RESEARCH ARTICLE

Prostate Cancer: A Hospital-Based Survival Study from Mumbai, India

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Abstract

<u>Background</u>: Prostate cancer is common in elderly men, especially in western countries, and incidences are rising in low-risk populations as well. In India, the age-standardized rates vary between registries. Under these circumstances we have estimated the survival of prostate cancer patients based on age, family history, diabetes, hypertension, tobacco habit, clinical extent of disease (risk group) and treatment received. <u>Materials and Methods</u>: The present retrospective study was carried out at the Tata Memorial Hospital (TMH), Mumbai, India. During years 1999-2002, some 850 prostate cancer cases, including 371 new cases, treated in TMH were considered as eligible entrants for the study. Five-year survival rates using actuarial and loss-adjusted (LAR) method were estimated. <u>Results</u>: The patient population was distributed uniformly over the three age groups. A larger proportion of the patients were diagnosed at 'metastatic stage' and hormone treatment was most common. 20% patients had history of diabetes and 40% with hypertension. The 5-year overall survival rate was 64%. Survival was 55%, 74% and 52% for '<59 years','60-69 years' and '>70 years' respectively. Non-diabetic (70%), hypertensive (74%), with family history (80%) of cancer, with localized-disease (91%) and treated with surgery, either alone or in combination, (91%) had better survival. <u>Conclusions</u>: The present study showed that prostate cancer patients with localized disease at diagnosis experience a better outcome. Local treatment with either surgery or radiation achieves a reasonable outcome in prostate cancer patients. A detailed study will help in understanding the prognostic indicators for survival especially with the newer treatment technologies available now.

Keywords: Prostate cancer - survival rate - risk-group - India - prognostic factors

Introduction

Prostate cancer is the most commonly diagnosed cancer in western men, and incidence is rising rapidly in most countries, including low-risk populations. Prostate cancer is the second most frequently diagnosed cancer of men (913000 new cases, 13.8% of the total) and the fifth most common cancer overall. Nearly three-quarters of the registered cases occur in developed countries (658000 cases) (Ferlay et al., 2010).

Incidence rates of prostate cancer vary by more than 25-fold worldwide, the highest rates are in Australia/New Zealand (104.2 per 100,000), Western and Northern Europe, Northern America Incidence rates are relatively high in certain developing regions such as the Caribbean, South America and sub-Saharan Africa. The lowest age-standardised incidence rate is estimated in South-Central Asia (4.1 per 100,000) (Ferlay et al., 2010). With an estimated 258000 deaths in 2008, prostate cancer is the sixth leading cause of death from cancer in men (6.1% of the total). Because PSA testing has a much greater effect on incidence than on mortality, there is less variation in mortality rates worldwide (10-fold) than is observed for incidence (25-fold), and the number of deaths from prostate cancer is almost the same in developed and developing regions. Mortality rates are generally high in predominantly black populations (Caribbean, 26.3 per 100,000 and sub-Saharan Africa, ASRs 18-19 per 100,000), very low in Asia (ASR 2.5 per 100,000 in Eastern Asia for example) and intermediate in Europe and Oceania. In India, the age-standardized rates (per 105) vary between Delhi (11.5), Mumbai (6.3), Chennai (5.2), Bangalore (6.0) and Barshi (1.6) (NCRP, 2007).

Survival from prostate cancer have improved over the years, as a result of earlier diagnosis. There are not many studies from India reporting on prostate cancer survival. Thus the present study aims to report the survival rates of prostate cancer patients.

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Materials and Methods

The present study, a retrospective study, was carried out at the Tata Memorial Hospital (TMH), Mumbai, India. The hospital registered 850 histologically proven cancer of prostate between the years 1999-2002. Of these 371 cases treated in TMH and were considered for inclusion in the study. The following criteria was applied for inclusion of cases in the present study (i) diagnosed as primary prostate cancer (ii) those who are not treated outside of TMH (iii) those who have completed the initial treatment fully.

The exclusion criteria was (a) Prostate cancer cases diagnosed and treated elsewhere before attending TMH (b) Not proven histologically as primary prostate cancer (c) Who did not complete the initial Cancer –directed-treatment fully. Thus the total number of prostate cancer cases eligible for analysis in the present study was 371.

A regular follow-up was done periodically for all the cases. Patients who missed their appointments/do not attend for follow-up visits were sent pre-paid post cards enquiring their health status. Follow-up information was updated through hospital visits/letters/telephones Mumbai Cancer Registry. All Mumbai resident deaths were matched with the Mumbai cancer registry. The cases are followed up periodically and the closing date was December 2009. The endpoint of the study was overall survival.

The study group was classified into '<60, 60-69, and 70+ years' age groups, 'residents of Mumbai' and 'non-residents' based on place of residence, and 'literate' and 'illiterate' groups based on education. Prognosis and treatment is based on a grading system, generally the Gleason system which allots grades from 1-10 based on how much the cells in the cancerous tissue resemble normal prostate tissue. A score of 2-4 is considered as low grade (localized), 5-7 as intermediate grade (loco-regional) and 8-10 (metastasis) as high grade. Treatment was classified into three groups; (1) those treated by surgery, either alone or in combination with other treatment, (2) those treated by radiation, either alone or in combination with other treatment, and (3) those treated by hormone therapy, either alone or in combination with other treatment.

Statistical methods

The Actuarial survival rate method (AR) was used to calculate survival rates (Berkson and Gage, 1950). The proportion of lost to follow-up was high and varied within and between groups. Also the risk of losses and deaths were not independent, which violated the assumption of the actuarial method. Thus Loss-Adjusted Survival Rate (LAR) proposed by Ganesh (1995) was applied to obtain the corrected survival rates for various groups (Ganesh, 1995). This method takes into account the losses in different strata by adjustment to obtain the corrected survival rates. Estimated deaths are obtained by logistic regression method in those with complete follow-up and then subsequently these estimates were applied to those with incomplete follow-up. Thus by applying the LAR method, survival rates were obtained for each of the categories are reported. Univariate and multivariate

analysis was carried out to compute the survival rates and also the prognostic factors.

Results

Table 1 describes the patient characteristics with regard to age, residence, religion, literacy, life-style habits as chewing, smoking, alcohol drinking, family history of cancer, medical history viz, diabetes, hypertension etc, disease risk-group as 'localised', 'loco-regional', and 'metastasis'.

Age was classified broadly into three categories viz. '<60 years', '60-69 years' and '>69 years'. It is seen that between the age '60-69 yrs' constitute a major proportion (42%) among the cases diagnosed. Most of the patients were from outside Mumbai (82%). Literacy rate was very low (9%). 71% of patients were diagnosed as 'Metastasis stage' and major proportion of patients received hormone therapy (78%). 13% had diabetic history and 22% had hypertension history. Only 5% had family history of cancer and 17% were tobacco-users in our study.

The actuarial survival rates (AR) and loss-adjusted survival rate (LAR) for factors considered are reported.

The median follow-up of patients was 40 months. 114 patients remained alive, excluding 89 deaths, at the end of the 5-year follow-up period. The endpoint was overall survival. The Overall five-year actuarial survival rate for prostate cancer was 62% while the LAR was 90%. It is seen that patients in the age-group 60-69 years had the best prognosis and the five-year survival rate was 76% and the difference in the outcome was statistically significant

Table 1. Characteristics of Prostate Cancer Patients Studied at TMH -1999-2002

Characteristics		Number	Percent
Total Cases		371	
Age	<60	106 (29%)	29
	60-69	158 (42%)	42
	70+	107 (29%)	29
Place of Residence	Mumbai	65 (18%)	18
	Non-Mumbai	336 (82%)	82
Literacy	Literate	35 (9%)	9
	Illiterate	306 (91%)	91
Risk Group	Localised	94 (25%)	25
	Locoregional	16 (4%)	4
	Metastasis	261 (71%)	71
Primary Treatment Recd.	Surgery	55 (15%)	15
	Radiation	26 (7%)	7
	Hormone	288 (78%)	78
	Chemotherapy	2	2
Co-morbid conditions	Diabetes		
	Yes	49 (13%)	13
	No	244 (66%)	66
	Unknown	78 (21%)	21
	Hypertension		
	Yes	80 (22%)	22
	No	213 (57%)	57
	Unknown	78 (21%)	21
Habits	Tobacco users	62 (17%)	17
	Non-tobacco users	221 (83%)	83
Family History of cancer	Yes	19 (5%)	5
	No	256 (69%)	69
	Unknown	96 (26%)	26

(p=0.001). The survival rates based on literacy status, although were different but not significant (p=0.45). Survival by risk-group showed that the prognosis became poorer with the advancement of disease i.e. metastatic – disease patients had a 53% five-year survival. The survival became poorer with the progressive years of follow-up. Patients with localized-disease showed a 91% survival at the end of 5 years. Surgically-treated patients, treated either as a single or in combination with other treatment modalities, showed a 91% five-year survival, whereas radiation-treated and hormone-treated patients had a five-year survival of 88% and 57% respectively.

Analysis based on life-style habits and co-morbid conditions are also described in Table 2. No statistically significant difference (p=0.64) was noted between the diabetic (71%) and non-diabetic (68%) patients survival rates. However it was observed that patients with hypertension history (77%) had a better survival than those without history of hypertension (66%), although not significant (p=0.08). In both of above two conditions, the difference could possibly be attributed to the time since diagnosis and duration of the treatment taken. There was no significant difference in survival rates for tobacco-usage. The rates were 99% and 68% for tobacco-users and non-users respectively. Family history played an important in determining the survival. Those with family history had better survival (82%) than those without family history of cancer (67%).

In general it is seen that the corrected survival rates by LAR method when compared with the actuarial (AR) method showed the possible bias caused due to the losses on follow up.

Table 2. Survival Rates: Loss-adjusted Survival Rates (LAR) and Actuarial Survival Rate (AR) for Prostate Cancer by Various Factors

Characteristics		No.	% LAR (AR)			p-value
			1- year	3-year	5-year	
All Cases		371	90 (92)	75 (74)	64 (62)	
Age	<60	6	86 (87)	69 (70)	60 (55)	
	60-69	158	94 (96)	84 (84)	76 (74)	0.001
	70+	107	89 (90)	65 (65)	51 (52)	
Literacy	Literate	35	90 (91)	75 (74)	64 (63)	0.45
	Illiterate	336	94 (100)	74 (69)	69 (59)	
Risk Group						
Localized		94	98 (98)	93 (93)	91 (91)	
Loco-regional		16	100 (100)	88 (81)	88 (81)	0.001
Metastasis		261	87 (81)	67 (66)	53 (48)	
Primary Treatment recd						
Surgery (S, S+..)		55	98 (98)	95 (95)	91 (91)	
Radiation (R,R+..)		26	92 (91)	92 (91)	88 (84)	0.001
Hormone (H, H +..)		288	89 (91)	69 (68)	57 (54)	
Co-morbid condition						
Diabetes	Yes	49	90 (93)	78 (78)	71 (65)	0.64
	No	244	91 (93	81 (82)	68 (70)	
Hypertension	Yes	80	92 (94)	87 (89)	77 (74)	0.08
	No	213	91 (92)	78 (78)	66 (66)	
Habits						
Tobacco users		62	87 (91)	73 (79)	69 (66)	0.8
Non- users		221	92 (93)	81 (83)	68 (68)	
Family History of cancer						
Yes		19	95 (94)	82 (80)	82 (80)	0.015
No		256	90 (92)	78 (78)	67 (66)	

Discussion

Estimation of survival rate is of primary importance since it will indicate the effect of new treatment, if any, compared, to standard treatment. Also the length of survival is the measure which is used for computing survival rates. Both of these require that the patients be followed-up over a period of time. In some Western countries, there is a centralized registration system across the country, which makes it a lot easier to obtain follow-up information. Such systems don't exist in most of the developing countries, including India. There are very few cancer survival reports from India, mainly because of poor patient follow-up and incompleteness in death registration system. Although there are methods to improve the follow-up response, it is difficult to obtain 100% follow-up and thus the limitations to undertake survival studies. Also the standard methods available in the literature for calculating survival rates are based on 'certain assumptions'. Violation of these assumptions will only result in biased estimation of survival rates by direct application of standard methods, like the actuarial method. Thus the method suggested by Ganesh (1995) has been applied to calculate the survival rates, which corrects for the losses to follow-up.

It is known that prostate cancer is an old-age disease occurring more among the elderly population, in India as in other parts of the world. The present study, one of the few studies on prostate cancer survival, is an hospital-based follow-up study of histologically confirmed prostate cancer patients, seen at TMH between the year 1999-2002. The total patients eligible for study was 371 cases. An attempt has been made to study the factor, demographic and clinical, that influence the survival of a prostate cancer patient. The LAR reported are adjusted for only losses to follow-up, and not adjusted for the background factors. In a large study, based on database of UK Association of Cancer Registries and British Association of Urological Surgeons, the overall five-year survival for prostate cancer patients was reported to be 81% (SWPHO, 2008) however the rates was 64% in the present study.

Age is known to be an important factor that determines the prognosis. Patients aged in '60-69' years had the best survival at advance. The effect of age on prognosis of prostate cancer has been shown to serve in other studies (Grönberg 1994) and in others 1995; Alikian et al., 1997).

Stage or disease, diagnosed as a critical determinant in prostate cancer survival. In addition to stage at diagnosis, tumor grade play an important role in prostate cancer survival, for grade reflected the cell differentiation and/or Gleason score. In a UK SEER report the 10-year relative survival was 100% for localized, 99% for those with loco-regional tumor and only for metastasis (Altekruse 2010). The analysis undertaken by South West Public Health Observatory, shows that the five-year survival rates for localized disease patients are 98.6% whereas it was 32.6% for those with metastasis (SWPHO, 2008). However in the present study the 5-year LAR survival rates for localized was 91%, 88% for loco-regional and 53% for metastasis patients. This shows that the prognosis becomes poorer with the increase in extent

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of spread of disease.

Over the years, effective treatment has been offered which has translated into better survival rates for prostate cancer patients. Surgically-treated patients, treated either as a single or in combination with other treatment modalities, showed a 91% five-year survival, whereas radiation-treated and hormone-treated patients had a five-year survival of 88% and 57% respectively in the present study. A study from Geneva cancer registry suggested that the 10-year survival rates were 83% for surgery, 75% for radiotherapy and 41% for hormone therapy (Merglen et al., 2007). Recently published results from a retrospective analysis suggested that prostate cancer patients with localized disease but positive margins do derive a survival benefit from adjuvant radiation therapy (Dillman, 2010).

Since an US study reported diabetes as an independent predictor of prostate cancer mortality (Coughlin, 2004) and thus the authors wanted to explore the effect of diabetes on prostate cancer survival. .The present study when analysed with respect to the diabetic history didn't show any statistical difference in survival rates.

It was observed that patients with hypertension history (77%) had a better survival than those without history of hypertension (66%). In both of above two conditions, the difference could possibly be attributed to the duration since diagnosis and duration of the treatment taken.

Data from three large prospective studies reported higher death rates from prostate cancer in current cigarette smokers, and inconsistent findings in incidence studies suggested that smoking might adversely affect survival in prostate cancer patients (Rodriguez, 1997). In the present study, there was clearly no significant difference in survival rates among tobacco-users, the 5-year survival rates being 69% and 68% for tobacco-users and non-users respectively.

It is known that family history plays an important role determining the risk for some cancers. One of the studies in assessing the role of family history in prognosis of prostate cancer, reported that patients with a family history of prostate cancer had a somewhat better prognosis than the patients with a negative family history, though the difference did not reach statistical significance (p=0.08) (Bratt et al., 1998) which is in agreement with the present study findings, This could possibly be due to the fact that those with family history could be visiting for periodical medical check-ups, which probably helped to be diagnosed at earlier stage of disease and thereby have better prognosis.

The above study, one of the few studies on prostate cancer survival, has shown that age at diagnosis, stage of disease, family history, diabetes, hypertension and treatment are important determinants for prognosis. The five-year Overall survival rate was 64%. Patients in the age group of '60-69 yrs' had the best prognosis. Concurrently those who had no history of diabetes,, those with hypertension history (74%), those with family history (80%) of cancer, those diagnosed with localized-disease (91%) and those treated with surgery, either alone or in combination (91%) had better survival than their respective counterparts. Tobacco use didn't show any significant effect on survival in this study.

To summarize, the present study showed that, prostate cancer patients with localized disease have better outcome. Local treatment with either surgery or radiation achieved a reasonable outcome in prostate cancer patients in the present study group. A more detailed clinical study will be helpful in understanding the prognostic indicators for survival especially with the newer treatment technologies available now.

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