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Original article

The Relationship Between Prostate Volume, Prostate-Specific Antigen and Age in Saudi Men with Benign Prostatic Conditions

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ABSTRACT

Objectives: To assess the relationship between prostate volume (PV), prostate specific antigen (PSA) and age in a cohort of Saudi men from the Urology Department, King Abdul Aziz University Hospital, Jeddah, Saudi Arabia.

Methods: Medical records of 447 Saudi men aged 20-89 years with benign prostatic conditions seen between January 2003 and June 2009, were reviewed, retrospectively. Cases with PSA >10 ng/ml, proven prostate cancer, previous prostate surgery or those who received 5-alpha reductase inhibitors (5-ARIs) were excluded. The study population was categorized into seven successive age groups (20-89 years). The variables of age, PV and PSA were examined. Using mean PV of the 20-29 years age group and mean PSA of the 40-49 years age group as reference points, percentage differences in mean PV and mean PSA in subsequent age groups were determined. A p-value <0.05 was considered significant. Findings in Saudi patients were compared to other ethnicities.

Results: 447 men were enrolled with mean age 64.2 years, mean PV 35.2 cc (range 7-184 cc) and mean PSA 2.2 ng/ml (range 0.18-10 ng/ml). Overall, 62% (277/447) had PV <30 cc and 8.7% (39/447) had PV ≥50 cc. Among individual age groups, most men had PV <30 cc, except the 70-79 years age group where 55.2% (53/96) had PV >30 cc. Percentage differences of PV and PSA in 80-89 years age group (+150% and +70%, respectively) were lower than in the 60-69 and 70-79 years age groups (+187% and +160%; +207.2% and +220% for PV and PSA, respectively). All variables demonstrated significant weak correlations; except PV and PSA which showed a significant positive relationship (p <0.0001; r=0.441).

Conclusion: PV and PSA are significantly and strongly correlated. PV and PSA in Saudi men are closer to Asian than white ethnicities.

Key Words: Prostate, volume, prostate specific antigen, prostatic hyperplasia, Saudi Arabia

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INTRODUCTION

Prostate volume (PV) varies widely throughout man's lifetime, and in the course of different prostatic diseases, including benign prostatic hyperplasia (BPH)[1,2]. Both PV and serum prostate-specific antigen (PSA) are key predictors of clinical progression and response to medical therapy in patients with BPH, thus helping to select the regimen for medical treatment (alpha-blockers, 5-alpha-reductase inhibitors (5-ARI), or their

combination)[7-11]. PV also has implications in episodes of acute urinary retention (AUR)[12]; predicts the outcome of trial without catheter (TWOC) after AUR and future need for BPH-related surgery[7,10]. Moreover, protocols for transrectal ultrasound (TRUS) guided biopsies and detection rates of prostate cancer (PCa) vary according to different PV and PSA levels[13]. Therefore, knowledge of PV and PSA is imperative for understanding the natural history of prostatic diseases, and as criteria for diagnostic and therapeutic decision-making.

To our knowledge, the differences in PV in Saudi men among different age groups are unknown. The aim of this study was to assess PV and serum PSA levels in Saudi men with benign prostatic conditions in different age groups (20-89 years), as compared to those reported for men of different ethnicities[4,6,14-17].

MATERIALS AND METHODS

Medical records of Saudi men aged 20-89 years from the Urology Department, King Abdul Aziz University Hospital, Jeddah, between January 2003 and June 2009 were retrospectively reviewed after institutional review board approval. The indications for evaluation were lower urinary tract symptoms (LUTS) and/or infertility work-up and included digital rectal examination (DRE), TRUS determination of PV and serum PSA testing in men ≥40 years old. Men age ≥40 years with suspicious findings on DRE, TRUS and/or serum PSA (≤10 ng/ml) who proved to have benign conditions on TRUS guided biopsies were included in the study. Men with PSA >10 ng/ml, proven PCa, previous prostate surgery or treatment with 5-ARIs were excluded from the study. The study population was categorized into seven successive age groups (20-89 years).

Statistical analysis was performed using SPSS® software version 11 (SPSS, Inc., Chicago, Illinois), examining variables of age, PV and PSA frequencies in overall population and among different age groups. Using Chi-square test, a 2-tailed P-value <0.05 was considered significant. Correlations of age, PSA and PV were performed using Pearson's correlation coefficient (r). Using mean PV of the 20-29 years age group and mean PSA of the 40-49 years age group as reference points, the percentage differences in mean PV and mean PSA in subsequent age groups were determined. PV and PSA findings in Saudi men were compared to those of other ethnic origins in reports entailing comparable study populations[4,6,14-17].

RESULTS

A total of 447 men fulfilling the inclusion criteria were included in the study. The mean age was 64.2 years, mean PV was 35.2 (range 7-184) cc and mean PSA was 2.2 (range 0.18-10) ng/ml. PV and PSA varied widely over different age groups (Table 1). Frequencies of different PV among age groups are shown in Table 2. Overall, 62% (277/447) had PV <30 cc and only 8.7% (39/447) had prostates ≥50 cc. Among men aged ≥40 years, 57.6% (231/401) had PV <30 cc, while only 9.7% (39/401) had prostates ≥50 cc. Among individual age groups, most men had PV <30 cc, except the 70-79 years age group where more patients (55.2%; 53/96) had PV >30 cc. In the limited number of patients in the 80-89 years age group (n = 16) we found 62.5% with PV <30 cc. The percentage differences of PV and PSA in the 80-89 years age group (+150% and +70%, respectively) were lower than those found in the 60-69 and 70-79 years age groups (+187% and +160%; and +207.2% and +220%, respectively) (Table 3). Age demonstrated significant (p <0.0001) but weak positive correlations with PV (r=0.306) and PSA (r=0.324). Only PSA and PV showed a significant and strong positive correlation (p <0.0001; r=0.441) (Table 4). Comparing our findings to other studies, PV and PSA values in Saudi men were found to be closer to those of Asian ethnicities[15,16] than European and American white men[4,6,14] (Table 5).

Table 1: Prostate volume and PSA levels among men of different age groups.

Age (years)		n	PV (cc)		PSA (ng/ml) *	
Group	**Mean**		**Mean ± SD**	**Range**	**Mean ± SD**	**Range**
20-29	27.2	11	13.8 ± 3.1	9.9-18	--	--
30-39	34.4	35	16.1 ± 7.3	7-28	--	--
40-49	45.2	63	23.8 ± 11.1	8-90	1.0 ± 0.4	0.18-4.2
50-59	54.6	102	32.2 ± 14.6	12.3-84	1.6 ± 0.6	0. 43-5.6
60-69	64.7	124	39.6 ± 18.7	8.9-112	2.6 ± 1.1	0.27-10
70-79	73.6	96	42.4 ± 20.4	7.5-184	3.2 ± 1.9	0.34-10
80-89	84.3	16	34.5 ± 17.9	12.6-76	1.7 ± 0.8	0.4-3.1
All men*	64.2	447	35.2 ± 22.5	7-184	2.2 ± 1.5	0.18-10

PV=prostate volume, PSA=prostate-specific antigen. * PSA was determined in men aged ≥ 40 years old.

Table 2: Frequency distribution of different prostate volumes (PV) among men of different age groups.

Age group	PV < 30 cc n/total (%)	PV 30-39 cc n/total (%)	PV 40-49 cc n/total (%)	PV ≥ 50 cc n/total (%)
20-29	11/11 (100%)	0	0	0
30-39	35/35 (100%)	0	0	0
40-49	51/63 (81%)	7/63 (11.1%)	3/63 (4.8%)	2/63 (3.2%)
50-59	61/102 (59.8%)	22/102 (21.6%)	9/102 (8.8%)	10/102 (9.8%)
60-69	66/124 (53.2%)	27/124 (21.8%)	19/124 (15.3%)	12/124 (9.7%)
70-79	43/96 (44.8%)	25/96 (26%)	15/96 (15.6%)	13/96 (13.5%)
80-89	10/16 (62.5%)	2/16 (12.5%)	2/16 (12.5%)	2/16 (12.5%)
All men	277/447 (62%)	83/447 (18.6%)	48/447 (10.7%)	39/447 (8.7%)

Table 3: Percentage differences in mean PV and mean PSA in consecutive age groups, as compared to the reference points of the 20-29 and 40-49 year age groups, respectively.

Age (years)	PV		PSA	
	% difference	**P***	**% difference**	**P***
20-29	RP=13.8 ± 3.1 cc	n/a	n/a	n/a
30-39	+16.7%	= .1439	n/a	n/a
40-49	+72.5%	< .0001	RP=1.0 ± 0.4 ng/ml	n/a
50-59	+133%	< .0001	+60%	<.0001
60-69	+187%	< .0001	+160%	<.0001
70-79	+207.2%	< .0001	+220%	<.0001
80—89	+150%	= .0004	+70%	=.0034

*P-values for the differences of mean PV and mean PSA in consecutive age groups as compared to RP.
PV=prostate volume, PSA=prostate-specific antigen, RP=reference point, n/a=not applicable.

Table 4: Correlations of age, PSA and PV.

	Age		PV	
	r	p value	r	p value
Age	--	--	.306	<.0001
PV	.306	<.0001	--	--
PSA	.324	<.0001	.441	<.0001

PV=prostate volume, PSA=prostate-specific antigen, r= Pearson correlation coefficient.

DISCUSSION

Prostatic size varies significantly throughout man's life. Berry and coworkers found that average prostate weight increased from about 20 grams in men aged 40 years to 38.8 grams in men aged above 80 years[1]. PV and PSA are key predictors of clinical progression, response to medical treatment and prostate-related events in patients with prostatic diseases[3-9,18,19]. DRE, despite being widely used to identify an enlarged prostate, lacks sensitivity, requires an experienced examiner, and is subject to inter-observer variability[3,20,21]. TRUS remains the gold standard for PV measurement, although it is not feasible in all patients because of lack of availability, high cost and patient inconvenience[22]. Thus, serum PSA has been extensively studied as a proxy marker to estimate PV[3-9]. In a study by Bohnen et al[3], PV >30 cc was found in 52 % of men with PSA ranging from 1.1–1.5 ng/ml and in 65% with PSA ranging from 1.6–2.0 ng/ml. The authors concluded that a serum PSA level >1.5 ng/ml could be a functional cut-off value to recognize men with PV more than 30 cc. A number of studies have shown that risk of BPH clinical progression is maximum in men with PV ≥30 cc and PSA >1.5 ng/ml[8,9,18,19]. In a retrospective study, patients with PV >40 cc who were treated with different alpha-blockers demonstrated increased risk of treatment failure[23]. In another study[24], patients receiving tamsulosin and having smaller total PV responded better on flow parameters. According to the BPH guidelines of the European Association of Urology, PV >30–40 cc is an indication for 5-ARI therapy in patients with moderate-to-severe LUTS[11]. Thus, patients with bothersome LUTS and PV ≤40 cc may achieve maximum benefit using alpha-blocker medication, while in those with PV ≥40 cc, 5-ARI therapy (with or without an alpha-blocker) is appropriate[25].

We evaluated the relationship between PV, PSA and age in Saudi men with benign prostatic conditions. To the best of our knowledge, this is the first demographic study reporting on the PV in Saudi men of different age groups. We have chosen 30 cc as cut-off value to dichotomize the PV, because in clinical practice a PV ≥30 cc is commonly described as an ''enlarged prostate''[26], and it was recognized in several studies as a cut-off for response to medical therapy and clinical progression[9,11,18,19]. In our study, 62% of all Saudi men had PV <30 cc while only 8.7% had prostates larger than 50 cc. The reported PVs in our study are clearly smaller than those reported in European[4,14] and American studies[6] involving predominantly white men. Among Saudi men aged ≥ 40 years, 57.6% had PV <30 cc and only 8.7% had prostates ≥ 50 cc. Comparatively, in a European study from the Netherlands, involving 1859 patients aged 40-80 years with symptomatic BPH and no evidence of prostate cancer, 26.3% had PV <30 cc and 30.1% had prostates >50 cc[4]. Additionally, 55.2% of Saudi men aged 70–79 years showed a PV >30 cc compared to 83% reported in a similar age group of white men[4].

The PV and its relationship to PSA are reported to be variable in different races[4,6,14-17]. The PV in Japanese[15] and Korean[16] men was reported to be lower than in white men[4,6,14]. Additionally, the relationship between PSA and total PV in Asian men is dissimilar to white men where more PSA per unit prostate volume has been noted in Japanese and Taiwanese men[15,17]. Of note, the reported mean PSA (5.9 ng/ml) in the study on Taiwanese men[17] was higher than in other studies[4,6,14], including ours. The Taiwanese study was based on biopsy proven BPH in patients who underwent TRUS biopsy due to increased PSA. The authors acknowledged that this was a limitation of their study hindering the applicability of their

Table 5: Comparison of prostate volume and PSA in Saudi men vs. other ethnicities.

Ethnicity	Population	n [pts]	Age [years] mean (range)	PV [cc] mean (range)	PSA [ng/ml] mean (range)
Saudi [Current study]	Patients with LUTS secondary to benign prostatic disease and/or infertility	447	64.2 (20-89)	35.2 (7-184)	2.2 (0.18-10)
White (European) [4]	Patients with symptomatic BPH and no evidence of prostate cancer	1859	63.5 (40-80)	43.9 (9–186)	3.1 (0.1–10.0)
White (European) [14]	Patients with LUTS suggestive of benign prostatic enlargement	354	70.2 (45-91)	40.1 --	3.9 --
Predominantly white (Americans) [6]	Patients with symptomatic BPH and no evidence of prostate cancer	4448	63.7 (40-80)	43.7 --	2.6 --
Japanese [15]	Patients with at least moderate LUTS and clinical BPH	535	67.1 (43-89)	30.2 (5-140.3)	2.3 (0.2-9.9)
Korean [16]	Patients with LUTS and BPH	5716	64.3 (50-79)	36.9 --	2.2 --
Taiwanese [17]	Patients with LUTS and pathologically proven BPH	233	71.4 (42-89)	43.1 (10.5-104.6)	5.9 (0.5-9.9)

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

data to the general Taiwanese population[17]. The PV and PSA values in our Saudi patients were found to be closer to those of Asian ethnicities[15,16] than those of European and American white men[4,6,14]. However, the study designs, methodologies and populations involved in these studies are not identical; hence the comparison of such findings should be interpreted with caution. Nevertheless, our findings raise the question whether special PV and PSA cut-off values for medical therapy of BPH are justified in Saudi patients - probably lower than those in white races. Moreover, the results of the current study further support our previous findings[27] questioning the validity of a PSA cut-off of 4 ng/ml for TRUS guided biopsies for prostate cancer detection in Saudi patients and suggesting a lower PSA cut-off value for biopsies.

Although traditionally BPH has been considered a chronic and progressive condition[2], some authors have reported on the phenomenon of prostatic atrophy associated with aging in some men[14,28,29]. In the Baltimore Longitudinal Study of Aging[28], studying primarily white men without prostate cancer who underwent pelvic magnetic resonance imaging (median age 58 years, range 30-74), the PV increased at a median rate of 0.6 cc per year (range -9.9 to 62.1), corresponding to a median 2.5% annual change. Overall, 61.9% of men had prostate growth, 1.4% had a stable prostate size and 36.7% had a decrease in prostate size during the study period[29]. In a Japanese study[29], Tsukamoto et al examined the longitudinal changes in PV in 67 men with LUTS and at least 2 serial TRUS measurements. Prostate volume increased in 70%, remained stable in 15% and decreased in 15% of men[29]. Furthermore, Vesely et al from Sweden reported on the relationship between age, PV, PSA, symptom score and uroflowmetry in men with LUTS[14]. They reported progressive increase of mean PV (48.2ml) and mean PSA (5.4 ng/ml) in the <80 years age group as compared to the <54 years age group (27.5 ml and 1.5 ng/

ml, respectively). Nevertheless, in the 75-79 years age group they found a decrease in both PV and symptom score, while PSA remained unchanged[14]. In our study, the 80–89 years age group demonstrated a majority (62.5%) with PV <30 cc, denoting smaller prostates in this particular group as compared to the preceding younger 50-59, 60-69 and 70-79 age groups, where 59.8%, 53.2% and 44.8% had PV <30 cc, respectively. Additionally, using PV of the 20-29 years age group and PSA of the 40-49 years age group as reference points, the percentage differences of PV (+150%) and PSA (+70%) in the 80-89 years age group are lower than those found in the 60-69 and 70-79 years age groups (+187% and +207.2% for PV; and +160% and +220% for PSA), respectively. Although these findings can be explained by the hypothesis of prostatic atrophy[14,27,28], our findings cannot necessarily endorse this hypothesis and we caution about their interpretation, as the sample size of the 80-89 years age group is very small and there is lack of longitudinal follow-up of individual patients.

We recognize that our study was limited by its retrospective cross-sectional design and its relatively small single-center study population. The clinical cohort was selected on the basis of symptoms, thus it is not a typical community-based sample. Our findings need to be better characterized by prospective, multicenter, long-term longitudinal studies entailing larger cohorts of randomly selected community-based populations.

Conclusions

Changes in PV and PSA are highly variable among different ages. Age demonstrated significant but weak positive correlations with PV and PSA. Only PSA and PV showed a significant and strong positive correlation. PV and PSA values in Saudi men were found to be closer to those of Asian ethnicities than European and American white men.

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