

Prostate Cancer Diagnosis-What to Expect in the Thai Population?

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Objective: To study the prostate cancer detection rates upon transrectal ultrasound (TRUS) guided biopsy in relation to prostate-specific antigen (PSA) and digital rectal examination (DRE) included risk factors for prostate cancer diagnosis.

Materials and Methods: 1,176 patients who underwent TRUS prostate biopsy between 2002 to 2008 were enrolled to the study. The prostate cancer detection rates with reference to PSA level and DRE finding were investigated. Logistic regression analysis was performed on age at biopsy, clinical symptoms, prostate-specific antigen (PSA), and DRE findings to identify significant risk factors. The correlation of DRE findings in combination with PSA value was also analyzed.

Results: Referring to patients with normal DRE, the cancer detection rates were 10.8%, 12.9%, 21.3%, 42.6% and 77.8% in patients with PSA <4, 4 to 10, 10.01 to 20, 20.01 to 50 and >50 ng/ml, respectively. According to patients with abnormal DRE, the cancer detection rates were 15.0%, 20.7%, 41.2%, 60.5% and 84.8% in patients with PSA <4, 4 to 10, 10.01 to 20, 20.01 to 50 and >50 ng/ml, respectively. Additionally, the age at biopsy, PSA level and DRE finding were the significant risk factors for prostate cancer diagnosis while clinical symptom was not. The data revealed that normal DRE finding in combination with PSA level was statistically significant when PSA level was above 20 ng/ml. Similarly, the abnormal DRE finding in combination with PSA level was statistically significant when PSA level was above 10 ng/ml.

Conclusion: Thai men appeared to have lower prostate cancer detection rate when compared to the Western population. The age at biopsy, PSA level and DRE finding were the significant risk factors for prostate cancer. Besides, the combination of DRE and PSA level increased the accuracy and were the best tool for prostate cancer screening.

Keywords: Prostate cancer screening, Prostate cancer risk factors, Transurethral ultrasound guided prostate biopsy, Prostate-specific antigen, Digital rectal examination

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Prostate cancer is a growing threat to world population. Although the rate of incidence and mortality of prostate cancer in native Asian populations are reported to be much lower when compared to other ethnic groups⁽¹⁻⁵⁾, the burden of increasing morbidity and mortality in most parts of the world due to prostate cancer imposes an urgent need for preventive measures. Therefore, while a large number of studies on prostate cancer have focused on the areas where prostate cancer is commonly reported, such as the United States and United Kingdom^(1,4,5). The present study proposes to highlight certain key points following a nearly decade-long investigation in an area where prostate cancer is less common, or probably, least.

Since the prostate-specific antigen (PSA) era (90's),

there were significantly more prostate cancer detection than the past decade⁶. However, Thai men considerably genetically and physiologically differed from the Western population. According to National Thailand Cancer Database, the prevalence of prostate cancer is 7.5: 100,000. Hence, the clinical application of PSA in Thai men should be thoroughly investigated. Moreover, Thai specific data are beneficial for counseling of transrectal ultrasound (TRUS) guided prostate biopsy for suspected Thai prostate cancer. To date, large scale study on prostate cancer Thai population is inadequate. Herein, the prostate cancer rates upon TRUS guided biopsy in relation to DRE and PSA level in the Thai population. In addition, the risk factors of prostate cancer detection upon TRUS guided biopsy were also explored.

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Materials and Methods

The patients without previous diagnosis of prostate cancer were examined at the urology unit of Rajavithi Hospital, Thailand, between January 2002 and April 2008. These patients met any or combinations of following inclusion criteria: (1) presence of abnormal digital rectal examination

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(DRE) (hard consistency or irregular surface prostate gland); (2) elevated prostate specific antigen (PSA) above 4 ng/ml. The study was approved by Ethical Committee (EC number 53173).

After enrollment, 1,176 patients (mean age 65 year) were included in the study, and their informed consents were obtained. All patients had received 500 mg of ciprofloxacin and fleet enemas before they underwent TRUS guided prostate biopsy followed by systematic random biopsy by using the Panther 2002 ADI (B-K Medical, Gentofte, Denmark). All TRUS with prostate biopsy procedures were performed by the first author (D.A).

Logistic regression analysis was performed on age at biopsy, clinical symptoms, prostate-specific antigen (PSA), and digital rectal examination (DRE) findings. Statistical significant is $p < 0.05$.

Results

Logistic regression analysis revealed that prostate cancer was associated with age at biopsy, PSA level, and DRE findings; and there was no statistically significant association with clinical symptoms (Table 1).

According to Table 1, total of 1,176 patients were studied with the mean age of 65 years and a range of 45 to 87 years. The peak age range was 61 to 70 years and accounted for 42.83% (418 patients) of the entire study population.

Of all patients across age groups, malignancy was identified in 295 patients (30.23%) while 681 patients (69.77%) had benign prostatic tumors. In the peak age range, malignancy was detected in 123 patients, accounting for 12.60% of all cases.

Table 1 demonstrated that older age at biopsy over

60 years were significantly correlated with higher risk of prostate cancer, with patients aged 61 to 70 years (OR, 1.90; 95% CI, 1.22 to 2.98; $p < 0.001$); aged 71 to 80 years (OR, 2.26; 95% CI, 1.43 to 3.58; $p < 0.001$); and aged over 80 years (OR, 4.57; 95% CI, 2.50 to 8.35; $p < 0.001$).

Additionally, Table 1 indicated that PSA elevation and DRE findings were also significantly correlated with the development of prostate cancer.

According to the data, an amelioration of PSA level was associated with an increasing risk of prostate cancer where PSA level of 4.01 to 10.00 ng/ml (OR, 1.21; 95% CI, 0.53 to 2.80; $p < 0.001$); PSA level of 10.01 to 20.00 ng/ml (OR, 2.60; 95% CI, 1.12 to 6.02; $p < 0.001$); PSA level of 20.01 to 50.00 ng/ml (OR, 6.64; 95% CI, 2.81 to 15.68; $p < 0.001$); and PSA level exceeding 50 ng/ml (OR, 29.50; 95% CI, 11.84 to 73.50; $p < 0.001$).

Table 1 also pointed out that normal DRE and abnormal DRE findings were correlated to prostate cancer with a significantly higher prostate cancer risk of an abnormal DRE findings (OR, 3.42; 95% CI, 2.50 to 4.69; $p < 0.001$).

Upon investigation, patients with normal DRE was 72.95% (712). The correlation between DRE findings in combination with PSA value was shown in Table 2.

Clearly, Table 2 shows that normal DRE findings in combination with PSA level were of statistically significant, with PSA level of 20.01 to 50.00 ng/ml (OR, 6.11; 95% CI, 2.00 to 18.64; $p < 0.001$); and PSA level exceeding 50 ng/ml (OR, 28.88; 95% CI, 8.90 to 93.69; $p < 0.001$).

A significant correlation of abnormal findings combined with PSA level were PSA level of 10.01 to 20.00 ng/ml (OR, 3.97; 95% CI, 1.06 to 14.83; $p < 0.001$); PSA level of 20.01 to 50.00 ng/ml (OR, 8.67; 95% CI, 2.20 to 34.15;

Table 1. Risks of prostate cancer stratified by age, symptoms, PSA level and DRE findings

| Factors | Total No. | Malignancy (n = 295) | No malignancy (n = 881) | OR (95% CI) | p-value |
|----------------|-----------|-------------------------|----------------------------|------------------------|---------|
| Age (years) | | | | | <0.001* |
| ≤60 | 167 | 30 (17.9%) | 137 (82.1%) | 1 | |
| 61 to 70 | 418 | 123 (29.4%) | 295 (70.6%) | 1.90 (1.22 to 2.98) | |
| 71 to 80 | 317 | 105 (33.1%) | 212 (66.9%) | 2.26 (1.43 to 3.58) | |
| >80 | 74 | 37 (50%) | 37 (50%) | 4.57 (2.50 to 8.35) | |
| Symptoms | | | | | 0.182 |
| Obstructive | 455 | 128 (28.1%) | 327 (71.9%) | 1 | |
| Irritative | 214 | 62 (28.9%) | 152 (71.1%) | 1.04 (0.73 to 1.49) | |
| Others | 307 | 105 (34.2%) | 202 (65.8%) | 1.33 (0.97 to 1.81) | |
| PSA | | | | | <0.001* |
| ≤4 | 57 | 7 (12.2%) | 50 (87.8%) | 1 | |
| 4.01 to 10.00 | 413 | 60 (14.5%) | 353 (85.5%) | 1.21 (0.53 to 2.80) | |
| 10.01 to 20.00 | 251 | 67 (26.7%) | 184 (73.3%) | 2.60 (1.12 to 6.02) | |
| 20.01 to 50.00 | 137 | 66 (48.2%) | 71 (51.8%) | 6.64 (2.81 to 15.68) | |
| >50 | 118 | 95 (80.5%) | 23 (19.5%) | 29.50 (11.84 to 73.50) | |
| DRE | | | | | <0.001* |
| Normal | 712 | 118 (16.6%) | 531 (83.4%) | 1 | |
| Abnormal | 264 | 114 (43.2%) | 150 (56.8%) | 3.42 (2.50 to 4.69) | |

*statistically significant at $p < 0.05$

Table 2. Risk of prostate cancer concerning DRE findings in combination with PSA

| PSA | Total No. | Malignancy (n = 295) | No malignancy (n = 881) | OR (95% CI) | p-value |
|----------------|-----------|-------------------------|----------------------------|--------------------------|---------|
| DRE: normal | | | | | <0.001* |
| ≤4 | 37 | 4 (10.8%) | 33 (89.2%) | 1 | |
| 4.01 to 10.00 | 326 | 42 (12.9%) | 284 (87.1%) | 1.22 (0.41 to 3.62) | |
| 10.01 to 20.00 | 183 | 39 (21.3%) | 144 (78.7%) | 2.23 (0.75 to 6.69) | |
| 20.01 to 50.00 | 94 | 40 (42.6%) | 54 (57.4%) | 6.11 (2.00 to 18.64) * | |
| >50 | 72 | 56 (77.8%) | 16 (22.2%) | 28.88 (8.90 to 93.69) * | |
| DRE: abnormal | | | | | <0.001* |
| ≤4 | 20 | 3 (15.0%) | 17 (85.0%) | 1 | |
| 4.01 to 10.00 | 87 | 18 (20.7%) | 69 (79.3%) | 1.48 (0.39 to 5.60) | |
| 10.01 to 20.00 | 68 | 28 (41.2%) | 40 (58.8%) | 3.97 (1.06 to 14.83) * | |
| 20.01 to 50.00 | 43 | 26 (60.5%) | 17 (39.5%) | 8.67 (2.20 to 34.15) * | |
| >50 | 46 | 39 (84.8%) | 7 (15.2%) | 3.157 (7.28 to 136.98) * | |

* statistically significant at $p < 0.05$

$p < 0.001$); and PSA level exceeding 50 ng/ml (OR, 31.57; 95% CI, 7.28 to 136.98; $p < 0.001$).

Discussion

Since the 1990s⁷, Catalona et al have explored many important hallmark studies on the clinical application of PSA for decision making on TRUS guided prostate biopsy^(6,7). Due to the significantly differences on the implication of elevated PSA level and the probability of having prostate cancer between Thai and Western population, it would be inappropriate for Thai counselling men based on Western population data. The present study demonstrated the prostate cancer detection upon TRUS guided biopsy in relation to DRE and PSA level, and specified risk factors of prostate cancer in the Thai population.

The present results showed that the cancer detection rates with reference to PSA in Thai men were much lower than that reported in the Western population. In the Prostate Cancer.

Prevention Trial⁽⁸⁾, the cancer detection rate was 15.2% in patients who had normal DRE and PSA <4.0 ng/ml, compared to 10.8% in the present study. According to the present study, prostate cancer detection rate of Thai patients (12.9%) with normal DRE was lower than those reported by Catalona and colleagues (20.7%) at the same level of PSA (4.1-9.9 ng/ml)⁽⁷⁾. Similarly, the cancer detection rate of Thai patients with abnormal DRE (20.7%) was lower than those reported by Gerstenbluth and colleagues (40.8%) at the same level of PSA (4.1 to 9.9 ng/ml)⁽⁹⁾. According to Gerstenbluth et al⁽⁹⁾, the cancer detection rates were 73.6%, 90.3% and 93.8% for patients with PSA 20 to 29.9, 30 to 39.9 and 40 to 49.9 ng/ml, respectively. These data were much higher than our results of 48.2% in patients with PSA 20.1 to 50 ng/ml. Additionally, the prostate cancer detection rates in this study appeared to be much lower than those in the Western population.

The present study also illustrated the importance of a proper DRE. Patients with abnormal DRE had much

higher cancer detection rates of up to +193.4% when compared to patients with normal DRE at the PSA range of 10.01 to 20 ng/ml. Concerning 114 patients (17.68% of the entire study population) with both abnormalities of DRE and malignancy, a significant correlation was identified when abnormal DRE findings were in combination with elevated PSA level from 10.01 to 20.00 (a level lower than the PSA level of patients with both normal DRE and no malignancy). This result suggested whether DRE findings may affect the outcome of prostate cancer screening, or more specifically, if elevated PSA level screening alone is sufficient. Many research studies have currently suggested the elevated PSA levels as a more accurate predictor of prostate cancer than the DRE and recommended its application for prostate cancer screening^(10,11). In contrast, the present study demonstrated that DRE was appropriate for assessing the urological patient.

The data from Table 1 and Table 2 indicated the differences in the prostate cancer detection rate from elevated PSA level screening with and without DRE. Clearly, the odds ratio of prostate cancer detection between elevated PSA level (1.21, 2.60, 6.64 and 29.50; all $p < 0.001$) and the combination of elevated PSA level with the DRE (1.22, 2.23, 6.11 and 28.88; all $p < 0.001$) were similar. In addition, the elevated PSA level and the abnormal DRE findings generated the contrasting evidences with increased prostate cancer risk (1.48, 3.97, 8.67 and 31.57; all $p < 0.001$).

To date, this research is the largest study on prostate cancer detection upon TRUS guided prostate biopsy in the Thai population. The information is beneficial for consideration of TRUS guided prostate biopsy in suspected Thai prostate cancer. The present study showed that a much lower prostate cancer detection rate in Thai men should be considered as an important factor prior to decision on TRUS guided prostate biopsy. However, further investigation on the lower cancer detection rate in the Thai population within the same range of PSA will be examined.

Additionally, the present study also pointed out that the combination of DRE and elevated PSA level could be

used as the sensitive marker and the best tool for prostate cancer detection.

Conclusion

Thai men appeared to have lower prostate cancer detection rate when compared to those of the Western population. Age at biopsy, PSA level and DRE finding were the significant risk factors. Combination of DRE and PSA level increased the accuracy of the detection and were the best tools for prostate cancer screening. Further study would be focused on the specific conduction of the proper prostate cancer screening guideline for Thai population.

What is already known on this topic?

Nowadays, PSA level was used for prostate cancer screening test. The common indications for TRUS guided prostate biopsy are PSA level above 4 ng/ml or abnormal DRE finding.

What this study adds?

Thai men have lower prostate cancer detection rate in all PSA level ranges when compared previous study from the Western data. Age at biopsy, PSA level and DRE finding were the significant risk factors. This study clearly showed that DRE is still necessary for prostate cancer screening although some studies questioned about the benefit of DRE. Combination of DRE and PSA level increased the accuracy of detection and were the best tool for prostate cancer screening.

Potential conflicts of interest

The authors declare no conflict of interest.

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