RESEARCH ARTICLE

Prostate Cancer in Younger and Older Patients: Do We Treat Them Differently?

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Abstract

Diagnostic and therapeutic strategies of prostate cancer may largely influenced by patients' age at presentation. This study is aimed to evaluate the characteristics, diagnostic and treatment strategies in prostate cancer patients in our centres. A cross-sectional analytic study of prostate cancer data in two main referral cancer centres, Cipto Mangunkusumo General Hospital and Dharmais National Cancer Centre from 1995-2010, was therefore performed. Patients were divided into 2 sub-populations; below 60 years (younger patients) and 75 years old and above (older patients). PSA levels, diagnostic modalities, Gleason score and therapeutic options were analysed for both and compared using bivariate analysis. 152 patients were <60 years and 210 were ≥75 years. There was no statistical difference in mean PSA level (797.9ng/mL vs 345.3 ng/mL, respectively; p>0.05) and diagnosis was made by biopsy in majority of patients in both groups (68.2% and 71.6% in younger and older groups respectively). Most presented with an advanced disease stage (65.1% and 66.0%, respectively) and there was no statistically significant difference in mean Gleason scores f (8.1 vs 7.7; p>0.05). Primary androgen deprivation therapy (PADT) was the main treatment for overall patients (48.0% and 50.7%, respectively). Radiotherapy and radical prostatectomy are the main therapeutic modalities for younger patients with local and locally advanced disease (39.6% and 35.4% respectively), while the majority of older patients with the same disease stage were treated with radiotherapy and PADT (45.8% and 39.0% respectively). Differences observed in treatment modalities were statistically significant (p<0.0003). We conclude that there is no difference in disease clinical aggressiveness of the two groups but significant differences were obseved in therapeutic strategies utilised with younger and older patients.

Keywords: Prostate cancer - young - elderly - treatment - clinical agressiveness - Indonesia

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Introduction

It is acknowledged that prostate cancer occurs predominantly in elderly patients, with peak incidence occurring between the ages of 70 and 74 years (Klein et al., 2007). Nevertheless, studies have documented an age migratory pattern toward an increase of prostate cancer cases in younger age groups (50-59 years)and though rarely in age groups below 40 years (Yang et al., 2010). National data documented in the participating two centres in this study, revealed peak incidence of prostate cancer diagnosis is in population between 66-72 years (Umbas ., 2005). This may mainly contributed to the widespread adoption of prostate-specific antigen (PSA) testing, which has also led to escalating proportion of men being diagnosed with early stage and low or intermediate grade prostate cancer (Wong et al., 2006; Astigueta et al., 2010; Yang et al., 2010)

As the number of diagnosis being made increased in younger population, many issues arise in relation to tumour aggressiveness, diagnostic and therapeutic strategies. Although uncommon, prostate cancer in younger individuals is associated with atypical clinical presentation, more aggressive pathologic findings and poorer outcomes (Astigueta, 2010; Li et al., 2011). Regardless of the facts mentioned above, only little is documented considering the pattern, clinical behaviour and outcomes of prostate cancer in younger individuals. The adjustments and alteration made in the diagnostic or therapeutic strategies have also not been reported well.
Equivalently, the discussion on prostate cancer in elderly population also raised many issues and controversies. A number of literatures documented how management of localised prostate cancer is considered sub-optimal especially in senior adults population[8]. Thus, many have questioned the role of primary hormonal treatment in elderly patients with localised or locally advanced disease (Berger et al., 2009; Cooperberg and Konety, 2009; Droz et al., 2010) Despite such findings, there is currently no well-documented data available in stratifying tumour

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characteristics, diagnostic strategies or treatment options in this group of patients.

This paper is aimed to evaluate the diagnostic and treatment strategies, which have been used in prostate cancer patients in our centres. Through such evaluation, we would be expected to see pattern in the differences of diagnostic modalities and management strategies in younger and older individuals diagnosed with prostate cancer.

Materials and Methods

Study Design

This is an analytical study, which is conducted cross-sectionally to describe possible differences in patients' characteristics, presentation of disease, disease progression as well as diagnostic and treatment strategies in younger patients (below 60 years old) and older patients (75 years old and above) with prostate cancer.

Study Population

Study population includes all patients with prostate cancer presented to Department of Urology, Cipto Mangunkusumo Hospital and Departement of Urology, Dharmais National Cancer Centre Hospital from 1995-2010. Patients will be classified in accordance to their age at diagnosis into two groups; younger patients, which include patients with age at diagnosis below 60 years and older patients, which include those with age at diagnosis 75 years old and above.

Procedures

Patient presenting with clinical signs and symptoms of prostate cancer underwent a thorough clinical history taking and physical examination. This was followed by PSA total level measurement. Biopsies were performed trans-rectally to cases, in which prostate cancer is suspected. This is evident from PSA level above 4ng/mL or digital rectal findings suggestive of prostate cancer. In cases where prostate cancer was not suspected, patient directly underwent trans-urethral resection of prostate or open prostatectomy as indicated. The pathologic diagnosis of prostate cancer was made from specimens obtained by biopsies, TURPs and open prostatectomies. Data were obtained from medical records in the two participating centres.

Variable Identifications

Independent variable in this study age at diagnosis. The data were then reviewed for PSA level at the time of diagnosis, diagnostic modalities used, pathologic scoring, disease stage at presentation and therapeutic options chosen as dependent variables.

Data Analysis

Descriptive data includes patients' demographic and disease characteristics. The data were then analysed as comparative proportion (bivariate analysis) in order to detect any statistically significant characteristics in both younger and older sub-populations. Analysis results with p value<0.05 were regarded as statistically significant.

Results

From 1995 to 2010, 503 patients within the designated age groups were documented. These patients were divided into two subpopulations; those who were below 60 years of age (152 patients) and those who 70 years of age and above (210 patients) at the time of diagnosis.

PSA levels were measured in all patients. Overall mean PSA level in our patients was 461.22 ng/mL (median 60.9). Mean PSA in younger patients was higher, although not significantly different than in older patients (797.90ng/mL, median 62.6 vs 345.30 ng/mL, median 57.4; p>0.05). Diagnosis of prostate cancer was made based on histopathology findings of specimens obtained fromtrans-rectal prostate core biopsy, transurethral resection (TURP) or open prostatectomy. The proportion of diagnostic modalities utilised in both subpopulations is described by Table 1.

Most patients in both groups came in an advanced stage (65.1% and 66%) for younger and older subpopulations respectively. Comparison of disease stage at presentation in both subpopulations revealed no statistically significant difference (p>0.05).

Mean Gleason score in younger group is 8.1 (median 9.0; range 4-10) and in older group is 7.7 (median 8;

Table 1.

No. of	<60 years	>75 years
Study Sub-Populations		
No. of patients	152 patients	210
Median	55 years	78
Range	23-59 years	75-92 year
Diagnostic Modalities (TUR-P = Trans- Urethral Resection of Prostate		
TUR-P	46 (31.3%)	52 (25%)
Biopsy	105 (68.2%)	151 (71.6%)
Open prostatectomy	1 (0.7%)	7 (3.4%)
Disease Stage at Presentation (Based on AJCC Staging System for Prostate Cancer)		
Disease stage at presentation		
1	1 (0.7%)	2 (1%)
2	40 (26.3%)	50 (23.9%)
3	8 (5.3%)	7 (3.3%)
4	99 (65.1%)	138 (66%)
Incomplete	4 (2.6%)	13 (5.7%)
Therapeutic options (data for all patients; stage 1 - 4)		
RP	18 (11.8%)	0
RT	19 (12.5%)	27 (12.9%)
PADT	74 (47.3%)	106 (50.7%)
WW	5 (3.3%)	5 (2.4%)
CT	19 (12.5%)	55 (26.3%)
Refused	17 (11%)	17 (7.7%)

Table 2. Therapeutic Modalities (Data for Stage 1-2 Patients Only and Stage 1, 2 and 3 Patients Only)

	St.I and II		St. I, II, III	
	<60	>75	<60	>75
RP	17 (41%)	1 (1.2%)	17 (35.6%)	0
RT	16 (40%)	46 (50.0%)	19 (39.6%)	27 (45.8%)
PADT	2 (5%)	35 (38.4%)	5 (10.4%)	23 (39.0%)
WW	0	4 (4.9%)	0	3 (5.1%)
CT			0	4 (6.8%)
Refused	6 (15%)	45 (6.1%)	7 (14.6%)	2 (3.4%)

range 4-10) respectively. The difference in Gleason score between both groups is not statistically significant (p >0.05).

Therapy modalities were grouped into the following; watchful waiting (WW), open/laparoscopic radical prostatectomy (RP), radiotherapy (RT), primary androgen deprivation therapy (PADT) and chemotherapy (CT). Minority of patients refused to underwent any therapy (14.6% and 3.4% in younger and older subpopulations respectively).

Almost half (47.3%) patients who were below 60 years received primary hormonal therapy as the main modality of treatment. A slightly greater proportion is also seen in the older patients (50.7%). Radical prostatectomy was performed in 18 cases (11.8%) in younger subpopulation, while none was performed in older subpopulation. Fifty-five patients (26.3%) in older subpopulation received secondary chemotherapeutic agents, while only 19 patients (12.5%) received the same therapeutic modality in younger subpopulation.

Patients with organ-confined disease (stage 1, 2 and 3) at the time of diagnosis were analysed profoundly for their choices of therapeutic modalities.

Radiotherapy and prostatectomy were the most form of therapy performed in population below 60 years (39.6% and 35.4% respectively). In older population, radiotherapy was also performed in the majority of patients (45.8%), followed by primary androgen deprivation therapy (39%). These differences in proportion are all statistically significant (p = 0.003).

When the data was stratified to include only patients with stage 1 and 2 diseases (local disease), similar findings were observed as shown in Table 2.

Discussion

As documented in most literatures (Klein et al., 2007; Li J et al., 2011), both centres involved in this study also experienced an increasing trend of prostate cancer diagnosis. However, this pattern of increase is unlikely to be the result of widespread adoption of PSA testing alone. This is reflected in the characteristics of the majority of our patient, who distinctly came to seek for medical care in an advanced disease stage. Moreover, the means PSA level in both younger and older groups are 797.90 ng/mL and 317.37 ng/mL respectively. Such high means of PSA levels are indicative of advanced disease stage or metastatic prostate cancer.

Newcomer et al. concluded that the introduction of PSA testing results in the increase in the incidence of local-regional disease and the decrease in the incidence of metastatic disease (Newcomer et al., 1997). Similar finding is also documented by Derweesh et al., stating that non-palpable cancers (AJCC clinical stage pT1C) currently account for 75% of newly diagnoses disease (Derweesh et al., 2004). The fact that the number of pT1C cases is increasing in other centres in relation to escalating incidence of prostate cancer is therefore not the case in our centres. Data reported by Umbas et al. recorded only a minor increase in the number of pT1C cases.The number of prostate cancer presented in an advanced stage still hold a major proportion in spite of the increase in early prostate cancer detection an the widespread adoption of PSA screening.

This is reflected on the fact that most of our patients were detected with stage 4 disease at the time of diagnosis (65.1% of patients below 60 years and 64.9% of patients above 70 years). Astigueta et al. reported that advanced prostate cancer is uncommon in young adults (below 50 years) (Astigueta et al., 2010). In contrary, both centres in this study observed a large number of younger patients presented in an advanced stage, although the age cut off point used in the study is 10 years older (below 60 years). Our finding is similar to case report by series of case reports by Kanto et al. (2002), Suzuki et al. (2004) and Sasaki et al. (2004) (Kanto et al., 2002; Sasaki et al., 2004; Suzukui et al., 2008). Kanto et al. reported only one case that was thought curable, in which the patient's cancer was detected by chance occult blood test (Kanto et al., 2002).

The diagnosis of prostate cancer is mainly made from prostate biopsy specimens for both subpopulations, as both centres adopt the same policy of performing trans-rectal prostate core biopsy in patients with PSA level of more than 4 ng/mL or in any patients whom digital rectal examination results were suggestive of prostate malignancy.In a small number of cases diagnosis of prostate cancer was obtained from trans-urethral resection of prostate (31% in younger age group and 24% in older age group) and open prostatectomy (0.7% in younger age group and 2.9% in older age group). Recall that the range of PSA levels in our study extend from 0.2 – 60,350 ng/mL. Patients presented with PSA levels below 4 ng/mL and normal digital rectal examination would have directly underwent TUR-P or open prostatectomy.

Gleason score has long been accepted as a powerful predictor of prostate adenocarcinoma behaviour and disease progression (Benaim et al., 2002; Herman et al., 2002). It is regarded as a fundamental determinant of disease biology and prognosis (O'Dowd et al., 2001). Mean Gleason score in younger and older group in this study is 8.1 (median 9.0; range 4-10) and 7.5 (median 7; range 2-10) respectively. Mean Gleason score in our younger population is significantly higher compared to our older patients (p=0.019). This is in accordance to the results reported by most authors, which stated that prostate cancer in younger individuals would have poorer prognosis and more aggressive biological behaviour (Jadeja et al., 1994; Kanto et al., 2002; Sasaki et al., 2004; Suzuki et al., 2008; Astigeuta et al., 2010).

The overall number of radical therapy (radical prostatectomy and radiotherapy) in our centres is relatively low (11.8% in younger individuals and 0.2% in older individuals). This is an implication of the low detection rate of diseases in early stage (local regional disease). As most patients came with stage 4 diseases, the proportion of patient underwent primary hormonal treatment in both younger and older sub-populations are equally high (47.3% and 48.7% respectively). Radiotherapy is utilised in 12-13% of both sub-populations (for all ages).

Early stage diseases in both sub- populations were analysed separately to see the differences in our management strategies. Literatures suggested that younger

patients with early stage disease are the most suitable candidates for radical prostatectomy (Astigueta et al., 2010). This is also reflected in our findings, where 41% of our younger patients with early disease stage underwent radical prostatectomy. Radiotherapy, however also appears as one of the therapeutic mainstay in this group of patients. Unfortunately, no reasons other than the patients' preference could be related to such result.

In contrary, radical prostatectomy is no longer the main option of therapy in older individuals. The procedure was performed in only 1 case of our older patients with early disease stage. Radiotherapy is selected as the main therapy in half of our older patients population, followed by primary hormonal treatment in 38%. These results are in line with current reports, where androgen deprivation therapy is described as an effective choice of therapy (Stangelberg et al., 2008; Cooperberg et al., 2009). Although watchful waiting is increasingly considered as an option (Stangelberger et al., 2008; Berger et al., 2009), our data revealed only 4.9% of patients were managed conservatively. This is attributable to the large number of high-grade tumour as reflected by the high mean of Gleason score, thus higher likelihood of aggressive disease progression.

There are additional points that could make this study better. Identification of risk factors, especially in younger subpopulation would allow us to analyse whether PSA level screening in high-risk individuals will have significant benefits as suggested by many. Another weakness of this study is the unavailability of prostate cancer specific survival.

In conclusion, the incidence of prostate cancer in both centres involved in this study is increasing, although a large proportion of patient were still presented in an advanced stage of disease. Gleason score is significantly higher in younger population with prostate cancer, thus indicate a more aggressive disease clinical behaviour. There are significant differences in therapeutic strategies in younger and older patients. This indicates that age alone has influenced our selection of therapeutic modalities. Further survival analysis is an important aspect the needs to be done in the future.

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