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Research Article

Well Responses of Clinical Symptoms and Prostate Specific Antigen Follow up in Advanced Stage Prostate Cancer Patients in One Year Managed by Hormonal Therapy

Zuhirman Zamzami,

M.D, Urologist, Ph.D

Urology Division,Surgery Department, Medical Faculty, Riau University

Abstract:

Purpose: To evaluate the responses of clinical symptoms and prostate specific antigen (PSA) follow up in advanced stage prostate cancer patients in one year of hormonal therapy

Materials and Methods: We reviewed medical records of advanced prostate cancer patients consisting of age, clinical symptoms, digital rectal examination (DRE), PSA levels, Gleason Score (G S) – histopathology grading, bone scan and hormonal therapy, follow up of clinical symptoms and PSA levels in one year of hormonal therapy in Arifin Achmad Regional General Hospital, Pekanbaru, Riau Province, Indonesia. Statistical analysis of univariate was used. Approval on the study was obtained from the Ethical Review Board for Medicine and Health Research, Medical Faculty, University of Riau.

Results: There were 36 advanced stage cancer patients in this study in which mostly (36.1%) in 51-60 and 61-70 year age groups. Most (52.8%) clinical symptom was urinary retension and most (69.4%) DRE was abnormal. Initial PSA levels were mostly (52.8%) > 100 ng /ml. All histopathology findings were adenocarsinoma and the Gleason Score (GS) with histopathology grading were mostly (63.9%) 8 -10 with poorly differentiated. Bone scan showed metastases in 69.4% patients. Management was mostly (63.9%) Androgen Deprivation Therapy. The clinical symptoms was least found until nine months and PSA levels also were normal in nine months of follow up after hormonal therapy.

Conclusion: We found well responses of clinical symptoms and PSA follow up in advanced stage prostate cancer patients in one year managed by hormonal therapy.

Keywords: Hormonal therapy, Advanced stage prostate cancer, Clinical symptom, Prostate Specific Antigen, Follow up.

INTRODUCTION

Prostate cancer is the fourth most frequent cancer of all malignancies in men. About 1.1 million people worldwide were estimated to be diagnosed with prostate cancer by 2012, the estimation number of new cases was around 137.9 per 100 people and nearly 70% of cases occurred in developed country. The incidence of prostate cancer increased worldwide with the highest rate in Australia, America, and in Europe, whereas the lowest rate of prostate cancer occured in Asia [1]. Data of Indonesian Society of Urologic Oncology (ISUO) 2011 during 2006-2010 showed there were 971 prostate cancer patients. The average age was 68.3 years old and this case mostly occur in age group 70-79 (37.6%). Diagnostic modalities used for this case, especially biopsy, counted for 563 cases (57.9%). Patients were mostly (50.5%) found in advanced stage [2].

The choice of prostate cancer treatment depends on several aspects: tumor grading, staging, co-morbidity, patient preference, life expectancy at diagnosis, and the Prostate Specific Antigen (PSA) level in the blood. Hormonal therapy was introduced by Huggins and Hodges in 1941 to treat advanced stage prostate cancer and is used until now for primary treatment of prostate cancer [3,4,5]. Hormonal therapy is an option for high grade prostate cancers (53.8%) and is often selected in older patients [6]. Bilateral subcapsular orchiectomy is still the most widely used initial therapy for 307 cases (31%). Anti-androgen drugs were used on 182 patients (18%), radical prostatectomy were used in 89 patients (9%), radiotherapy were used on 63 patients (6%) and the rest are active monitoring, chemotherapy and combination therapy [7]. Hormonal therapy should be followed up to detect disease progression. The purpose of follow-up is to monitor therapeutic response, detect therapeutic compliance, detect complications of hormonal therapy. A minimum follow-up time was 3-6 months after the hormonal therapy began. Examination of PSA levels, serum testosterone, and symptom evaluation were done to assess therapeutic response [1].

Data showed the incidence of advanced stage prostate cancers increases with the chief management is hormonal therapy [8]. We were interested in evaluating the follow-up of clinical symptoms and PSA levels in advanced prostate cancer patients managed by hormonal therapy in Arifin Achmad Regional

General Hospital, Pekanbaru, Riau Province, Indonesia in 2010-2016.

MATERIALS AND METHODS

We reviewed medical records of all advanced stage prostate cancer patients of Arifin Achmad Regional General Hospital Pekanbaru Riau Province in January 2010 until December 2016. The data collected consisted of age, clinical symptoms, digital rectal examination (DRE), prostate specific antigen (PSA) levels, Gleason Score (GS) with histopathology grading, bone scan, hormonal therapy such as androgen deparivation therapy (ADT), bilateral orchiectomy, and combination of ADT with radiotherapy, follow-up of clinical symptoms and follow-up of PSA levels in the month 3 rd, 6 th, 9 th and 12 th after the hormonal therapy. Statistical analysis of univariate was used. Approval on the study was obtained from the Ethical Review Board for Medicine and Health Research, Medical Faculty, University of Riau.

RESULTS

Table 1. Frequency distribution of in advanced prostate cancer patients according to age

Age group (year)	N	f (%)
41-50	1	2.7
51-60	13	36.1
61-70	13	36.1
71-80	6	16.6
81-90	3	8.3
TOTAL	36	100

Table 2. Frequency distribution of in advanced prostate cancer patients according to clinical symptoms

Clinical Symptom	N	f(%)
LUTS	15	29.4
Urinary Retension	21	41.2
Hematuria	8	15.7
Pelvic bone pain	7	13.7
Total	51	100

Table 3. Frequency distribution of in advanced prostate cancer patients according to digital rectal examination (DRE)

DRE	N	f(%)
Normal	11	30.6
Abnormal	25	69.4
Total	36	100

Table 4. Frequency distribution of in advanced prostate cancer patients according to PSA level in advanced prostate cancer patients

PSA level (ng/ml)	N	f(%)
≤ 4	2	5.5
4.01 – 10	3	8.3
10.1 – 20	3	8.3
20.1 – 50	6	16.7
50.1 – 100	4	11.1
> 100	19	52.8
Total	36	100

Table 5. Frequency distribution of advanced stage prostate cancer patients according to histopatology grading with Gleason Score (G S) in advance prostate cancer patients

G S (Histopathology grading)	N	f(%)
2 – 4 ***(well differentiated)***	4	11.1

5 – 7 *(moderately differentiated)*	9	25
8– 10 *(poorly differentiated)*	23	63.9
Total	36	100

Table 6. Frequency distribution of advanced prostate cancer patients according to bone scan findings

Bone Scan		**f (%)**
Wihout Metastasis	1	30.6
Metastasis	5	69.4
Total	5	100

Table. 7 Frequency distribution of advanced prostate cancer patients according to Androgen Deprivation Therapy (ADT)

Hormonal Therapy		**f (%)**
ADT	3	63.9
Bilateral Orchidectomy	)	27.8
ADT + Radiotherapy		8.3
Total	5	100

Table. 8 Frequency distribution of clinical follow up in advanced prostate cancer patients after Androgen Deprivation Therapy(ADT).

Clinical symptoms	**After ADT**	**Month -**			
		3rd	6th	9th	12th
LUTS	9 (25%)	11 (68.7%)	8 (80%)	5 (100%)	0 (0%)
Urinary retension	19(52.8%)	2 (12.5%)	0 (0%)	0 (0%)	0 (0%)
Hematuria	3 (8.3%)	3 (18.7%)	2 (20%)	0 (0%)	0 (0%)
Bone pain	5(13.8%)	0(0%)	0 (0%)	0 (0%)	0 (0%)
Total	36 (100%)	16 (100%)	10 (100%)	5 (100%)	0 (0%)

Table 9. Frequency distribution of in advanced prostate cancer patients according to Prostate Spesific Antigen (PSA) levels

PSA level	**Initial PSA level**	**PSA level after month-**			
		3th	6th	9th	12th
≤4	2 (5.5%)	8 (22.2%)	22 (61.1%)	32 (88.9%)	36 (100%)
4.1-10	3 (8.3%)	13 (36.1%)	10 (27.7%)	4 (11.1%)	0 (0%)
10.1-20	3 (8.3%)	10 (27.7%)	4 (11.1%)	0 (0%)	0 (0%)
20.1-50	6 (16.6%)	2 (5.5%)	0 (0%)	0 (0%)	0 (0%)
50.1-100	4 (11.1%)	3 (8.3%)	0 (0%)	0 (0%)	0 (0%)
>100	18 (50%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	36 (100%)	36 (100%)	36 (100%)	36 (100%)	36 (100%)

DISCUSSION

There were 103 adenocarcinoma of prostate consisting in which 36 patients were advanced stage prostate cancer in this study. Advanced stage prostate cancer patients mostly (36.1%) in 51- 60 and 61- 70 year groups, and the lowest (2.8%) in age group 41-50 years (See in Table 1). Mostly (52.8%) clinical symptoms of advanced prostate cancer patients were urinary retension followed by lower urinary tract symptoms (LUTS) 25%, bone pain 13.9% and hematuria 8.3% (See in Table 2). Mostly (69.4%) abnormal prostate findings (hard noduls) were found in DRE findings but there were 30.6% normal prostate findings in DRE (See in Table 3). Mostly (50%) the PSA level in this study > 100 ng/ml, 42.4% in PSA level 4 -100 ng/ml but there were 5.5 % of the PSA level below 4 ng/ml (See in Table 4). Mostly (63.9%) Gleason Score were 7-10 with histopathology grading poorly differentiated in this (See Table 5). The presence of metastasis was 69.4% in bone scan findings but there was 30.6% bone scan findings without metastasis in the advanced stage prostate cancer patients (See in Table 6).

Mostly (63.9%) Androgen Deprivation Therapy (ADT) was managed by advanced stage prostate cancer patients followed by bilateral orchiectomy (27.8%) and ADT with radiotherapy (8.3%) (See in Table 7). In month 3rd follow up of clinical symptoms in advanced stage prostate cancer patients with hormonal therapy there were increasing of LUTS (68.7%),

decreasing of urinary retension (12.5%) and hematuria (12.5%) but without bone pain symptom. In the month 6th follow up of clinical symptoms in advanced staged prostate cancer patients with hormonal therapy showed there were no symptoms of urinary retension nor bone pain but there were LUTS and hematuria. In the month 9th follow up of clinical symptoms in advanced staged prostate cancer patients with hormonal therapy showed there was only LUTS. In month 12th follow up showed all patients were without clinical symptoms (See in Table 8).

The PSA level after managed by hormonal therapy began to decrease in month 3rd follow up and even there was no PSA level more than 100 ng/ml but mostly becoming 50 ng/ml and below. The PSA level after managed by hormonal therapy decrease in month 6th follow up mostly becoming 10 ng/ml and below. The PSA level after managed by hormonal therapy decrease in month 9th follow up mostly becoming below 4 ng/ml. The PSA levels after managed by hormonal therapy decrease in month 12th follow up were`all within normal limit (See in Table 9).

DISCUSSION

There were 103 adenocarcinoma of prostate consisting in which 36 patients were advanced stage prostate cancer included in this study. Table 1 showed advanced stage prostate cancer patients mostly (36.1%) in 51- 60 year group and also 36.1% in 61-70 year group, and the lowest (2.8%) in age group 41-50 years (See in Table 1).Prostate cancer generally affects men over 50 years of age. The results of this study were similar to a study by Glady et al (2015) [8].

Mostly (52.8%) clinical symptoms of advanced stage prostate cancer patients were urinary retension followed by lower urinary tract symptoms (LUTS) 25%, bone pain 13.9% and hematuria 8.3% (See in Table 2). One patients might suferred from more than one symptoms. This study showed that most patients were in the advanced stages. Most prostate cancers in developing countries are often diagnosed at an advanced stage. A study by Mahadi (2009) that said prostate cancer patients came with LUTS as the chief complaint but with varying symptoms [9].

The finding of abnormal DRE in the form of hard nodules is an indication of prostate biopsy needed to make the diagnosis. Although it is not 100% accurate, DRE as a basic prostate cancer examination is important. In this study, mostly (69.4%) abnormal prostate findings were found in DRE findings but there were 30.6% normal prostate findings in DRE (See in Table 3). A study by Schroder et al (1998) in 473 prostate cancer patients 55.8% found abnormal DRE findings [10].

PSA is an important marker in diagnosis, follow-up, and determining prognosis for prostate cancer. Advanced stage prostate cancer incidence at baseline PSA > 100 ng/ml was higher than in the PSA group in the 0-99 ng / ml range [11]. Mostly (50%) the PSA level in this study > 100 ng/ml, 42.4% in PSA level 4 -100 ng/ml but there were 5.5 % of the PSA level below 4 ng/ml (See in Table 4). Similar results obtained by Umbas et al (2011), there are 190 patients with advanced prostate cancer with PSA over 100 ng / ml or in 66.5% of all prostate cancer patients at Cipto Mangunkusuma Hospital and Dharmais Cancer Hospital Jakarta, Indonesia from January 1995 to December 2007 [11].

A grading system with a Gleason Score (G S) is often used to help distinguishing the histologic characteristics of prostate cancer. Grade 1-5 is a marker of tumor gland architecture. The degree of histology of the prostate gland was determined in the G S and divided into 3 gradings namely well, moderately, poorly differentiated. In this study, the degree of histopathology in advanced prostate cancer patients in our hospital was mostly poorly differentiated (GS: 7-10) in 63.9% patients, and lowest (11.1%) was well differentiated (GS: 2-4). This result was lower than by Putriyuni et al (2010) found the histopathology grading in most (86.6%) prostate cancer patients were poorly differentiated in 76 cases [12].

Prostate cancer is a malignancy in urology resulting in most (65 – 75%) bone metastasis compared to other metastasis. The standart bone metastasis diagnosis currently used is bone scan examination with 99m Tc methilen diphosponat (MDP) [3]. In this study, the result of bone scan examinations in advanced stage prostate cancer patients in our hospital showed 69.4% with positive metastasis but 30.6% with negative metastasis. This study suited the theory explaining that mostly (70%) advanced stage prostate cancer patients metastasis were to bones especialy to lumbar vertebrae and pelvic bone. The metastatic pathogenesis of prostate cancer to the bones due to the presence of a venous vascular plexus from the prostate to the vertebrae called the Batson plexus [14].

Hormonal therapyis the first-line standard management of advanced stage prostate cancer patients currently used. In our study, advanced prostate cancer patients mostly (63.9%) managed by ADT, 27.8% by bilateral orchidectomy and 8.3% by ADT with radiotherapy [3,8]. The management of hormonal therapy for advanced-stage prostate cancer is the primary choice. A study by Fellow et al (1992) proved that orchiectomy might reduce the risk of distant metastases in patients with prostate cancer [15]. Similar study conducted by Akaza et al (2006) showed that ADT therapy might slow the progression of disease in advanced stage prostate cancer [16].

Clinical symptoms needed to be assessed are lower urinary tract symptoms (LUTS), urinary retension, hematuria and bone pain [17]. Follow-up of the clinical symptoms is mandatory. Patients should be seen regularly to check for possible symptoms of the problem. Advanced stage prostate cancer patients are important for examining the possibility of early symptoms of spinal cord compression, In month 3rd follow up of clinical symptoms in advanced stage prostate cancer patients with hormonal therapy there were increasing of LUTS (68.7%), decreasing of urinary retension (12.5%) and hematuria (12.5%) but without bone pain symptom. In the month 6th follow up of clinical symptoms in advanced stage prostate cancer patients with hormonal therapy showed there were no symptoms of urinary retension nor bone pain but there were LUTS and hematuria. In the month 9th follow up of

clinical symptoms in advanced staged prostate cancer patients with hormonal therapy showed there was only LUTS. In month 12th follow up showed all patients were without clinical symptoms (See in Table 8). We suggest that the clinical symptom follow up in advanced prostate cancer patient might be enough for 12 months after managing by hormonal therapy. Prostate-specific antigen (PSA) is a good marker for prostate cancer follow-up. Thet treatment response can be assessed by using serum PSA level changes as a surrogate endpoint for survival in newly diagnosed prostate cancer metastasis patients. PSA levels can help show how the responses of prostate cancer treatment are, although not only from PSA levels but also from clinical symptoms. The follow-up results of PSA level after managing by hormonal therapy began to decrease in month 3 and the PSA level became in normal limit month 12 in our hospital. This study supports that the management by hormonal therapy for advanced stage prostate cancer patients result in the PSA level back to normal [19,20]. The weakness of this study might be that we did not differentiate the results of clinical symptoms and PSA level follow up in each of the three kinds of hormonal therapy.

CONCLUSION

We found well responses of clinical symptoms and PSA follow up in advanced stage prostate cancer in one year after managed by hormonal therapy**.** We suggest that the clinical symptoms and PSA levels follow up in advanced prostate cancer patients might be enough for 12 months after managed by the hormonal therapy.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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