Five-Year Follow-up of Prostate Cancer in Siriraj Hospital

SUCHAI SOONTRAPA, M.D.*, ANUPHAN TANTIWONG, M.D.*,
SUNAI LEEWANSANGTONG, M.D.*, THONGCHAI BHANALAPH, M.D.*

Abstract

Objective: To determine the clinical features, tumor characteristics, and treatment outcomes of Thai men with prostate cancer.

Material and Method: We retrospectively evaluated the clinical features, tumor characteristics, and treatment outcomes of 95 patients who were registered in Siriraj Hospital from 1993 to 1995. A survival end point in each stage was determined.

Results: The mean age was 72.37. The distributions of stage were 7.5 per cent for stage A, 1.1 per cent for stage B, 67.7 per cent for stage C, and 23.7 per cent for stage D. The prognosis of a clinical localized disease appeared good. Most patients with a urinary symptom were highly associated with stage C or stage D disease and were treated by hormonal therapy. With a maximal follow-up of 60 months, the median survival of stage C and D patients was 45 and 12 months, respectively.

Conclusion: Most Thai patients with prostate cancer were older than the life expectancy of Thai men. They presented with urinary symptoms and had locally advanced or advanced disease. With hormonal treatment, their prognoses were not impressive.

Key word : Prostate, Prostatic Neoplasm, Carcinoma

SOONTRAPA S, et al
J Med Assoc Thai 2000; 83: 236-242

Despite being the most common visceral malignancy among men in many Western countries, prostate cancer is the ninth most common malignancy in Thai men[1]. The incidence of prostate cancer is 3.8/100,000[1]. This is very low compared to that of Western men[2]. Because of cost effectiveness in a low incidence country, screening by prostatic specific antigen (PSA), digital rectal examination (DRE), or transrectal ultrasound for early detection of prostate cancer has not been widely used in Thailand. The majority of prostate cancer patients registered in our hospital were

* Division of Urology, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

diagnosed with a urinary symptom. At present, there are only a few reports of prostate cancer from Southeast Asia. The data of prostate cancer in men from this region including Thailand are limited in the literature. To determine the clinical features, tumor characteristics, and treatment outcomes of prostate cancer in Thai men, we retrospectively evaluated 95 patients who were registered in our hospital from 1993 to 1995.

MATERIAL AND METHOD

A total of 95 patients with prostate cancer were diagnosed at Siriraj Hospital, Mahidol University, Thailand, from 1993 to 1995. We retrospectively evaluated ages, histories, symptoms, physical examinations including DRE, blood chemistries including PSA, radiographic investigations including chest X-ray, CT scan, or bone scan, histological examinations, and treatment options by their inpatient record forms. Diagnosis was made by histological specimens from either a prostatic biopsy or a transurethral resection prostatectomy (TURP). Staging was determined by the Jewett-Whitmore system[3,4] by use of the DRE, histological specimen of either prostate gland (from prostatic biopsy or transurethral resection) or pelvic lymphnode (from diagnostic lymphadenectomy), and radiological investigations: chest X-ray, pelvic CT scan, or bone scan. The follow-up results were determined from the follow-up record forms and letters sent to the patients or their families to report the present condition of the patients or the date and cause of death if any patient died before the date of evaluation. The survival time in each patient was counted from the first date that the patients received their treatment to the date of evaluation or date of death. The maximal follow-up of these patients was 60 months. To evaluate the results of the treatment, the survival end points in each stage cohort were determined. Kaplan-Meier method was used to calculate the survival end points[5].

The majority of patients, who had locally advanced disease (stage C) or advanced disease (stage D) and could not be treated by definitive treatment, would receive either bilateral orchiectomy monotherapy or bilateral orchiectomy plus antiandrogen therapy. The survival end points of the patients treated with bilateral orchiectomy monotherapy and those treated with bilateral orchiectomy plus antiandrogen therapy were calculated using the Kaplan-Meier method. The comparison of the survival plots was made with using the Logrank Test[5].

Table 1. Clinical features and tumor characteristics of 95 patients.

	%
Age distribution	
40-49	3.2
50-59	8.4
60-69	27.4
70-79	36.8
> 80	24.3
Presentation symptom	
Prostatism	57.5
Urinary retention	17.9
Hematuria	12.7
Bone pain	9
No symptom	8.9
Clinical stage at the presentation	
A	7.5
B	1.1
C	67.7
D	23.7
Tumor differentiation	
well	28
moderate	43
poor	29

RESULTS

The distributions of the ages, presenting symptoms, tumor differentiations, and clinical stages are shown in Table 1. The mean age was 72.37 (sd = 10.84). The most common presentation symptom was prostatism (57.5%) which was defined as urinary frequency, difficult to urinate, dysuria, hesitancy, or the combination of these symptoms. The most common type of pathological tumor was moderate differentiation adenocarcinoma (43%).

To evaluate the treatment results stage by stage, the survival end points were determined. Of 95 patients, 2 were excluded from our analysis due to incomplete data. Of 7 patients with clinical stage A, 3 underwent radical prostatectomy. Only one patient had a pathological organ confined disease (33% organ confined rate). This patient is still alive after follow-up of 26 months after surgery. The other 2 patients had a pathological stage C disease in their radical prostatectomy specimens. Both received adjuvant hormonal therapy immediately after the operation. One patient is still alive after follow-up of 20 months. The other died 12 months after surgery because of other conditions. Four patients with clinical stage A disease were

managed by watchful waiting due to their advanced ages (over 75) or complicated medical conditions. After follow-up of 15 months, all are still alive. Only one patient had clinical stage B disease. At the age of 85, this patient was treated by symptomatic TURP for prostatism. He is still alive after follow-up of 18 months. For the patients treated by watchful waiting, any patient whose diseases progresses will be considered to receive hormonal therapy.

Most patients in our hospital presented with a stage beyond localized disease. Of 63 patients with stage C disease, 59 were treated by immediate androgen ablation therapy, 2 were treated by radiation therapy, and other two were treated by watchful waiting with subsequent androgen ablation therapy if their disease had progressed. Fifty six patients who had prostatism or other urinary symptoms were palliatively managed by TURP. The overall survival graph for stage C patients is shown in Fig. 1. The median survival was 45 months.

For 22 patients with stage D disease, all were immediately treated by androgen ablation therapy. Fifteen patients were symptomatically managed by TURP. The overall survival graph for stage D patients is shown in Fig. 2. The median survival was 12 months and no one survived beyond 60 months.

Several forms of androgen ablation therapy were used in patients with stage C and D diseases but the predominant methods were bilateral orchiectomy and bilateral orchiectomy plus antiandrogen. Bilateral orchiectomy monotherapy was used in 31 patients. To improve survival, bilateral orchiectomy plus antiandrogen was used in the other 42 patients (33 with flutamide and 9 with cyproterone acetate). Kaplan-Meier graphs of the overall survival end points in each treatment cohort, bilateral orchiectomy monotherapy and bilateral orchiectomy plus antiandrogen, are shown in Fig. 3. The outcomes in the combined androgen blockade cohort failed to demonstrate any survival benefit. With the use of the Logrank test in the comparison, no significant difference in the distribution of the overall survival was found ($p > 0.31$).

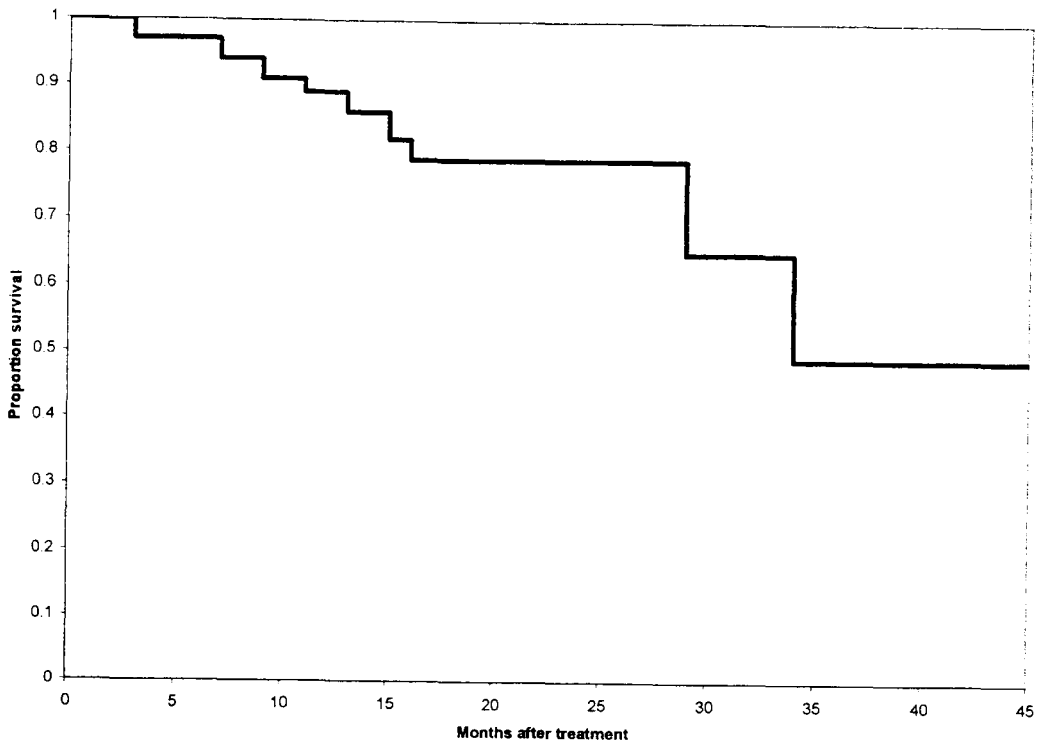

Fig. 1. Kaplan-Meier plots for overall survival in the patients with stage C prostate cancer.

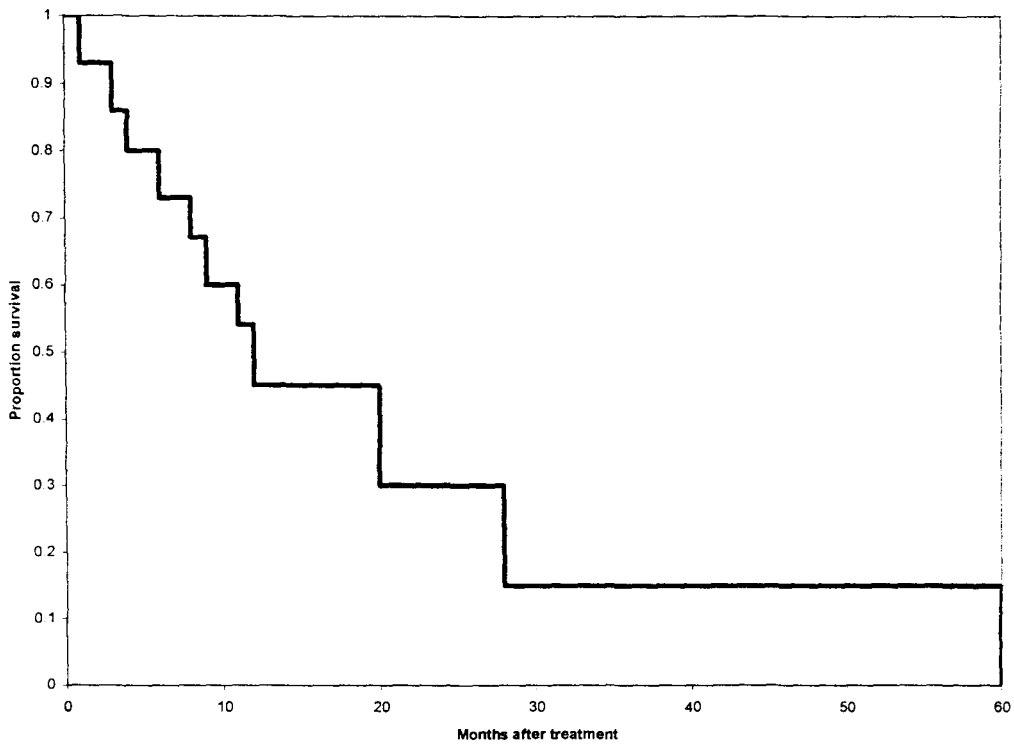

Fig. 2. Kaplan-Meier plots for overall survival in the patients with stage D prostate cancer.

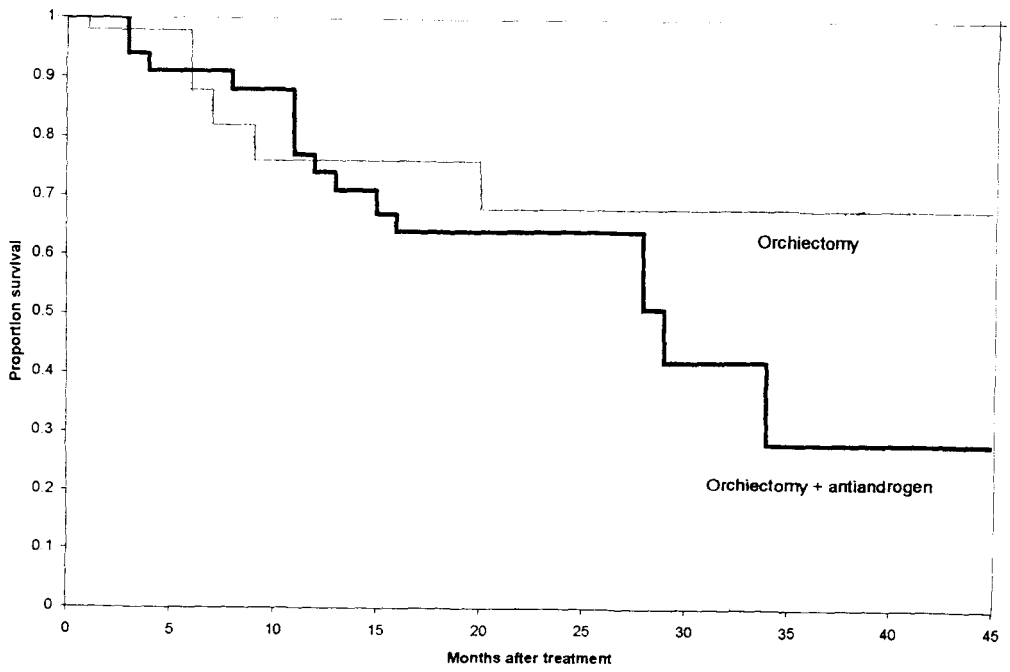

Fig. 3. Kaplan-Meier plots for overall survival in the stage C and D prostate cancer patients treated with bilateral orchiectomy monotherapy or bilateral orchiectomy plus antiandrogen.

DISCUSSION

Prostate cancer incidence is low among Thai men[1]. In several Western countries, the incidences have increased since the PSA era[2]. Even though PSA has been available in our hospital since 1991, the majority of patients still present with locally advanced disease or advanced disease. Of 95 patients, 75 presented with prostatism or urinary retention and eighty per cent of them had clinical stage C or D. All of the patients who suffered from bone pain had clinical stage D. Our data showed that the urinary symptom or bone pain is highly associated with locally advanced or advanced stage of disease. Only 8.9 per cent of the patients who registered in our hospital had no symptom and were diagnosed because of elevated PSA. In addition, only 8.6 per cent had clinical localized disease and 66 per cent of the patients who underwent radical prostatectomy had pathological stage C. Regarding age distribution, we found that only 39 per cent of the patients were younger than 70 years old and only 11.6 per cent of the patients were younger than 60 years old. This indicated that most patients registered in our hospital not only presented at old age but also presented with a stage of disease that could not be cured by definitive treatment.

For patients with clinically localized disease at presentation, the prognosis appears to be good. Eighty seven per cent of the patients are still alive. Only one patient died because of other conditions after 12-months follow-up. However, the survival expectation in localized disease is 10 to 15 years. The longest follow-up in our patients with localized disease was only 26 months. Thus, it is not sufficient to criticize their outcomes because the follow-up period is too short to determine.

Whenever tumors extend beyond the prostatic capsule and could not be totally excised, the patients would not be cured from prostate cancer. For locally advanced or advanced disease, more than 90 per cent of the patients in our hospital were treated by androgen ablation therapy. Hormonal therapy has been the palliative treatment for the past 50 years[6]. Despite high response rates[7], tumors progress to the androgen independent stage[8]. The survival outcome of our patients with stage C and D diseases was unsatisfactory. For stage C, the median survival was 45 months. For stage D, the survival results were extremely poor. The median survival was only 12 months and none of them survived beyond 5 years.

Importantly, while the mean age of the patients with prostate cancer was 72.37, the life expectancy of Thai men from 1990 to 1995 was only 65.85 year old[9]. Considering the mean age and age distribution of our patients with prostate cancer, we found that most patients were older than the life expectancy of Thai men. These figures as well as the low incidence of the disease suggested that prostate cancer might not be a disease that significantly caused the mortality of Thai men in the general population. Even though our data showed that the outcomes of the treatments in most patients who had locally advanced and advanced disease were not impressive, most of them would survive beyond the age of 76 in stage C and 73 in stage D. Extrapolating the data above, we suggest that the use of sereening may be less justified in Thailand where the incidence is low. However, it must be kept in mind that screening data in Thailand does not yet exist.

In our hospital, bilateral orchiectomy is the standard method for androgen castration. Recently, we combined bilateral orchiectomy with antiandrogen to prolong the survival. As illustrated in Fig. 3, the outcome was disappointing. However, we can not conclude this comparison in our data because of several limitations. First, this was not a randomized study and the sample size was small. Secondly, two antiandrogen compounds were used for combined androgen blockade (CAB). There may be some efficacy bias between the two compounds. At present, there is controversy of the survival benefit of CAB compared to the conventional methods among the randomized studies[10]. To improve survival in advanced disease, several investigators advocated CAB strategy for metastatic disease[11]. Some studies showed a significant survival benefit[12,13]. On the other hand, others failed to demonstrate that result[14,15]. Since controversy of the survival benefit of CAB remains unsolved, the value of using CAB is still questionable. The cost of using CAB is higher than using bilateral orchiectomy[10]. For a developing country such as Thailand, regarding survival, cost effectiveness, age distribution, and life expectancy in Thai men as discussed above, we suggest the use of bilateral orchiectomy monotherapy should remain a good option for advanced stage of prostate cancer in Thailand.

SUMMARY

The incidence of prostate cancer in Thailand is low. The majority of patients present aged over 70 and prostatism or urinary retention are highly associated with locally advanced disease or advanced disease. Prostate cancer in men who are younger than 60 years old is uncommon. For patients with clinically localized disease at presentation, prognosis appears very good. For patients with locally advanced disease, the median survival is less than 4 years. For patients with metastatic disease, the prognosis is extremely poor. Seventy per cent died before two years and none survived beyond 5 years. Importantly, the majority of prostate cancer patients presented at an age that is beyond the life expectancy of Thai men. Despite the poor outcomes of the treatment in locally advanced and advanced disease, prostate cancer may not significantly effect the mortality of Thai men in the general population.

(Received for publication on August 19, 1999)

REFERENCES

1. Vatanasapt V, Martin N, Sriplung H, et al. Cancer in Thailand 1988-1991. IARC Techical report No.16, International Agency for Research on Cancer (WHO), Lyon Cedex, France, 1993: 108-9.
2. Landis SH, Murray T, Bolden S, et al. Cancer statistics. Ca Cancer J Clin 1998; 48: 6-29.
3. Whitmore WF Jr. Hormonal therapy in prostate cancer. Am J Med 1956; 21: 679-713.
4. Jewitt HJ. The present status of radical prostatectomy for stage A and B prostate cancer. Urol Clin North Am 1975; 2: 105-24.
5. Dawson-Saunder B, Trapp RG. Methods for analyzing survival data. In Dawson-Saunder B, Trapp RG. Basic & Clinical Biostatistics, 2 nd edn, Connecticut: Appleton & Lange. 1994: 188-209.
6. Huggins C, Hodes CV. Studies of prostatic cancer. 1. The effects of castrations, of estrogen and of androgen injections on serum phosphatases in metastatic carcinoma of prostate. Cancer Res 1941; 1: 293-307.
7. Byar DP, Corle DK. Hormone therapy for prostate cancer: results of the Veterans Administration Cooperative Urological Research Group studies. Nation. Cancer Inst Monogr 1988; 7: 165-70.
8. Bruchovsky N, Rennie PS, Coldman AJ, et al. Effects of androgen withdrawal on the stem cell composition of the Shionogi carcinoma. Cancer Res 1990; 50: 2275-82.
9. Public health statistic A.D. 1992. Central Information Center, Health Statistic Division, Bureau of Health Policy and Plan, Permanent Secretory, Office for Ministry of Public Health, Thailand, March 1994: 19.
10. Leewansangtong S, Crawford ED. Maximal androgen withdrawal for prostate cancer therapy: current status and future potential. Endocrine Related Cancer 1998; 5: 325-39.
11. Labrie F, Dupont A, Belanger A, et al. New hormonal treatment in cancer of the prostate: combined administration of an LHRH agonist and an antiandrogen. J Steroid Biochem 1983; 19: 999-1007.
12. Dijkman GA, Janknegt RA, De Reijke TM, et al. Long-term efficacy and safety of nilutamide plus castration in advanced prostate cancer, and the significance of early prostate specific antigen normalization. International Anandron Study Group. J Urol 1997; 158: 160-3.
13. Crawford ED, Eisenberger MA, McLeod DG, et al. A controlled trial of leuprolide with and without flutamide in prostatic carcinoma. N Engl J Med 1989; 321: 419-24.
14. Prostate Cancer Trialists' Collaborative Group. Maximum androgen blockade in advanced prostate cancer: An overview of 22 randomized trials with 3283 deaths in 5710 patients. Lancet 1995; 346: 265-9.
15. Crawford ED, Eisenberger MA, McLeod DG, et al. Comparison of bilateral orchiectomy with or without flutamide for the treatment of patients with stage D2 adenocarcinoma of the prostate. Results of NCI intergroup study 0105 (SWOG and ECOG). J Urol 1997; 157 (4 suppl):336.

ผลการติดตามการรักษา 5 ปี ในผู้ป่วยมะเร็งต่อมลูกหมากในโรงพยาบาลศิริราช

สุชาย สุนทราภา, พ.บ., อนุพันธ์ ตันติวงศ์, พ.บ.*,*
สุนัย ลีวันแสงทอง, พ.บ., ธงชัย พรรณลาภ พ.บ.**

วัตถุประสงค์: เพื่อศึกษาถึงลักษณะทางคลินิก, คุณสมบัติของเนื้องอก และผลของการรักษาผู้ป่วยมะเร็งต่อมลูกหมากในคนไทย

ผู้ป่วยและวิธีการ: การศึกษานี้เป็นการศึกษาย้อนหลังผู้ป่วย 95 ราย ที่ได้รับการวินิจฉัยว่าเป็นมะเร็งต่อมลูกหมากในปี 2536 จนถึง ปี 2538 โดยการพิจารณาถึงลักษณะทางคลินิก, คุณสมบัติของเนื้องอก และผลของการรักษาโดยพิจารณาจากระยะเวลาที่มีชีวิตอยู่หลังจากการรักษาของผู้ป่วยในระยะต่างของโรค

ผล: อายุเฉลี่ยของผู้ป่วยคือ 72.37 ปี สัดส่วนของผู้ป่วยที่ได้รับการรักษาตามระยะของโรค คือ ระยะ A 7.5%, ระยะ B 1.1%, ระยะ C 67.7%, และระยะ D 23.7% ในผู้ป่วยระยะแรกกล่าวคือ มะเร็งยังอยู่ในต่อมลูกหมากเท่านั้นจะมีการพยากรณ์โรคดี ผู้ป่วยส่วนใหญ่ที่มาด้วยอาการของปัสสาวะลำบากนั้นจะมีอยู่ในระยะ C และ D และได้รับการรักษาด้วยวิธีลดฮอร์โมนเพศชาย จากการติดตามผลการรักษาใน 5 ปี พบว่าระยะเวลามีชีวิตเฉลี่ยในระยะ C คือ 45 เดือน และในระยะ D คือ 12 เดือน

สรุป: ผู้ป่วยไทยส่วนใหญ่ที่เป็นมะเร็งต่อมลูกหมากมีอายุมากและเกินอายุเฉลี่ยของชายไทย นอกจากนั้นผู้ป่วยเหล่านี้มีอาการปัสสาวะลำบาก และอยู่ในระยะที่ลุกลามไปนอกต่อมลูกหมากแล้ว การรักษาด้วยการลดฮอร์โมนเพศชายในผู้ป่วยกลุ่มนี้จะได้ผลการรักษาที่ไม่ดีนัก

คำสำคัญ : ต่อมลูกหมาก, เนื้องอก, มะเร็ง

สุชาย สุนทราภา และคณะ
จดหมายเหตุทางแพทย์ ฯ 2000; 83: 236–242

* สาขาวิชาศัลยศาสตร์ยูโรวิทยา, ภาควิชาศัลยศาสตร์, คณะแพทยศาสตร์ศิริราชพยาบาล, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10700