

# *Radical Prostatectomy and Oral Flutamide for Prostatic Cancer in Pramongkutklao Hospital*

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Serum prostate-specific antigen (PSA) was used as an outcome measure in new patients who were admitted to Urologic Division since January 1993 with prostatic cancer treated with 1) Retropubic radical prostatectomy (RRP) combined with bilateral orchidectomy, and 2) Flutamide combined with bilateral orchidectomy.

The new cases of prostatic cancer from January 1993 to January 1995, were selected into this prospective study to compare the outcome of two modalities of treatment. There were 12 patients who qualified to enter the study. Two forms of treatments were set for those new and untreated cases. There were 6 radical prostatectomies and 6 cases in oral flutamide. All cases were combined treatment with bilateral orchidectomy. Serum PSA was checked after treatment at 1 month, 3 months, and 6 months follow-up. The cost of treatment, complication and side effect of drug were included in the study.

In RRP and bilateral orchidectomy

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group, the mean age was  $68.1 \pm 4.2$  yr, preoperative serum PSA was  $37 \pm 32.7$  ng/ml. The mean age in oral Flutamide plus orchidectomy was  $66.3 \pm 8.8$  yr and serum PSA before starting treatment was  $50.1 \pm 32$  ng/ml. The age and pretreatment serum PSA were comparable in both groups. After the treatment in 1 and 3 months, there was significant difference of serum PSA change. The mean serum PSA in RRP group was 0.06 ng/ml in first month and 0.86 ng/ml in third month, while mean serum PSA in oral Flutamide was 11.8 ng/ml in first month and 6.9 ng/ml in third month of follow-up. At sixth month of follow up, there was reverse serum PSA in both groups. The mean serum PSA in oral Flutamide was 6.1 ng/ml while in RRP was 20 ng/ml. The RRP group

had poorly differentiated cell type in 4 patients and moderately differentiated adenocarcinoma in 2 cases. There were well differentiated adenocarcinoma in 3 cases and 3 moderately differentiated adenocarcinoma in 3 patients of oral Flutamide group.

The radical prostatectomy would be maximum advantage in young age group of prostatic cancer because of significant cure rate and low cost. Oral Flutamide would be the alternative treatment of choice in older patients.

Recent development of management prostatic cancer includes, 1) the success of nerve-sparing radical prostatectomy in early stage of prostate cancer to reduce complication rate of impotence and prolong survival, 2) development of many new anti-androgen drugs, 3) aggressive investigation to early detect prostatic cancer. In Thailand, retropubic radical prostatectomy (RRP) is not a popular procedure because most urologists disquiet about the intraoperative and post-operative complications. Meanwhile many new anti-androgen drugs such as Flutamide, Cyproterone acetate have been introduced for cure prostatic cancer, are more preferable because of the easiness to administer and avoiding operative complications. The purpose of this study is to compare the outcome of these two modalities of treatment between immediate combined RRP plus orchidectomy and orchidectomy with anti-androgen medication. The serum prostatic-specific antigen (PSA) was widely used in part for screening, diagnosis, prognostic and monitoring the cancer of prostate gland. Normal standard value of serum PSA in Pramongkutklao Hospital was 0.4-4 ng/ml.

## MATERIALS AND METHODS

In Pramongkutklao Hospital, there were 41 cases of prostatic cancer record in Urology

Division during January 1993-January 1994. The known cases of prostatic cancer who had been treated by bilateral orchidectomy previously were excluded. Only 17 cases were the new patients. They were diagnosed by transurethral resection in 13 cases and by biopsy after digital rectal examination in 4 cases. Pretreatment work-up before the definite treatment were serum Prostatic Specific Antigen (PSA) and Bone Scan. The five patients who had prostatic cancer stage D2, positive lesions of bone scan study were also excluded as the known cases. Treatment strategy was bilateral orchidectomy combined with retropubic radical prostatectomy (RRP) or bilateral orchidectomy combined with oral anti-androgen (Flutamide). Follow-up examination at 1, 3 and 6 months were done by serum PSA. In the RRP, MRI was performed for staging before starting treatment. The mean value of age and serum PSA of two groups were evaluated by non-parametric type and the Kolmogorov-Smirnov two sample test.

## RESULTS

The number of patients entered in RRP plus orchidectomy was 6 patients and in Flutamide plus orchidectomy was 6 patients. All patients were followed at least 6 months. The maximum duration of follow-up was 24 months.

### *RRP and Bilateral Orchidectomy Group:*

Criteria of RRP operation were, 1) patients were fit for operation, they did not have any major disease or serious conditions, 2) poorly differentiated adenocarcinoma on pathologic report. MRI was used for pre-operative staging of prostatic cancer, but we found 4 cases in 6 (66%) were understaged by MRI. There was positive lymph node in 2 cases (33%). We completed nerve-sparing retropubic prostatectomy in only one case, who had pre-operative serum PSA 4 ng/ml. The rest five cases were with local invasion to the neurovascular bundles. Most of cases who had serum PSA more than 10 ng/ml were upstaged after operation. Table 1 showed stag-



ing in RRP group.

Blood transfusion of two units were needed in all cases except in the case of complete nerve sparing RRP. The hospital stay was about 3 weeks before the retained Foley catheter was removed and cystoscopy was performed. Suprapubic cystostomy was done later in 2 cases because of blood clots retention. However, this suprapubic cystostomy did not delay the convalescence time. Post operative urinary incontinence completely returned to normal in average of 4 weeks. The maximum expense in a state - run hospital was

approximately 40,000 baht which was equal to the cost of Flutamide in only one year. The serum PSA in RRP group was dramatically lowered to undetectable level immediately after complete resection of prostatic cancer. The serum PSA dropped from the average level of 37 ng/ml to 0 ng/ml. There was one case that serum PSA in 6 months rose up 120 ng/ml. This case had metastasis to the lung and died 8 months later. All other cases were in good condition with weight gain and able to return to work as usual. Serum PSA as shown in Table 2 decreased to undetectable level.

**Table 1** Staging of Patients in RRP Group.

Age	Pre Op. Stage	Post Op. Stage	Pathologic	Pre Op. PSA
64 yr	stage A	stage A	Mod. Diff.	4 ng/ml
67 yr	stage B	stage B	Mod. Diff.	26 ng/ml
64 yr	stage A	stage B	Poorly Diff.	15 ng/ml
69 yr	stage A	stage B	Poorly Diff.	35 ng/ml
70 yr	stage B	stage D1	Poorly Diff.	97 ng/ml
75 yr	stage B	stage D1	Poorly Diff.	45 ng/ml

**Table 2** Serum PSA in RRP group.

Pre Rx Serum PSA	Post Rx 1 month	Post Rx 3 month	Post Rx 6 month
4 ng/ml	0 ng/ml	0 ng/ml	0 ng/ml
26 ng/ml	0 ng/ml	0.2 ng/ml	0.2 ng/ml
15 ng/ml	0 ng/ml	0 ng/ml	0 ng/ml
35 ng/ml	0 ng/ml	0 ng/ml	0 ng/ml
97 ng/ml	0.4 ng/ml	1 ng/ml	1 ng/ml
45 ng/ml	0 ng/ml	4 ng/ml	120 ng/ml
37* ± 32.5** ng/ml	0.06* ± 0.16 ng/ml	0.86* ± 1.58 ng/ml	20.2* ± 48.89 ng/ml

\*Mean value, \*\*Standard deviation

### Oral Anti-Androgen (FLUTAMIDE) and Bilateral Orchiectomy

There were 6 cases in this group. Their ages were 66, 69, 70, 64, 69 and 60 year-old respectively. The mean age was slightly younger than the RRP group (66.3 yr. VS 68.1

yr). The pathological report of prostatic adenocarcinoma was well differentiated in 3 cases and moderately differentiated in other 3 cases. The pretreatment serum PSA was averaged at 50 ng/ml. This group had work-up before treatment with bone scan and serum

**Table 3** Cost and Complication of RRP Group.

Blood Transfusion	1.5 ± 0.5 unit
Hospital stay	25 ± 3 days
Post OP Incontinence	Average 4 weeks
Direct cost of treatment	25,000-40,000 Baht (in State-Run hospital)

**Table 4** Pathology and Serum PSA in Oral Flutamide Group.

Age	Pathology	Pre Op PSA	Post Rx PSA 1 month	Post Rx PSA 3 months	Post Rx PSA 6 months
66 yr	Well Diff	40 ng/ml	20 ng/ml	9.5 ng/ml	9.5 ng/ml
69 yr	Well Diff	36 ng/ml	10 ng/ml	4 ng/ml	4 ng/ml
70 yr	Well Diff	1.6 ng/ml	2 ng/ml	2 ng/ml	2 ng/ml
64 yr	Mod. Diff.	70 ng/ml	15 ng/ml	10 ng/ml	5 ng/ml
69 yr	Mod. Diff.	95 ng/ml	20 ng/ml	12 ng/ml	12 ng/ml
60 yr	Mod. Diff.	58 ng/ml	4 ng/ml	4 ng/ml	4 ng/ml
66.3* ± 3.8**		50 ng/ml*	11.8 ng/ml*	6.9 ng/ml*	6 ng/ml*

\*Mean value, \*\*Standard deviation

**Table 5** Comparison of RRP and Oral Flutamide Group.

	RRP + Orchiectomy	Flutamide + Orchiectomy	P
Mean Age	68.1 ± 4.1 yr	66.3 ± 3.8 yr	NS
PSA Pre Rx	37 ± 32.7 ng/ml	50.1 ± 32 ng/ml	NS
PSA Post Rx 1 month	0.06 ± 0.16 ng/ml	11.8 ± 7.8 ng/ml	< 0.05
PSA Post Rx 3 months	0.86 ± 1.58 ng/ml	6.9 ± 4 ng/ml	< 0.05
PSA Post Rx 6 months	20.2 ± 48.8 ng/ml	6 ± 3.8 ng/ml	< 0.05

NS = not significant



PSA, but we were unable to make accurate staging in this group. However, the serum PSA was lowered after treatment significantly. Mean serum PSA 50 ng/ml in pre-treatment was down to 11.8 ng/ml in first month of treatment and 6.9 ng/ml in 3 months and finally in 6 months at 6 ng/ml. The side effects of drug were gynecomastia and GI discomfort in one case. The effect of combination hormonal treatment can maintain serum PSA in normal acceptable range. The cost of treatment was approximately 3,500 baht per month (42,000 baht per year).

## DISCUSSION

The data of both groups were compared to find out their effectiveness. The age and pretreatment serum PSA in both groups were not significantly different. But the outcome of treatment by measuring serum PSA after treatment at 1, 3 and 6 month were significantly different. ( $P < 0.05$ ). The difference of serum PSA was more than 10 ng/ml in the first and third month follow-up. At sixth month, one of the RRP group developed distant metastasis at lung and significantly rising of serum PSA. He was dead 8 months after operation. While in the oral Flutamide group, there was no death during follow-up.

We found that more than 40 per cent of case in group RRP was up-staged than before operation. Physician must be aware of the correct stage of prostatic carcinoma before deciding upon a method of treatment. The desire of accurate staging is still needed to reduce mortality after surgery. Lymphadenectomy with pathological verification may be the best way to avoid unnecessary operation in patient who would not benefit from RRP and this finding showed that surgical treatment only in advanced distant metastasis disease would not prolong survival time.<sup>1-3</sup> However, Chybowski and Oesterling showed serum PSA was the best predictive value only in bone metastasis.<sup>4,5</sup> The early and well localized disease would be maximum advantage by RRP because the cost of treatment was fixed as the cost of drug in one year<sup>6-8</sup> Zincke<sup>15</sup> reported

that combination of RRP with hormonal treatment in stage D1 prostatic cancer could prolong the survival and disease-free interval. The use of oral Flutamide in treating prostatic cancer became rapidly popular because of convenience and acceptable result. We also found good result of stage D2 prostatic cancer in using Flutamide treatment. Serum PSA was used to monitor the recurrence of prostatic cancer.<sup>11-13</sup> Oral Flutamide would be suitable in all older prostatic cancer patients. The combination of hormonal treatment as total androgen blockage and RRP are used in the advanced stage of prostatic cancer.<sup>14,15</sup>

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