Incidence of Prostate Cancer in Physical Checkup Population with Rising of Serum Prostatic Specific Antigen

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Abstract

Objective: To assess the prevalence of prostate cancer in northern Thailand.

Methods: This study was performed with a cohort study at the health check-ups clinic at University of Phayao Hospital from July 2021 until October 2021. In total, prostate gland check-ups and Prostate-specific antigen (PSA) screening was made available to 350 patients aged at least 45 years, and a number of parameters were recorded: International prostate symptom score (IPSS), Body mass index (BMI), Digital Rectal Examination (DRE) and Quality of Life score (QOL) score. Those patients whose PSA level was more than 4 ng/ml were advised to have a transrectal ultrasound (TRUS) biopsy of prostate. The cancer detection rate was determined on the basis of reported symptoms and the IPSS. Comparisons among data were assessed via the Chi-square test, while Spearman correlation was used to compare the PSA level and the Gleason score.

Results: For the study subjects, the median age was 63 years (45-81); median BMI was 23.4 (18.2-32.4) kg/m^2, median IPSS score was 11(0-32); median QOL score was 2(0-6); and median PSA was 1.23 (0.12-125.7) ng/ml. Upon biopsy, 7.54% of the sample participants (26/350) could be determined to have prostate adenocarcinoma. A majority of those cases exhibited localized lesions. Participants who considered themselves to have abnormal urination were more likely to also have prostate cancer. Only one prostate cancer case was discovered in a participant with mild LUTS, as indicated by IPSS below 8. Typically, prostate cancer occurred more frequently in males with high IPSS scores.

Conclusion: The PSA screening approach detected prostate cancer in 7.54% of healthy physical check-ups population. A majority of these cancer cases were already presenting symptoms. Patients with LUTS should be made aware of prostate cancer and PSA testing may be offered in such patients.

Keywords: International prostate symptom score, Prostate specific antigen, lower urinary tract symptoms

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อัตราการเกิดโรคมะเร็งต่อมลูกหมากในประชากรที่มาตรวจสุขภาพและพบว่ามีค่าแอนติเจนต่อมลูกหมากในเลือดสูง

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บทคัดย่อ

วัตถุประสงค์: การศึกษาครั้งนี้ได้ศึกษาถึงอุบัติการณ์ของการเกิดมะเร็งต่อมลูกหมากในภาคเหนือ ประเทศไทย

วิธีดำเนินการวิจัย: การศึกษานี้เป็นการศึกษาแบบ cohort study ในผู้ชายไทยที่เข้ารับการตรวจสุขภาพประจำปีที่โรงพยาบาลมหาวิทยาลัยพะเยา และอายุมากกว่า 45 ปีขึ้นไป จำนวน 350 คน ซึ่งได้รับการเชิญชวนและคำแนะนำในเรื่องของการตรวจเลือดเพื่อหาค่า PSA และทำการตรวจสุขภาพต่อมลูกหมาก ประกอบด้วย IPSS (International Prostatic Symptom Score) ดัชนีมวลกาย (Body mass index) QOL (Quality of Life) และการตรวจทางทวารหนัก (Digital rectal examination) ผู้ป่วยที่มีค่า PSA สูงกว่าปกติ จะได้รับคำแนะนำให้รับการตรวจ ชิ้นเนื้อของต่อมลูกหมากดูว่ามีมะเร็งหรือไม่ ผลทางการตรวจทางพยาธิสภาพของต่อมลูกหมากได้นำมารวบรวม และทำการศึกษาดูถึงอัตราการตรวจพบมะเร็งต่อมลูกหมากในกลุ่มผู้ป่วยที่มีอาการผิดปกติของการถ่ายปัสสาวะในระดับความรุนแรงและช่วงอายุต่าง ๆ กัน และใช้ Spearman correlation ในการหาความสัมพันธ์ระหว่างค่า PSA และ Gleason score

ผลการวิจัย: ค่ามัธยฐานอายุของผู้เข้าร่วมโครงการ, IPSS, QOL, BMI และค่ามัธยฐานเฉลี่ยของ PSA มีค่าเท่ากับ 63 ปี, 11, 2, 23.4 kg/m2 และ 1.23 ng/ml ตามลำดับ ในผู้ป่วยจำนวน 350 คน พบว่ามีผู้ป่วยจำนวน 26 คนที่ตรวจพบมะเร็งต่อมลูกหมากจากการทำ biopsy ผู้ป่วยส่วนใหญ่จะเป็นโรคมะเร็งอยู่ในระยะเริ่มต้น ทั้งนี้ผู้ป่วยที่มีมะเร็งต่อมลูกหมากนั้น จะมีอาการของการขับถ่ายปัสสาวะผิดปกติ นอกจากนี้ยังไม่พบผู้ป่วยที่เป็นมะเร็งต่อมลูกหมากรายใดเลยที่มีค่าความผิดปกติของการถ่ายปัสสาวะไม่มากนัก (IPSS < 8) จากการศึกษาตรวจพบว่ามีมะเร็งต่อมลูกหมากมีแนวโน้มเพิ่มขึ้น ในผู้ป่วยที่มีอาการถ่ายปัสสาวะผิดปกติที่รุนแรงขึ้น

สรุป: จากการศึกษาครั้งนี้พบว่าการตรวจพบมะเร็งต่อมลูกหมากในผู้ป่วยที่เข้ารับการตรวจสุขภาพต่อมลูกหมากมีร้อยละ 7.54 โดยที่จะพบว่าผู้ป่วยที่เป็นมะเร็งนั้นจะมีอาการของการถ่ายปัสสาวะที่ผิดปกติแล้ว ดังนั้นการตรวจเลือด เพื่อหาค่า PSA อาจจะมีประโยชน์ในผู้ป่วยที่มาพบแพทย์ด้วยอาการขับถ่ายปัสสาวะที่ผิดปกติโดยก่อนเจาะเลือด แพทย์ควรจะให้คำแนะนำถึงข้อดีข้อเสียของการตรวจเลือดดังกล่าว

คำสำคัญ: แบบสอบถามอาการของต่อมลูกหมาก สารบ่งชี้มะเร็งในต่อมลูกหมาก อาการทางเดินปัสสาวะส่วนล่าง

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Introduction

Nowadays, Prostate cancer is that the second most typical cancer found in men. There are currently almost 1.5 million new cases annually. For middle-aged and older men in the developed world, prostate cancer is diagnosed more frequently than any other neoplasm. In Thailand, the current prostate cancer rate is 8.6 cases for every 100,000 men[1], making it the fourth most prevalent form of cancer in males. It is rare in men under 40 years of age, but become increasingly common as men age beyond their fifties.

Prostate cancer does not occur with uniform prevalence across Asia; it varies significantly between regions.The incidence and mortality in Thailand are respectively 8.63/100,000 and 5.9/100,000 (GLOBOCAN, 2020)[1]. Throughout Asia as a whole it is the fourth most common form of cancer found in men, and it is becoming increasingly common. It tends not to affect men aged below 40, but the incidence rises with age once men reach 50. For the periods from 1992–1995, 1998–2002 and 2007–09, the respective prostate cancer incidence rates were 3.1/100,000, 5.0/100,000, and 7.7/100,000[3]. These rates were higher for prostate cancer at advanced stages than the data reported from the United States and Europe, as well as South Korea, Taiwan, and Japan[4-7]. In the year 2000 to analyze the stage of the detected prostate cancer, a majority of cases were detected in stage C, at 67.7% of all cases (stage A = 7.5%, stage B = 1.1%, and stage D = 23.7%). In the later stages, C and D, the median survival rates are much lower at 45 months and 12 months respectively[8]. Importantly, as more PSA screening is carried out, and public awareness of prostate cancer rises, the proportion of cases detected in the earlier stages is increasing.

When assessing and treating prostate cancer in Thailand, it is normal to take comorbidity and life expectancy into consideration. The Thai Male life expectancy stands at 77.5 years, placing the country slightly behind the USA or the more developed countries in Europe and Asia. Leading Thai hospitals have established multidisciplinary teams in order to manage the care of prostate cancer patients. Team members typically include medical and radiation oncologists, urologists, radiologists and pathologists in addition to professional multidisciplinary teams[10]. Nowadays, PSA is the most widely-used testing method, and when prostate cancer is suspected, PSA is supplemented by evidence from a digital rectal examination. It has been found that prostate cancer is more likely to be found in males whose IPSS score is high[13]. A biopsy is recommended if the PSA level exceeds 4 ng/ml.

The predictive values for sensitivity, specificity, false-positive, and false-negative severally are 95.8, 66.2, 33.8, and 4.2%. The impediment of PSA testing is that it is a high sensitivity, however a low specificity in giving a detection of prostate cancer which can cause a trouble in clinical practice.

The most common presenting symptoms of patients with prostate cancer vary from asymptomatic, lower urinary tract symptoms (LUTS) of metastasis symptoms such as pathologic fracture or bone pain. A majority of cases are initially identified when conducting PSA along with digital rectal examination (DRE) at screening appointments, or sometimes at a check-up for LUTS. Prostate biopsies typically comprise twelve cores following transrectal ultrasound. It is unusual in Thailand for a transperineal prostate biopsy to be performed. If the PSA level remains high after completion of the initial biopsy, it may be necessary to undergo a second biopsy or Magnetic Resonance Imaging (MRI) -prostate gland. Tantiwong *et al*. featured 928 elderly male participants, with a prostate cancer prevalence of 1.42% with a 95% confidence interval (0.4%-2.5%). To address the issue of cost-effectiveness when conducting prostate cancer screening, those authors advocated the use of DRE at the start of the screening process as a means of improving the overall cost-effectiveness[4]. The use of PSA for prostate cancer check-ups is more common, and males with LUTS are often advised by urologists to undergo PSA testing, which allows cancer to be detected at an earlier stage. Sathitkarnmanee *et al*. examined 129 males aged at

least 45 years, reporting that prostate cancer was found in 6.2% of the participants. The ROC curve analysis indicates that a PSA cut-off level at 4 ng/ml might be appropriate to Thailand for prostate cancer-screening to be carried out[6].

Increased public awareness of prostate cancer has affected in greater interest in check-ups which make use of the PSA test. In Thailand, however, it is difficult to find data concerning the prostate cancer prevalence in those who participate in screenings which would provide important information about their ages and symptoms. This current research study does indicate prostate cancer prevalence using stratification of the data by both symptoms and a range of other relevant factors which include age, Body mass index (BMI), International prostate symptom score (IPSS), Prostate-specific antigen level (PSA), digital rectal examination (DRE), and Quality of Life score (QOL) score.

Methods

The study was cohort study of 350 participants who attended physical health check-ups clinic and PSA screening at University of Phayao Hospital during July to October 2021. The participants were men in good health, aged at least 45 years, who were offered the opportunity to undergo a check-up of the prostate glands. The subjects were all given information about the PSA test, DRE, and prostate cancer. Those who wished to undergo the PSA test were fist invited to complete the checks for IPSS score and QOL score. Consultations for all participants were held with a urologist, and PSA testing was only then carried out with informed consent, along with the digital rectal examination. The participants were given counseling concerning their results for IPSS score, QOL score, and PSA level. Transrectal ultrasound guided biopsy of the prostate (TRUS-biopsy) was offered to those participants whose PSA level exceeded 4.0 ng/ml. A record of the symptoms analysis and cancer detection rate were collected from the pathological reports for further analysis. Patients were classified based on their level of severity of LUTS using IPSS score. The cancer detection rate were presented in the form of a percentage using a 95% confidence interval. Comparisons were drawn between the incidence rates in each group and the Chi-square test was used to perform the analysis. Furthermore, the PSA values for each of the groups were evaluated using the Kruskal Wallis H-test. The Spearman R test was used to assess correlation arising between the Gleason score and PSA level, and P value of less than 0.05 was defined as statistically significant difference.

Results

There were 360 healthy men participating in the healthy physical check-up scheme from the July to October 2021. Analysis of the PSA results from 350 of these participants was performed. The median age was 63 years (45-81); The median IPSS score was 11 (0-32), and median QOL score was 2 (0-6). Meanwhile, the median value for PSA was 1.23 (0.12-125.7) ng/ml, as shown in Table 1 Of 350 patients, 160 patients described themselves as normal voiding, whereas 90 patients and 100 patients responded as uncertain and abnormal voiding, separately.

PSA test presented as abnormal (more than 4 ng/ml) in 40 cases (11.43%). Having been counseled, patients with abnormal PSA decided to undergo TRUS-biopsy of prostate. The 40 abnormal PSA patients, 37 (10.57%) agreed to proceed with TRUS-biopsy. There were 7 (0.02%) patients with abnormal DRE. 6 of these 7 patients had elevated PSA more than 4.0 ng/ml. All of these PSA-elevated patients agreed to proceed with TRUS-biopsy.

Table 1:
Median values of Age, PSA, IPSS, BMI and QOL in studied population

	Median [Min-Max]
Age (years)	63 [45- 81]
PSA (ng/ml)	1.23 [0.12- 125.7]
IPSS	11 [0- 32]
BMI	23.4 [18.2 -32.4]
QOL	2 [0- 6]

26 patients were diagnosed to have prostate adenocarcinoma on biopsy. Prostate cancer was found more common in patients who described themselves as having abnormal urination than in others (Table 1). Stratifying patients into severity of LUTS using IPSS, there was no prostate cancer patient with mild degree of abnormal urination (IPSS less than 8) as shown in Table 2. Median values of PSA and cancer prevalence were shown increased in elderly men (Table 3).

24 out of 26 patients (92.31%) with prostate cancer were found to have localized prostate cancer on routine clinical staging for the cancer. 2 patients already had advanced disease, and they had been treated with hormonal therapy. Out of 24 patients with localized disease, 20 patients encountered laparoscopic radical prostatectomy, one patient encountered open radical prostatectomy, and the other selected other treatment such as radiation therapy or hormonal therapy.

The relationship between the PSA level and the Gleason score was analysed using the Spearman R test, revealing no correlation (Spearman R < 0.7, 95% CI = -0.1- 0.7). (Figure 1.)

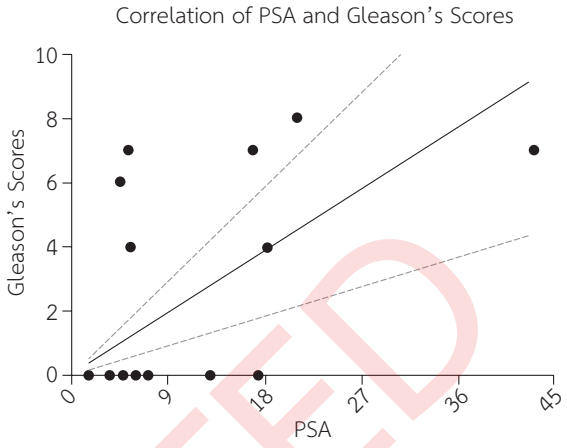

Figure 1: Correlation of PSA and Gleason score

Table 2:
Number of cancer found stratified by urinary symptom described by patients

		Total No.	No. of cancer found	Prevalence %	Prevalence 95%CI	p-value
Patients described their symptoms as	No abnormality	160	3	1.86	0.3-9.4	0.35
	Uncertain	90	8	8.89	3.3-14.5	
	Abnormal urinary symptoms	100	15	15.00	6.2-19.8	
IPSS	Mild (0-7)	160	3	1.88	0.3-9.4	0.10*
	Moderate (8-19)	160	14	8.75	3.1-12.6	
	Severe (20-35)	30	9	30	4.2-42.1	
Age(years)	40-49	55	2	3.64	0.2-7.1	0.27*
	50-59	105	5	4.76	1.7-10.5	
	60-69	133	12	9.02	2.8-26.3	
	70-79	57	7	12.3	3.1-42.1	

*Chi-SquareTest

Table 3:
Shows median values of PSA stratified by age group

Age (years)	Total No.	Median [Min-Max] PSA (ng/ml)	p-value
Mild (0-7)	110	1.14 [0.23-11.40]	0.04*
Moderate (8-19)	173	1.30 [0.18-56.1]	
Severe (20-35)	67	1.91 [0.33-125.7]	

*Kruskal Wallis-H test

Discussion

Since 2004, prostate cancer cases in Thailand have increased from 4.68% to 7.54% in 2021. It may be the case that this change results from dietary and lifestyle changes among the Thai male population, who have lower exercise levels, higher stress, and diets containing more fat. Significantly, the use of the PSA test may also have affected the incidence rate by allowing better detection. However, mass screening using the PSA test is not carried out in Thailand for all healthy males over 45 due to the doubtful cost-effectiveness of the method.

Following the development of PSA test , a significant shift has occurred towards early stage detection or prostate cancer, with Catalona *et al*. noting that the proportion of cases where the disease is discovered at the advanced stage is declining when patients are screened, in contrast to those who do not undergo screening[15]. Meanwhile, it was reported by Roehl *et al*. than around 60% of prostate cancers diagnosed since the introduction of PSA have been clinical T1c tumors; in contrast, before PSA around 70% of cases were found to be clinical T2 or greater[16]. In addition, the incidence rate for distant metastasis has dropped by half over the past ten years[17]. It is normally the case that when prostate cancer is diagnosed in patients at an earlier age, it will involve a tumor in its earlier stages. The effect of age upon the prevalence of early stage tumors was examined by Carter *et al*. who found that younger patients were more likely to have cancer which could still be treated successfully, and therefore the risk of mortality was lower[18]. It was also noted by Smith *et al*. that when prostate cancer is diagnosed in younger patients, this can be an independent predictor of an improved prognosis[19].

PSA screening in symptomatic patients could be favorable. In the present study prostate cancer was found in 1.86% of totally asymptomatic patients. In patients with symptoms, incidence rates have been reported to reach as high as 15%. No cancer cases were found in any participants in this study who had only mild symptoms, defined by IPSS score lower than 8. and the study finding that PSA screening leads to increased prostate cancer diagnoses. Although it is recommended by some clinical practice guidelines, PSA screening remain controversial. It is unclear whether screening improve overall and disease specific mortality, the most critical outcome for patients, or whether the overall benefits of screening outweighs the potential harms and costs of overdiagnosis and overtreatment. PSA screening may increase the detection of localized (Stage I and II) prostate cancer, and PSA screening may modestly decrease the incidence of advanced prostate cancer (Stage III and IV) this corresponded to few men diagnosed with advanced prostate cancer.The major limitation of this study, the reported harm evidence was not based on a comprehensive evaluation of the complications of TRUS-biopsy prostate and tremendous related complications among men who underwent screening versus those who did not.

Conclusion

The prostate cancer prevalence rate at the University of Phayao Hospital in healthy men undergoing PSA screening was reported to be 7.43%. In the present study, prostate cancer detection in asymptomatic patients was 1.86%. Patients with moderate to severe lower urinary tract symptoms were discovered to have more cancer than those without symptoms or mild symptoms, although this did not show significant difference. PSA testing may be provided together with counseling to the patients with moderate to severe lower urinary tract symptoms. Screening of prostate cancer in all men regardless of symptom is not recommended at this stage, as lack of evidences of long term survival benefit, cost-effectiveness of screening, and lastly, better quality of life of patients on a screening program. And a cut off PSA level of 4 ng/ml would be suitable for prostate cancer screening among the Thai population.

Conflict of interest

The authors declare no conflict of interest.

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