Prostate Int 4 (2016) 43–48

Contents lists available at ScienceDirect

Prostate International

journal homepage: http://p-international.com

Original Article

Relationship of age, prostate-specific antigen, and prostate volume in Indonesian men with benign prostatic hyperplasia

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ARTICLE INFO

Article history:
Received 22 August 2015
Received in revised form
4 March 2016
Accepted 7 March 2016
Available online 11 March 2016

Keywords:
Age
Benign prostatic hyperplasia
Indonesian men
Prostate specific antigen
Prostate volume

ABSTRACT

Background: To investigate the relationship between age, prostate specific antigen (PSA), and prostate volume (PV) in Indonesian men with histologically proven benign prostatic hyperplasia.
Methods: Data were generated from our BPH database from June 1994 until December 2013. Subjects were men with a minimum age of 40 years with chief complaint of LUTS or urinary retention, diagnosed with BPH. All patients underwent TRUS-guided prostate biopsy. Patients with PSA level >10 ng/mL were excluded from the study to exclude the possibility of occult prostate cancer. PV was measured with TRUS. Appropriate statistical tests were employed for data analysis.
Results: In all, 1638 patients were enrolled in our study. There was a statistically significant difference in PSA ($P = 0.03$) and PV ($P < 0.0001$) between age groups. Overall correlation between age, PSA, and PV were: i). Age and PV ($r = 0.12$, $P < 0.0001$); ii). Age and PSA ($r = 0.07$, $P = 0.008$); iii). PSA and PV ($r = 0.26$, $P < 0.0001$). Subgroup analysis in terms of indwelling catheter use versus without: i). Age 66.09 ± 8 years versus 65.38 ± 7.66 years ($P = 0.158$); ii). PSA 4.93 ± 2.62 ng/mL versus 4.68 ± 2.82 ng/mL ($P = 0.038$); iii). PV 47.58 ± 21.33 mL versus 41.43 ± 20.55 mL ($P < 0.0001$). Correlation between age, PSA, and PV in patients were similar in patients with and without indwelling catheter.
Conclusion: In Indonesian men with biopsy-proven BPH, both PV and PSA increased with ageing. Prostate volume was significantly correlated with PSA. Even though the results were weaker, these results are consistent with results in other sets of population. The results vary between different countries and thus, ethnicities. Indonesia is a populous a sociocultural and ethnically diverse country. Therefore, aside from PSA, age, and PV, when investigating men with BPH, ethnicity may also need to be taken into account.

1. Introduction

Benign prostatic hyperplasia (BPH) is a common progressive disease in the male aging population.[1] Although aging and androgens are established risk factors, the cause of BPH remains uncertain.[2,3] Several mechanisms were hypothesized to be involved in the progression of BPH including hormonal or vascular alterations, inflammation, epithelial/stromal interactions, and luminal/epithelial cell interactions.[2,3]

In the aging male, there is significant tissue remodeling taking place within the prostate. It was postulated that prostate growth is the result of a disturbed balance between apoptotic and proliferative activities with a net reduction in apoptotic activity. Histologic analysis showed a decreased apoptotic activity in glandular and basal epithelial cells of the prostate.[2–4] Thus, with increasing age there is a tendency of increasing prostate volume (PV).

Prostate-specific antigen (PSA) is a widely used tumor marker for prostate cancer.[5,6] Although it is well known that PSA is prostate specific, it is not a disease-specific biomarker. Several studies have examined the relationship between PSA and PV.[5,7–9] These studies consistently showed a positive correlation between PSA level and PV. However, these results were derived from Western and East Asian populations, and thus may not accurately reflect the conditions in an Indonesian population. Differences in ethnicity and geographical factors may exert differences in BPH characteristics in men.[10,11] The exact relationship between age, serum PSA, and PV in Indonesian men with histologically proven BPH has yet to be established. Thus, the aim of this study was to investigate the

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http://dx.doi.org/10.1016/j.prnil.2016.03.002

Table 1 Characteristics of 1638 patients.

Age (y)	65.67 ± 7.81
Age group (y)	
≤ 60	448 (27.4)
61–69	664 (40.5)
≥ 70	526 (32.1)
PSA (ng/mL)	4.78 ± 2.74
	0.02–10
PV (mL)	43.93 ± 21.08
	3–174
Indwelling catheter	
Yes	666 (40.7)
No	972 (59.3)

Data are presented as *n* (%) or mean ± SD.
PSA, prostate-specific antigen; PV, prostate volume.

relationship between age, PSA level, and PV in Indonesian men with histologically proven BPH.

2. Materials and methods

Data were generated from our BPH database from June 1994 until December 2013. These involved patients whose chief complaint was lower urinary tract symptoms or urinary retention who visited the Department of Urology of the "Cipto-Mangunkusumo" Hospital. The inclusion criteria were a minimum age of 40 years and a diagnosis of BPH (histopathologically proven). Patients with indwelling catheter were those with a history of urinary retention who failed trial without catheter with α blocker. All patients underwent standard clinical evaluation and PSA testing. Indication for prostate biopsy in our department was a PSA value of greater than or equal to 4 ng/mL or abnormal findings in digital rectal examination. Core biopsy was done with an 18-gauge needle, TRUS guided, using a spring-loaded biopsy gun (Bard Magnum). Our patients underwent a 6- to 12-core biopsy. Those patients with biopsy results of prostate cancer, atypical acinus, atypical small acinar proliferation, atypical adenomatous hyperplasia, and prostatic intraepithelial neoplasia were excluded from the study. Those who consumed 5α-reductase inhibitors and those with a PSA level of greater than 10 ng/mL (in order to avoid the possibility of occult prostate cancer) were also excluded from the study.

Patients were divided into three age groups: 60 years of age or younger, between 61 and 69 years of age, and 70 years of age and older. Based on the measurements obtained using TRUS, PV was calculated using the following formula: PV = height × width × length × 0.52. PV was categorized into Less than 30 mL, 31–40 mL, 41–50 mL, 51–100 mL, and greater than 100 mL.[12]

Descriptive statistics were used to characterize all variables. Prior to statistical analysis, numerical data were log-transformed for normalization. One-way analysis of variance (ANOVA) test and independent *t* test were used to analyze the differences in numerical data (age, PV, and PSA) among the different age groups and catheter use groups. Pearson's test for correlation was used to analyze the linear correlation between age, PSA, and PV. A *P* value of less than 0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics (IBM Corp., New York, United States; www.ibm.com/SPSS_Statistics) version 20.

3. Results

A total of 1,638 patients were included in our study. The characteristics of these patients are presented in Table 1. The median (range) PSA and PV in age groups ≤ 60 years, 61–69 years, and ≥ 70 years were 4.29 (0.1–9.93) ng/mL and 30.68 (3–141.29) mL, 4.61 (0.07–10) ng/mL and 38.92 (11.4–149) mL, and 4.8 (0.02–10) ng/mL and 40.48 (3–174) mL, respectively. There was a statistically significant difference in PSA ($P = 0.03$, one-way ANOVA test) and PV ($P < 0.001$, one-way ANOVA test) between age groups. These results are illustrated in Figs. 1A and 1B.

PSA was < 4 ng/mL in 715 (43.65%) patients. PV was ≤ 30 mL in 436 (26.6%) patients, 31–40 mL in 442 (27%), 41–50 mL in 296 (18.1%), 51–100 mL in 430 (26.3%), and > 100 mL in 34 (2.1%).

The correlation between age, PSA, and PV are illustrated in Fig. 2. The results of the subgroup analysis based on indwelling catheter use are presented in Table 2. The correlation between age, PSA, and PV in patients with and without indwelling catheter is illustrated in Fig. 3.

4. Discussion

BPH is age-related, and the prevalence increases with increasing age.[13,14] Among many factors that contribute to prostate

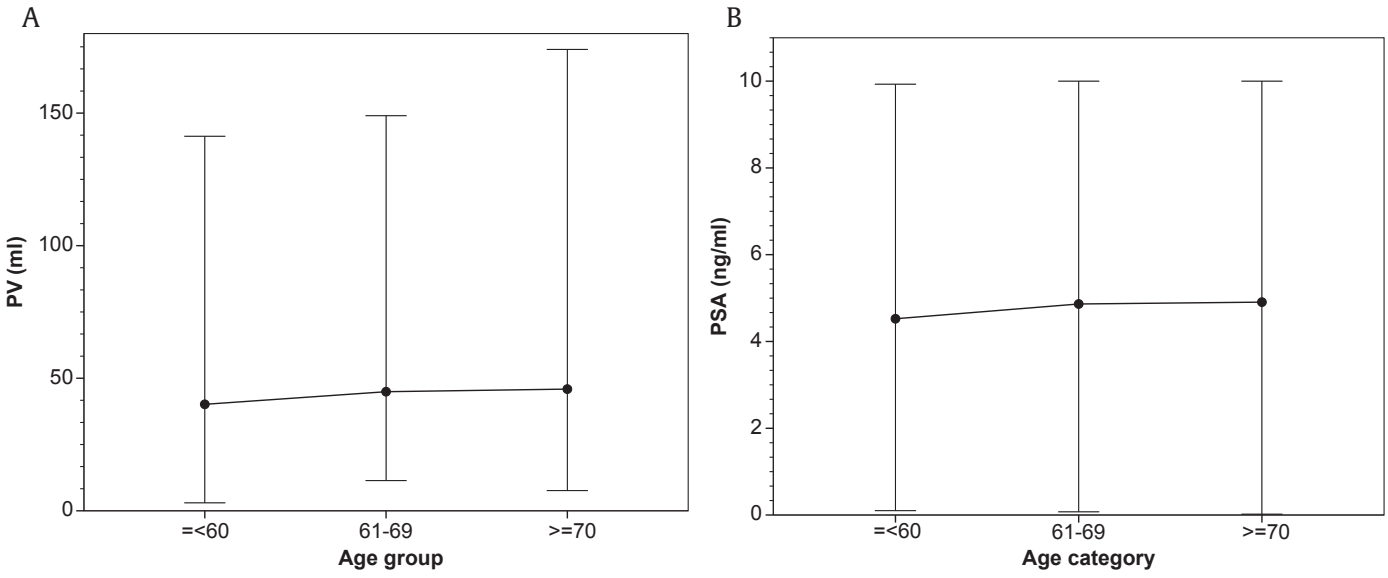

Fig. 1. Median and range values, by age group. (A) Prostate volume (PV). (B) Prostate-specific antigen (PSA).

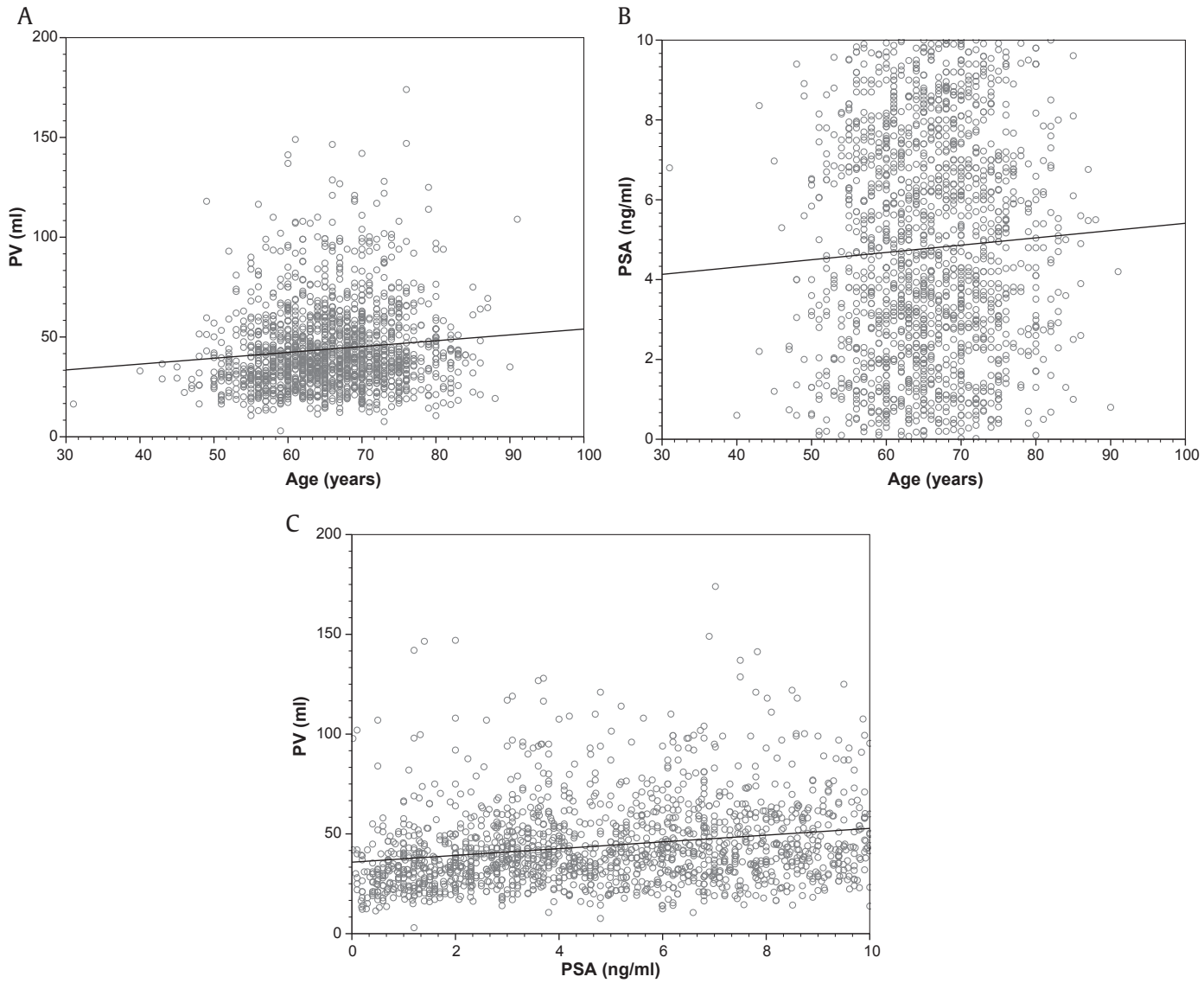

Fig. 2. Pearson's correlation coefficient. (A) Between age and PV ($r = 0.12$, $P < 0.001$). (B) Between age and PSA ($r = 0.07$, $P = 0.008$). (C) Between PSA and PV ($r = 0.26$, $P < 0.001$). PSA, prostate-specific antigen; PV, prostate volume.

enlargement in BPH, the two most well-known etiologic factors were aging and androgen.[3] Consistent with the theory that aging is an etiologic factor of BPH, our results showed a trend of increasing median PV with advancing age, with the highest PV recorded in the ≥ 70 years group and the lowest PV in the ≤ 60 years group. This increasing PV with aging is accompanied with an increasing trend of PSA with age. This result is consistent with studies in Indian, South Korean, Taiwanese, and Swedish populations (Table 3).[15–19] The correlation between age and PV in our study is the weakest ($r = 0.12$, $P < 0.001$). Consistent with results from other studies, PSA was positively correlated with age in our study. However, the correlation is the weakest ($r = 0.07$, $P < 0.008$) (Table 4) compared with results from other studies.[15–17] PSA has been suggested as an estimator for PV.[7,20,21] This is supported by the fact that prostate epithelial cells are responsible for circulating PSA, and several studies had documented a positive correlation between PSA and PV.[8,17,22,23] Hochberg et al[8] reported a correlation coefficient of 0.33–0.41 in a series of white patients. Studies in Japanese, South Korean, and Indian patients showed a positive significant correlation coefficient between PSA and PV of 0.65, 0.41, and 0.78, respectively.[15,17,23] Our study showed a similar but weaker correlation with a correlation coefficient of 0.26 ($P < 0.001$). The corresponding studies had a similar study design. The difference between the degree of correlation of age with PV and age with PSA is probably attributable to the ethnic or geographical factors that may influence prostatic growth.[10,11]

Table 2 Subgroup analysis based on catheter usage.

Variable	Indwelling catheter		*P*
	Yes	No	
Overall (y)	666 (40.7)	972 (59.3)	–
≤ 60	171 (10.4)	277 (16.9)	–
61–69	267 (16.3)	397 (24.2)	–
≥ 70	228 (13.9)	298 (18.2)	–
Age (y)	66.09 ± 8	65.38 ± 7.66	0.158 [a)]
PSA (ng/mL)	4.93 ± 2.62	4.68 ± 2.82	0.038 [a)]
PV (mL)	47.58 ± 21.33	41.43 ± 20.55	< 0.001 [a)]

[a)] Independent *t* test.
Data are presented as *n* (%) or mean ± SD.
PSA, prostate-specific antigen; PV, prostate volume.

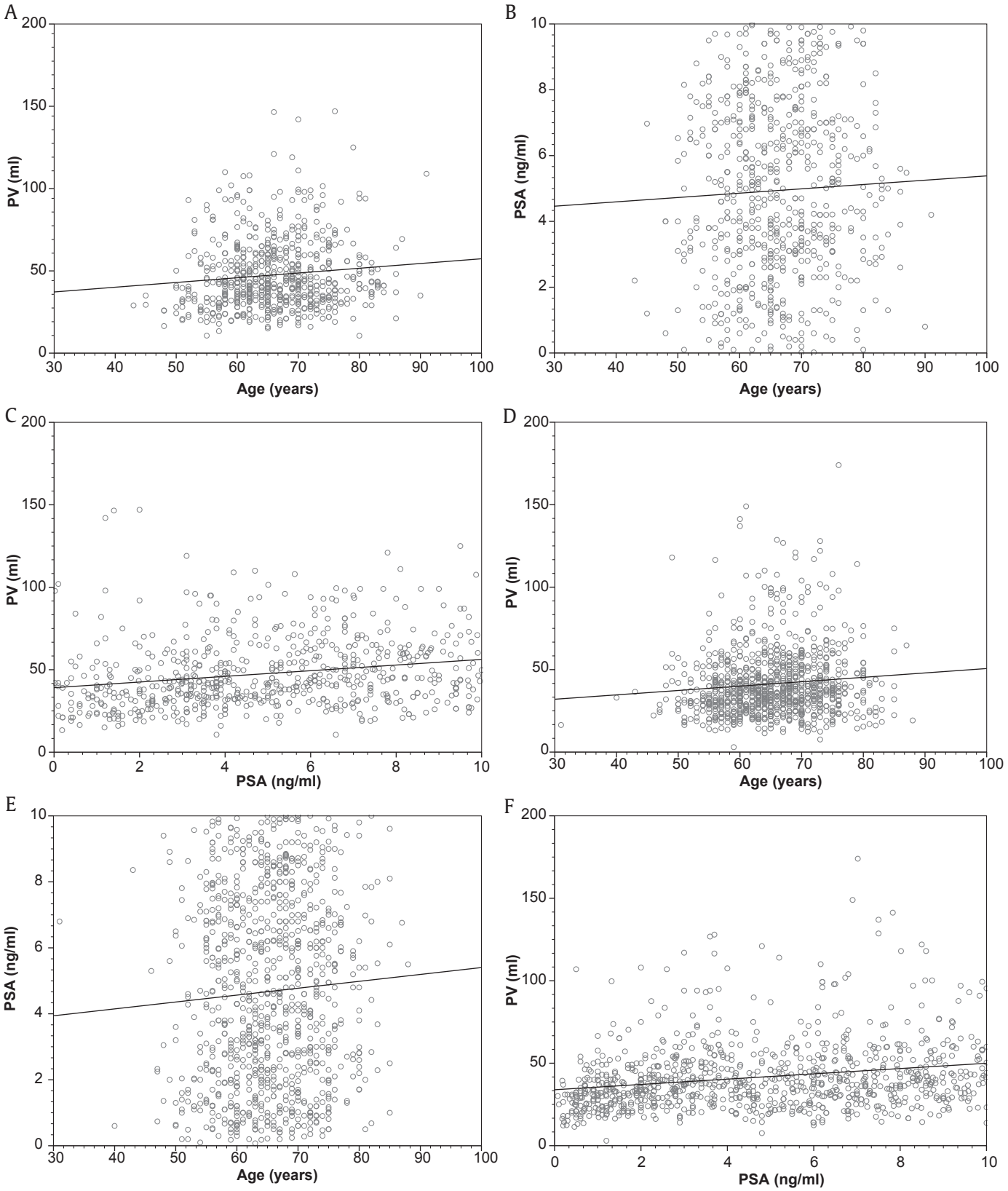

Fig. 3. Pearson's correlation coefficient in patients with (A–C) and without (D–F) indwelling catheter. (A) Between age and PV ($r = 0.13$, $P = 0.001$). (B) Between age and PSA ($r = 0.04$, $P = 0.267$). (C) Between PSA and PV ($r = 0.23$, $P < 0.001$). (D) Between age and PV ($r = 0.11$, $P = 0.001$). (E) Between age and PSA ($r = 0.08$, $P = 0.016$). (F) Between PSA and PV ($r = 0.28$, $P < 0.001$). PSA, prostate-specific antigen; PV, prostate volume.

Table 3 Correlation of age and prostate volume in different countries from various studies.

Country	Study	Correlation coefficient (r)	P
India	Baruah et al[15]	0.84	0.001
South Korea	Lee et al[17]	0.32	< 0.001
Taiwan	Liu et al[19]	0.31	< 0.001
Sweden	Vesely et al[16]	0.25	0.001
Indonesia	Our study	0.12	< 0.001

Table 4 Correlation of age and prostate-specific antigen in different countries from various studies.

Country	Study	Correlation coefficient (r)	P
India	Baruah et al[15]	0.77	0.001
South Korea	Lee et al[17]	0.17	< 0.001
Sweden	Vesely et al[16]	0.28	< 0.001
Indonesia	Our study	0.07	0.008

We have performed a subanalysis in patients with and without indwelling catheter, comparing age, serum PSA, and PV. Patients with indwelling catheter tend to have a higher serum PSA ($P = 0.038$) and PV ($P < 0.001$). PSA is an organ-specific biomarker of the prostate. Disruption of the normal anatomic prostatic tissue results in an increase in serum PSA. This increase may result from malignant or benign prostatic diseases or prostatic manipulation including catheterization.[24] It is also known that patients with higher PSA and PV tend have a greater risk of urinary retention and thus, catheterization.[25,26] Although aging is related to a higher risk for urinary retention,[27] results from our study showed that there was no difference in age in terms of indwelling catheter use. In both groups, PV was significantly correlated with age and PSA. Both groups showed similar coefficient correlation values.

Elevated serum PSA is observed in men with BPH, prostatitis, or prostate cancer. In another study conducted earlier in our center, from January 1995 to December 2014, the overall prostate cancer detection rate was 28.7%. With specific levels of PSA 4.0–9.9 ng/mL and 10.0–19.9 ng/mL, the prostate cancer detection rates were 9.3% and 13.1%, respectively. Meanwhile, the overall detection rate for PSA level 4.0–20 ng/mL was 11.3%, which was similar to that reported in a study by Shahab et al.[28,29] The indications for prostate biopsy in our center were PSA > 4.0 ng/mL or abnormal digital rectal examination (DRE) findings. We believed that the possibility of unintentionally including patients with prostate cancer had been minimized as much as possible as we enrolled only individuals with a PSA of ≤ 10.0 ng/mL and histopathologically proven BPH from either a transrectal prostate biopsy or a transurethral resection of the prostate (TURP) specimen.

The limitation of our study was that the correlations between PSA, age, and PV found in this study were weaker than those found in similar studies from other centers. This difference could be attributable to methodological differences between this and other studies; or there was a fundamental difference in the biology of prostate (including PV and PSA) in various ethnicities.[10,30,31] Indonesia, the most populous country in Southeast Asia, is a socioculturally and ethnically diverse country. The heterogeneity of our study population may account for the weak correlation coefficient between the investigated variables. Future studies may be necessary to explore the correlations in specific ethnicities. A prospective, multicenter, long-term longitudinal study is warranted to address this issue.

In Indonesian men with biopsy-proven BPH, both PV and PSA increased with aging. PV was significantly correlated with PSA. Even though the results were weaker, these results are consistent with the results in other population groups. Thus, aside from PSA, age, and PV, when investigating men with BPH, ethnicity may also need to be taken into account.

Conflicts of interest

None declared.

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