary prostate biopsies.** *PLoS One.* 2014; 9(9): e106933.
PubMed Abstract | Publisher Full Text | Free Full Text
28. Mochtar CA, Rahardjo D, Umbas R: **A higher PSA-density cut-off level in patients with intermediate PSA values for the early detection of prostate cancer.** *Gan To Kagaku Ryoho.* 2000; 27 Suppl 2: 514–22.
PubMed Abstract
29. Hwang SI, Lee HJ: **The future perspectives in transrectal prostate ultrasound guided biopsy.** *Prostate Int.* 2014; 2(4): 153–160.
PubMed Abstract | Publisher Full Text | Free Full Text
30. Putra PCA: **Final Data Biopsy RSCM 2008-2013.** Harvard Dataverse, V2. 2019. <http://www.doi.org/10.7910/DVN/JNNECM>

Open Peer Review

Current Peer Review Status: ?

Version 1

Reviewer Report 04 July 2019

<https://doi.org/10.5256/f1000research.20706.r50755>

© 2019 Roobol M et al. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Sebastiaan Remmers

Erasmus Medical Center, Rotterdam, The Netherlands

Monique Roobol

Department of Urology, Erasmus Medical Center, Rotterdam, The Netherlands

This paper evaluates predictors for a positive systematic biopsy. These predictors included PSA, age, prostate volume, and PSA density (PSAD). The authors concluded that PSAD was the best predictor for a positive biopsy based on ROC analysis.

The authors have done great work by including 1232 patients. The manuscript is nicely written. There are some considerations before accepting this manuscript for indexing:

- Why are men with normal DRE not included? If you only include men with abnormal DRE you will make a high risk cohort and you will miss tumour located on the ventral side of the prostate.
- In the method section, the authors describe that inclusion criteria were age >45 years and PSA >4 ng/ml. However, in Table 1 the range for men with positive biopsy was 35-89 and for men with negative biopsy 40-83. In addition, the range of PSA is 0.8 – 7740 ng/ml. A more proper way of reporting is by providing the median and the interquartile range.
- Figure 1 is composed of a section A and B. However, I do not see the added value of separating prostate volume from the rest of the predictors.
- The methodology is not sufficient to conclude that PSAD is the best predictor. Multiple testing will lead to biased results. The best methodology is to make a logistic model in which age and PSAD are used as predictor. Since PSA and prostate volume are combined into PSAD, it is not recommended to use both PSAD, and PSA and prostate volume in one model. On the basis of this model, it is possible to calculate an AUC and to make an individual prediction for a men.

Before an accurate message can be given, it is first important to take the previous considerations into account. The results of an Indonesian cohort will be of interest for both researchers and urologists.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

No

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Prostate cancer research; statistical methodology

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research