

Spectrum of Prostate Cancer in the Singapore General Hospital (1980 to 1985)

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Abstract

Introduction: Serum prostate specific antigen (PSA) testing has contributed to a dramatic rise in the incidence of prostate cancer diagnosed in the last decade in the West as well as in Singapore. Now prostate cancer is ranked as the sixth commonest cancer among men in Singapore. To form the basis for comparisons and to assess the trends and impact of these changes, we analysed the presentation, disease characteristics and outcome of treatment of patients with prostate cancer diagnosed in the pre-PSA era at the Singapore General Hospital (SGH). **Materials and Methods:** Of the 149 patients (1980 to 1985) registered in the database, 134 (90%) records with full follow-up data were available for the analysis. All patients were diagnosed and managed at SGH. Follow-up and death data were collected through clinic visit, phone interviews of the patients, relatives, family physicians and the death registry. Survival analysis was carried out using the Kaplan-Meier product limit method. **Results:** The mean age at diagnosis was 69.8 years. There were no significant changes with reference to each year during 1980 to 1985 and the mean number of diagnoses per year was 22.3. Of the 134 patients, 86% had either retention of urine or severe lower urinary tract symptoms and 14% had metastatic disease at presentation. Most histological diagnosis was made during prostatectomy; wherein 82% was found with transurethral resection of the prostate (TURP) and 12% in open prostatectomy, respectively. Pathological analysis during diagnosis revealed that 72.4% patients had metastatic disease. Of which, 57.5% had high-grade (Gleason >7) tumours. Among these, 82% underwent TURP to relieve urinary obstruction, while 26.1% received local irradiation to the prostate. Majority had hormone therapy shortly after diagnosis in the form of orchidectomy or oral diethylstilbestrol (76.1%). The median crude survival (26 months) was minimal for metastatic patients. **Conclusion:** The spectrum of prostate cancer in the pre-PSA era was characterised by high stages of high-grade disease, with very limited opportunity for successful treatment and hence survival.

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Introduction

Prostate cancer is the most prevalent cancer among men in the United States.¹ In Singapore, it is the sixth most common incidence of cancer among males and the age-adjusted rates have risen from 8.2 to 9.6 per 100,000 per year between 1987 and 1992.² Much of these changes have been attributed to the routine testing of asymptomatic males with serum prostate specific antigen (PSA) testing. In the West, there are emerging evidence that a "cull effect"³ has occurred and its incidence has begun to drop in the last few years. There is also evidence of significant stage migration towards clinically localised disease.⁴ Several reports have also documented improvement in survival.³ The incidence of prostate cancer in Singapore is still a fraction of that in the West. To form the basis for comparisons, in order to assess the trends and impacts of these changes, we need a clear picture of the pattern of

disease before and after the introduction of PSA testing. As a part of the continual effort to study this disease, we analysed the presentation, disease characteristics and outcome of treatment of patients with prostate cancer diagnosed in the pre-PSA era at the Singapore General Hospital (SGH).

Material and Methods

From the uro-oncology database of the Department of Urology, SGH, 149 consecutive patients were identified between the years 1980 and 1985. In Singapore, only in the late 1980s was PSA introduced to identify prostate cancer. Prior to this, proper diagnostic methods for symptomatic men were not available. Out of these 149 patients, complete follow-up records were available for 134 (90%) who formed the basis of this study. Primarily, all patients were diagnosed and managed at SGH. Follow-up and death data

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were obtained from clinic visit, phone interviews of the patients, relatives, family physician and the death registry. Survival analysis was carried out using the Kaplan-Meier product limit method. Patients who were still alive were censored in January 1998. Comparisons of survivorship between histological grades and different disease stages were made with the log-rank method.

Results

During the period 1980 to 1985, the mean age at diagnosis of prostate cancer was 69.8 years with a range of 40 to 92 years. The number of prostate cancer diagnosed ranged between 19 and 26 per year (Table I). The ethnic distribution of patients diagnosed with prostate cancer (Table I) is similar to the general racial distribution in Singapore.

Of the 134 analysable patients, nearly 86% ($n = 115$) of patients were identified with retention of urine and severe lower urinary tract symptoms (LUTS) and the remaining 13% ($n = 17$) were diagnosed with symptoms of metastatic disease such as bone pain, cord compression and general debilitation from systemic diseases (Table I). These diagnoses were principally made during transurethral resection of the prostate (TURP) in majority of the patients (81%, $n = 109$) and open prostatectomy (12%, $n = 16$).

TABLE I: CANCER INCIDENCE, DEMOGRAPHIC PROFILE AND PRESENTING SYMPTOMS OF PROSTATE CANCER DIAGNOSED DURING 1980-1985 IN SINGAPORE GENERAL HOSPITAL

	Percentage	No. of patients
Year		
1980	-	19
1981	-	25
1982	-	22
1983	-	19
1984	-	26
1985	-	23
Presenting symptom (%)		
ARU	51	68
LUTS	35	47
Metastasis	13	17
Asymptomatic	1	1
Diagnostic method (%)		
TURP	81	109
Open surgery	12	16
Biopsy	7	9
Racial distribution (%)*		
Chinese	77	103
Indian	4	5
Malay	13	17
Others	6	8

ARU: acute retention of urine; LUTS: lower urinary tract symptoms; TURP: transurethral resection of the prostate

* The ethnic distribution as quoted by national statistics is as follows: Chinese, 76.4%; Malay, 14.9%; Indian, 6.4%; Others, 2.3%

Pathology revealed adenocarcinoma in all patients; of which, nearly 57.5% ($n = 77$) were identified with a Gleason score of 8 to 10 and 23.6% ($n = 32$) showed moderate difference (Gleason score, 5 to 7), while only 18.9% ($n = 25$) carcinomas (Gleason score, 1 to 4) were well differentiated.

In the present series, since most of the patients had advanced stages of prostate cancer, only a minimal percentage of patients underwent radiation therapy alone (5.7%, $n = 8$). In contrast, the majority had TURP (82%, $n = 110$) to palliate local urinary obstruction. In addition, after the initial diagnosis, 77.6% ($n = 104$) and 55.2% ($n = 74$) of patients were found to be on hormonal therapy and oral diethylstilbestrol (DES), respectively; whereas, 41.6% ($n = 56$) had orchidectomy. A significant number of patients (22.4%, $n = 30$) did not undergo any therapy after being diagnosed as stage A with TURP.

The average follow-up period was 72 months and 52% of death is attributed to prostate cancer. The overall median crude survival was 34 months. Whereas, the median survival for patients with localised disease was 111 months [standard deviation (SD), 46.3 months] (Fig. 1), compared to those with metastatic disease at 26 months (SD, 27.9 months). The overall 5-year survival rate was 33.6%. The 5-year survival rate for those with localised and metastatic disease was 78.4% and 15.6%, respectively. This difference in survival was highly significant at $P < 0.001$. Median survival of well-differentiated prostate cancer was 31.9 months (0 to 104.0 months; SD, 39.7 months); whereas, the survival in moderately-differentiated tumour was 41.9 months (1.4 to 163.6 months; SD, 44.9 months) and in poorly-differentiated tumour was 24.9 months (0.6 to 117.5 months; SD, 34.9 months) (Fig. 2).

Discussion

In the pre-PSA era, patients were generally evaluated for prostate cancer only when they present with lower urinary symptoms. The present study supports the concept that symptomatic prostate cancers are generally of advanced stages and seldom curable. Seventy-two per cent of patients in the present series had metastatic disease at presentation with a median survival with treatment of only 26 months. The remaining patients had incidental diagnosis of prostate cancer at TURP, most had well-differentiated tumours generally as latent cancers. This is borne out by their excellent survival of 111 months despite the limited application of potentially curative therapy such as irradiation and the total absence of radical prostatectomy as a form of local treatment in that era. It will be enlightening to compare these numbers with those of the post-PSA era. Certainly, in the US, some of the series have reported lower (26% to 52%) metastatic disease at presentation in the modern era.⁵ Thus, while the incidence rates have risen in

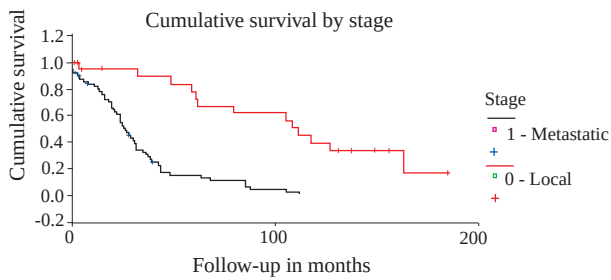


Fig. 1. Survival curves of localized (111 ± 46.3 months) and metastatic (26 ± 27.9 months) prostate cancer.

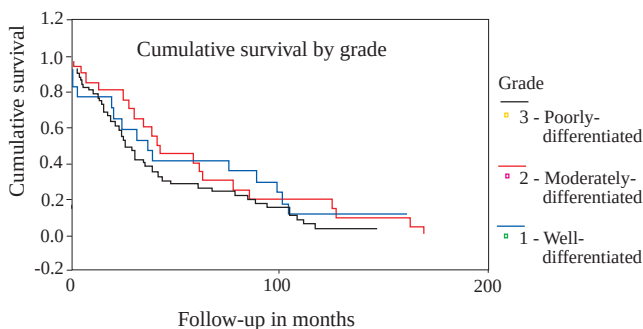


Fig. 2. Median survival of different histological grades (well, moderate and poorly differentiated) of prostate cancer.

the US, the mortality figures have remained relatively stable.

The number of patients with prostate cancer seen in this hospital was relatively stable during this period. This could be attributed to the relatively narrow period of observation although it could also reflect the true stable incidence before the advent of PSA testing. A comparison with later year's figure will be useful.

The mean diagnostic age of 69.5 (range 40 to 92) years is comparable to other series;⁶ although a later series of localised prostate cancer reported in 1995 had a mean age of 66.7 years, perhaps reflecting the lead time bias of those mainly asymptomatic patients.⁷

A report of cancer incidence in Singapore from 1993 to 1997² documented a rising incidence of prostate cancer over the last 30 years in Singapore. This increase was demonstrated in all ethnic groups. The age-adjusted risk of prostate cancer between 1993 and 1997 is 3 times that observed during the period 1968 to 1972. The age-adjusted relative risk for Indians and Malays was 0.7 and 1.0, respectively; with the risk in Chinese as the reference group.

Most of our patients had hormonal therapy as their primary therapy for prostate cancer, which is similar to previous studies done in the West.⁸ Most had either

orchidectomy, DES or both.⁹ In the present series, radiotherapy was also used as a single therapy or in combination in 35 patients. This reflects advanced stages of most of their diseases. Their survival also reflects the limited duration of control afforded by such treatment. Crude survival analysis was chosen in our analysis due to the difficulty in obtaining accurate information on the cause of death in many of our patients. Most of the elderly patients had significant co-morbid diseases at the time of diagnosis and death. Most of them also had advanced disease. It is often difficult to decide whether patients died of the disease or with the disease.

Conclusions

This series of patients with prostate cancer diagnosed in the pre-PSA era is characterised by the high stages and high grade of diseases of the majority of patients at presentation. Treatment opportunities were very limited and the short median survival emphasised the need for a better programme for prostate cancer diagnosis and treatment, perhaps with the use of PSA testing.

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