PSA Density in the diagnosis of prostate cancer in Chinese population：results from the Chinese Prostate Cancer Consortium

Zijian Song1, Jinke Qian2*, Yue Yang1, Hanxiao Wu1, Maoyu Wang1, Siyuan Jiang1, Fubo Wang1, Wei Zhang1#, Rui Chen1#, Chinese Prostate Cancer Consortium*

1 Department of Urology, Shanghai Changhai Hospital, The Second Military Medical University, Shanghai 200433, China.

2 Department of Urology, Binhai People's Hospital, Jiangsu Province, China

*** These authors shares first authorship.**

Contact Information:

Department of Urology, Shanghai Changhai Hospital

drchenrui@foxmail.com Rui Chen

zhangweinicky@qq.com Wei Zhang

INTRODUCTION AND OBJECTIVE

We performed this study to investigate the diagnostic performance of PSAD in a multicenter cohort of Chinese Prostate Cancer Consortium. Outpatients with a PSA greater than 4.0 ng ml^{-1} regardless of DRE results or a PSA less than 4.0 ng ml^{-1} but abnormal DRE results were included from 18 large referral hospitals in China.

MATERIAL & METHODS

The diagnostic performance of PSAD and the sensitivity and specificity for diagnosis of PCa and HGPCa at different cutoff values were evaluated. A total of 5220 patients were included in the study and 2014 (38.6%) of them were diagnosed with PCa.

RESULTS

In patients with PSA from 4.0 to 10.0 ng ml^{-1}, PSAD was associated with PCa and HGPCa in both univariate (OR=45.15 and p< 0.01, OR=25.38 and p< 0.01, respectively) and multivariate analysis (OR= 52.55 and p< 0.01, OR= 26.05 and p< 0.01, respectively). The AUCs of PSAD in predicting PCa and HGPCa in men with a PSA of 4.0-10.0 ng ml^{-1} were 0.627 and 0.630, respectively. With the PSAD threshold of 0.10, nearly all (89.9%) of HGPCa could be detected and avoid the biopsies in 20.0% of patients (356/1776 cases).

Among these patients avoided biopsies, only 30 cases were with HGPCa. The diagnostic performance of PSAD was higher than PSA in all PSA ranges. In patients with a PSA from 4.0-10.0 ng ml^{-1}, when the cutoff value of PSAD was 0.10, we could get a sensitivity of nearly 90% for both PCa and HGPCa.

Table 1. Univariate and multivariate analysis of variables at the time of biopsy in predicting the risk of PCa and HGPCa

Variables	PSA 4-10 ng/ml				All PSA			
	PCa		HGPCa		PCa		HGPCa	
	Odds ratio(95%CI)	P	Odds ratio(95%CI)	P	Odds ratio(95%CI)	P	Odds ratio(95%CI)	P
Age at biopsy(year)								
Univariate analysis	1.05(1.04-1.07)	<0.0001	1.06(1.04-1.08)	<0.0001	1.05(1.05-1.06)	<0.0001	1.05(1.04-1.06)	<0.0001
Multivariate analysis	1.07(1.05-1.08)	<0.0001	1.07(1.05-1.09)	<0.0001	1.06(1.05-1.07)	<0.0001	1.06(1.05-1.06)	<0.0001
PSAD								
Univariate analysis	45.15(15.70-129.83)	<0.0001	25.38(8.19-78.69)	<0.0001	1.15(1.12-1.19)	<0.0001	1.11(1.09-1.14)	<0.0001
Multivariate analysis	52.55(16.42-168.22)	<0.0001	26.05(7.53-90.07)	<0.0001	1.10(1.07-1.14)	<0.0001	1.08(1.05-1.10)	<0.0001
TRUS (Nodule) Positive VS Negative								
Univariate analysis	1.13(0.91-1.41)	0.2728	1.02(0.78-1.33)	0.8907	1.39(1.25-1.54)	<0.0001	1.29(1.16-1.43)	<0.0001
Multivariate analysis	1.06(0.83-1.35)	0.6303	0.93(0.70-1.24)	0.6252	1.38(1.23-1.55)	<0.0001	1.28(1.15-1.43)	0.0002
%fPSA								
Univariate analysis	0.07(0.02-0.30)	0.0003	0.09(0.02-0.48)	0.0049	0.02(0.01-0.05)	<0.0001	0.02(0.01-0.04)	<0.0001
Multivariate analysis	0.07(0.01-0.34)	0.0010	0.07(0.01-0.45)	0.0051	0.02(0.01-0.03)	<0.0001	0.01(0.01-0.03)	<0.0001

Table 2 Sensitivity, specificity, positive and negative predict value of the PSAD at different cutoff values in patients with 4-10 ng ml^{-1}

cutoff	Sensitivity (95% CI)		Specificity (95% CI)		HGPCa missed	Unnecessary Biopsies avoided
	PCa	HGPCa	PCa	HGPCa		
0.10	88.7(85.4-91.5)	89.9(85.8-93.1)	23.3(21.0-25.6)	22.2(20.1-24.4)	27/296(9.1%)	299/1325(22.6%)
0.11	83.8(80.1-87.1)	84.5(79.8-88.4)	28.5(26.1-31.0)	27.4(25.1-29.7)	45/296(15.2%)	367/1325(27.7%)
0.12	78.7(74.6-82.4)	80.7(75.8-85.1)	35.8(33.2-38.4)	34.7(32.2-37.1)	57/296(19.3%)	462/1325(34.9%)
0.13	73.8(69.5-77.8)	77.0(71.8-81.7)	42.4(39.7-45.1)	41.4(38.8-43.9)	67/296(22.6%)	554/1325(41.8%)
0.14	70.7(66.3-74.9)	74.0(68.6-78.9)	47.0(44.3-49.7)	45.8(43.2-48.4)	75/296(25.3%)	616/1325(46.5%)
0.15	64.8(60.1-69.2)	67.2(61.6-72.5)	52.5(49.8-55.2)	51.2(48.6-53.8)	96/296(32.4%)	688/1325(51.9%)
0.16	61.6(57.0-66.2)	63.9(58.1-69.3)	58.6(55.9-61.2)	56.9(54.3-59.4)	104/296(35.1%)	770/1325(58.1%)

With the PSAD threshold of 0.10: Nearly all (89.9%) of HGPCa could be detected. Avoid the biopsies in 19.5 % of patients (356/1776 cases). Among these patients avoided biopsies, only 30 (10.1%) cases were with HGPCa. In contrast, if the 0.15 cutoff was applied, there would be 96 (32.4%) HGPCa patients missed.

SUMMARY / CONCLUSION

The results of this study should be validated in prospective population-based multicenter studies

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REFERENCES

1.Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA *et al.* Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians* 2018; **68**: 394-424.

2.Center MM, Jemal A, Lortet-Tieulent J, Ward E, Ferlay J *et al.* International variation in prostate cancer incidence and mortality rates. *European urology* 2012; **61**: 1079-92.

3.Umbehr MH, Gurel B, Murtola TJ, Sutcliffe S, Peskoe SB *et al.* Intraprostatic inflammation is positively associated with serum PSA in men with PSA <4 ng ml(-1), normal DRE and negative for prostate cancer. *Prostate cancer and prostatic diseases* 2015; **18**: 264-9.

4.Simardi LH, Tobias-MacHado M, Kappaz GT, Taschner Goldenstein P, Potts JM *et al.* Influence of asymptomatic histologic prostatitis on serum prostate-specific antigen: a prospective study. *Urology* 2004; **64**: 1098-101.

5.Thorpe A, Neal D. Benign prostatic hyperplasia. *Lancet (London, England)* 2003; **361**: 1359-67.

6.Yoshida K, Honda M, Sumi S, Arai K, Suzuki S *et al.* Levels of free prostate-specific antigen (PSA) can be selectively measured by heat treatment of serum: free/total-PSA ratios improve detection of prostate carcinoma. *Clinica chimica acta; international journal of clinical chemistry* 1999; **280**: 195-203.

7.Benson MC, Whang IS, Pantuck A, Ring K, Kaplan SA *et al.* Prostate specific antigen density: a means of distinguishing benign prostatic hypertrophy and prostate cancer. *The Journal of urology* 1992; **147**: 815-6.

8.Benson MC, Whang IS, Olsson CA, McMahon DJ, Cooner WH. The use of prostate specific antigen density to enhance the predictive value of intermediate levels of serum prostate specific antigen. *The Journal of urology* 1992; **147**: 817-21.

9.Verma A, Onge JS, Dhillon K, Urology ACJTCJo. PSA density improves prediction of prostate cancer. 2014; **21**: 7312-21.

10.Jue JS, Barboza MP, Prakash NS, Venkatramani V, Sinha VR *et al.* Re-examining Prostate-specific Antigen (PSA) Density: Defining the Optimal PSA Range and Patients for Using PSA Density to Predict Prostate Cancer Using Extended Template Biopsy. *Urology* 2017; **105**: 123-8.