South African Family Practice 2015; 57(4):247–252
http://dx.doi.org/10.1080/20786190.2014.993859

S Afr Fam Pract
ISSN 2078-6190 EISSN 2078-6204

RESEARCH

Prostate cancer profile and risk stratification of patients treated at Universitas Annex Department of Oncology, Bloemfontein, Free State, during 2008 to 2010

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Background: Prostate cancer commonly occurs in older men. Since TNM staging excludes prostate-specific antigen (PSA) level and Gleason score, patients with prostate cancer are divided into risk groups when deciding on treatment options. This study determined the profile and risk stratification of patients with prostate cancer treated at the Department of Oncology, Universitas Annex in Bloemfontein, Free State, during 2008 to 2010.
Methods: This was a cross-sectional study with retrospective data collection. Information was gathered from 497 patient files on age, race, residence, Gleason score, PSA level, TNM stage, and initial treatment. The patients' risk group was determined from their Gleason score, PSA level, and T stage.
Results: Patients were mostly (45.7%) between 65 and 75 years of age and 72.8% were in the black race group. The largest percentage of patients had a Gleason score of 8 to 10 (43.7%), PSA level > 20 ng/ml (67.9%), and a T stage ≥ T3 (62.3%). Almost half of the patients (48.7%) had stage IV disease and 38.4% received palliative hormonal therapy as initial treatment. The majority of patients (82.5%) fell into the high risk group.
Conclusions: The majority of patients in each age group fell into the high risk group, which means that these patients were at a higher risk of developing metastatic prostate cancer. We recommend better education of our patient population and local clinic staff, so that people in the community can understand the prevalence of the disease, the symptoms and effect of the cancer, and that it is treatable if detected early.

Keywords: high risk, profile, prostate cancer, risk group, stratification

Introduction

Prostate cancer is an adenocarcinoma of the prostate gland and is more common in older men.[1]

The Gleason score is used to describe the histological grading of a tumour and is determined by histological examination of biopsy samples obtained from the prostate gland. Depending on the cellular pattern of the prostate cancer, a number from one to five is assigned to the most frequent and second most frequent patterns observed. These two numbers are added together to obtain the total Gleason score.[1] A Gleason score of 4 + 3 is indicative of a more aggressive prostate cancer than a Gleason score of 3 + 4.[2]

Prostate-specific antigen (PSA) is a glycoprotein secreted by the prostate gland. When the prostate gland enlarges, as is the case during prostate cancer, increased amounts of PSA are secreted resulting in an increased PSA blood level.[3] This PSA level, measured in nanograms per millilitre (ng/ml) of blood, is therefore used in the screening for prostate cancer.

The TNM system, endorsed by the American Joint Committee on Cancer, assesses the size and local infiltration of the tumour (T stage), whether the lymph nodes are involved (N stage), and if the tumour has distant metastasises (M stage).[4] Patients are assigned to one of four stages (stage I–IV) once the T, N, and M stages have been determined. This staging is considered when deciding on the appropriate treatment.[5]

Since TNM staging excludes the PSA level and Gleason score, patients are also divided into risk groups (high, intermediate, and low) when deciding on treatment options.

A patient's risk group is determined by the PSA level, Gleason score, and the T staging and refers to a patient's chances of developing metastatic disease. A commonly used system is that of the National Comprehensive Cancer Network (NCCN), where a prostate cancer patient is assigned to a risk group according to the criteria shown in Table 1.[6]

Each year between 250 to 350 new patients with prostate cancer are seen at the Universitas Annex Department of Oncology. The majority of these patients have financial constraints and are state patients. Treatment options available at the Oncology Department for patients with prostate cancer are active surveillance/watchful waiting, radical prostatectomy, local radiation, palliative hormonal therapy and palliative radiation. The treatment used depends on the stage of the cancer and the risk profile of the patient.

Motivation for the study

To our knowledge, no other study of this nature has previously been conducted in the Free State. Therefore, the information collected will bring about new insight into the age, race, geographical distribution, Gleason score, PSA level, overall TNM stage, T staging, risk stratification, and initial treatment of patients with prostate cancer treated at Universitas Annex Department of Oncology in Bloemfontein.

Aim

To describe the profile and risk stratification of patients with prostate cancer who received treatment during 2008 to 2010 at Universitas Annex Department of Oncology in Bloemfontein, Free State.

Table 1: Risk group stratification by PSA level, Gleason score, and T staging

Risk group	PSA level (ng/ml)	Gleason score	T staging
Low	≤ 10	< 7	T1c–T2a
Intermediate	10.1–20	3 + 4	T2b–T2c
High	> 20	4 + 3, 8–10	≥ T3

Methodology

This was a cross-sectional study with retrospective data collection. The files of patients with prostate cancer, who received treatment at Universitas Annex Department of Oncology during January 2008 to December 2010, were reviewed.

The population size was 505 patients. Files of patients that did not have sufficient information to calculate the risk group were excluded from this study.

Measurements

A coded data sheet was used to record the age, race, geographic location (place of residence), Gleason score, PSA level, overall TNM stage, T staging, risk group, and the initial treatment given for each patient. Each of these variables was assigned different categories. For the race and geographic location, an 'Other' category was added with space to specify.

The Department of Oncology provided the researchers with a list of names of all the patients with prostate cancer who received treatment at Universitas Annex during the study period. The patient files were obtained from the archives of the Department of Oncology. The recorded data were checked for errors by the researchers, who reviewed the files again before the data sheets were sent for analysis.

Pilot study

A pilot study was done at Universitas Annex Department of Oncology.

The first 20 files of 2008 were used for the pilot study as the changes that needed to be made on the data sheet were apparent within these first 20 files. The data recorded from the files used in the pilot study were included in the main study.

Analysis of data

Risk group stratification was based on the Gleason score, PSA level, and the T staging.[6] If one or more of the variables were missing from a file but the available variable(s) resulted in high risk stratification, the file was included in the data analysis as the missing variable(s) would not change the risk stratification. The variable with the highest number of missing values was the Gleason score, namely 9 (1.8%), followed by T staging (4) and PSA level (1).

The number and percentage of patients per category for each variable were determined. The PSA level, Gleason score, T staging, TNM stage, risk stratification, and initial treatment per age group as well as treatment per risk group and TNM stage per geographic location (not reported here) were also determined. This was done by the Department of Biostatistics, Faculty of Health Sciences at the University of the Free State.

Ethical aspects

The files remained in the Department of Oncology for the entire duration of the study. The names of the patients were not recorded on the data sheets.

Permission to conduct the research was obtained from the Acting Head of Department of Oncology and the Clinical Head of Universitas Academic Hospital. Permission was also obtained from the Ethics Committee of the Faculty of Health Sciences, University of the Free State.

Results

Of the 505 patient files, 497 (89.4%) patient files were analysed since the other eight files did not have sufficient information to calculate the risk group. Table 2 displays the demographic data of the study population.

Almost half of the patients (45.7%) were in the age group 65 to 75 years. The < 50 years age group had the smallest percentage of patients (1.0%). The majority of patients (72.8%) were black. Most of the patients were from the Free State (87.9%) followed by the Northern Cape (6.0%) and Lesotho (3.2%). Just under half (48.7%) of patients who were treated at Universitas Annex Department of Oncology had stage IV prostate cancer.

Using the criteria listed in Table 1 the researchers determined the risk group of each patient which is summarised in Table 3.

According to the patients' Gleason scores, PSA levels, and T staging, 82.5% were allocated to the high risk group.

Prostate cancer-specific variables in the four pre-determined age categories are shown in Table 4.

In each of the four age groups, the highest percentage of patients had a Gleason score of 8 to 10, a PSA level > 20 ng/ml, stage IV prostate cancer with T stage ≥ T3 resulting in a high risk group allocation.

Table 5 investigates the initial prostate cancer treatment per age group and per risk group.

Overall, the highest percentage of patients received palliative hormonal therapy (38.4%) followed by local radiation (16.7%), and active surveillance/watchful waiting (14.9%).

Almost a quarter of patients (20.5%) did not return for treatment and were categorised as lost to follow-up. This trend was seen in every age group. In the low risk group, most of the patients were lost to follow-up (39.1%).

Low risk patients were mainly treated through active surveillance/watchful waiting (32.6%). Most intermediate risk patients received radical prostatectomies (31.7%) while almost half of patients in the high risk group received palliative hormonal therapy (45.9%).

Discussion

Demographics

The largest percentage of patients (45.7%) with prostate cancer, treated during 2008 to 2010 at Universitas Annex Department of Oncology, were in the age group 65 to 75 years with only five

Table 2: Demographic data of patients with prostate cancer treated at Universitas Annex Department of Oncology during 2008 to 2010

	n	%
Age (years) (*n* = 497)		
< 50	5	1.0
50–64	141	28.4
65–75	227	45.7
> 75	124	25.0
Race distribution (*n* = 497)		
White	106	21.3
Black	362	72.8
Coloured	27	5.4
Asian	2	0.4
Area of residence (*n* = 497)		
Fezile Dabi*	58	11.7
Thabo Mofutsanyane*	82	16.5
Motheo*	184	37.0
Xhariep*	29	5.8
Lejweleputswa*	84	16.9
Northern Cape	30	6.0
North West	9	1.8
Eastern Cape	2	0.4
Lesotho	16	3.2
Other	3	0.6
Prostate TNM cancer stage (*n* = 495)		
Stage I	43	8.7
Stage II A	55	11.1
Stage II B	73	14.8
Stage III	83	16.8
Stage IV	241	48.7

*Five district municipalities of the Free State[7]

(1.0%) patients younger than 50 years. This was expected as prostate cancer most commonly occurs in men between the ages of 65 to 75 years and is seldom found in men younger than 50 years.[1]

According to data from Census 2011, the black population constituted 79.2% of South Africa's total population.[8] Most of the patients (72.8%) in this study population were in the black race group. This race distribution is representative of the population stratification in South Africa and does not necessarily mean that prostate cancer is more common in the black race group.

The Oncology Department at Universitas Annex is a national reference centre. Patients from other provinces can either go to oncology centres in their province or be referred to Universitas Annex Oncology Department. However, for patients from the Free State Province and Lesotho the Oncology Department at Universitas Annex is the only centre for referral. As expected, the majority of patients (87.9%) were from the Free State with most of the patients (37.0%) coming from the Motheo district municipality. The rest of the patients mainly came from Lesotho (3.2%), since Lesotho does not have the facilities to treat these patients, and Northern Cape (6.0%) as the Oncology Department in the Northern Cape does not possess its own radiation machine and has to send patients to Universitas Annex.

Baseline cancer characteristics and risk group stratification of study population

A large number of patients (43.7%) had a Gleason score of 8 to 10 indicating that 4 out of every 10 patients with prostate cancer treated at Universitas Annex Oncology Department had high risk prostate cancer based on their Gleason score.

The majority of patients (67.9%) had a PSA level > 20 ng/ml. PSA levels tend to rise as the prostate enlarges or with metastatic disease. A PSA level > 20 ng/ml is indicative of a more advanced cancer.[6]

A large number of patients (48.7%) treated at the Oncology Department presented with stage IV prostate cancer. A possible reason for this could be due to insufficient screening of patients for prostate cancer in the geographic locations referring these

Table 3: Risk group stratification of patients with prostate cancer according to their Gleason scores, PSA levels, and T staging

	Low risk group		Intermediate risk group		High risk group	
	n	%	*n*	%	*n*	%
All (*n* = 497)	46	9.3	41	8.3	410	82.5
Gleason score (*n* = 488)						
< 7	139	28.5				
3+4			63	12.9		
4+3					73	15.0
8–10					213	43.7
PSA level (ng/ml) (*n* = 496)						
≤ 10	96	19.4				
10.1–20			63	12.7		
> 20					337	67.9
T staging (*n* = 493)						
T1–T2a	136	27.6				
T2b–T2c			50	10.1		
≥ T3					307	62.3

Table 4: Distribution of the Gleason score, PSA level, TNM stage, T staging, and risk group stratification according to age groups

	< 50 years		50–64 years		65–75 years		> 75 years	
	n	%	*n*	%	*n*	%	*n*	%
Gleason score (*n* = 488)								
	***n* =5**		***n* = 139**		***n* = 223**		***n* = 121**	
< 7	2	40.0	46	33.1	69	30.9	22	18.2
3+4	0	0	18	13.0	25	11.2	20	16.5
4+3	0	0	19	13.7	36	16.1	18	14.9
8–10	3	60.0	56	40.3	93	41.7	61	50.4
PSA level (ng/ml) (*n* = 496)								
	***n* = 5**		***n* = 141**		***n* = 227**		***n* = 123**	
≤ 10	2	40.0	42	29.8	36	15.9	16	13.0
10.1–20	0	0	19	13.5	27	11.9	17	13.8
> 20	3	60.0	80	56.7	164	72.3	90	73.2
Prostate TNM cancer stage (*n* = 495)								
	***n* = 5**		***n* = 141**		***n* = 225**		***n* = 124**	
Stage I	2	40.0	16	11.4	18	8.0	7	5.7
Stage II A	0	0	20	14.2	19	8.4	16	12.9
Stage II B	0	0	19	13.5	42	18.7	12	9.7
Stage III	0	0	23	16.3	36	16.0	24	19.4
Stage IV	3	60.0	63	44.7	110	48.9	65	52.4
T staging (*n* = 493)								
	***n* = 5**		***n* = 140**		***n* = 224**		***n* = 124**	
T1–T2a	2	40.0	46	32.9	60	26.8	28	22.6
T2b–T2c	0	0	18	12.9	23	10.3	9	7.3
≥ T3	3	60.0	76	54.3	141	63.0	87	70.2
Risk group (*n* = 497)								
	***n* = 5**		***n* = 141**		***n* = 227**		***n* = 124**	
Low	2	40.0	18	12.8	19	8.4	7	5.7
Intermediate	0	0	17	12.1	14	6.2	10	8.1
High	3	60.0	106	75.2	194	85.5	107	86.3

Table 5: Initial prostate cancer treatment per age group and per risk group

			Per age group								Per risk group					
			< 50 years		50–64 years		65–75 years		> 75 years		Low		Intermediate		High	
	All (*n* = 497)		(*n* = 5)		(*n* = 141)		(*n* = 227)		(*n* = 124)		(*n* = 46)		(*n* = 41)		(*n* = 410)	
Initial treatment	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Active surveillance/watchful waiting	74	14.9	0	0	11	7.8	35	15.4	28	22.6	15	32.6	8	19.5	51	12.4
Radical prostatectomy	30	6.0	0	0	19	13.5	10	4.4	1	0.8	6	13.0	13	31.7	11	2.7
Local radiation	83	16.7	0	0	28	19.9	48	21.2	7	5.7	6	13.0	9	22.0	68	16.6
Palliative hormonal therapy	191	38.4	2	40.0	49	34.8	84	37.0	56	45.2	1	2.2	2	4.9	188	45.9
Palliative radiation	17	3.4	1	20.0	5	3.6	11	4.9	0	0	0	0	0	0	17	4.2
Lost to follow-up	102	20.5	2	40.0	29	20.6	39	17.2	32	25.8	18	39.1	9	22.0	75	18.3

patients to Universitas Annex; hence, the patients presenting with late stage prostate cancer.

Most patients (62.3%) presented with a T stage ≥ T3. In our opinion the reason for the advanced local T stage is that patients tend to wait for progression in local symptoms before they seek help.

T2b–T2c had the lowest percentage of patients (10.1%). Screening methods, such as regular PSA testing and rectal evaluation of the prostate, will lead to earlier detection of stage T1–T2a prostate cancer.

To determine the risk group of a patient the Gleason score, PSA level, and T staging are taken into account (Table 1).[6] Corresponding to the large number of patients with a Gleason score of 8 to 10, PSA level of > 20 ng/ml, and T stage ≥ T3, it is not surprising that the majority of the study population (82.5%) fell into the high risk group.

Impact of age on prostate cancer variables and risk group stratification

The age group with the highest percentage of patients (60.0%) with a Gleason score of 8 to 10 was the < 50 years age group. However, there were only five (1.0%) patients in this age group. As a result, it does not give a general representation of the patients in the < 50 years age group within the population and it is difficult to draw conclusions regarding the results of this particular age group. A retrospective review done by Heyns, Fisher, Lecuona and Van der Merwe[9] also showed a very small percentage of patients in this age group with only 3% of their patients younger than 50 years.

Patients in the > 75 years age group had the second highest percentage of patients (50.4%) presenting with a Gleason score of 8 to 10. This is unexpected as patients in this age group usually have slower-growing tumours with a lower Gleason score.

In each age group the majority of the patients (between 56.7% and 73.2%) had a PSA level > 20 ng/ml.

The largest percentage of patients in each age group (between 44.7% and 60.0%) presented with stage IV prostate cancer showing that advanced stage disease affected patients in all age groups.

Initial treatment of study population

The highest percentage of patients (38.4%) received palliative hormonal therapy. A reason for the use of palliative hormonal therapy in this study population was that most patients fell into the high risk group and presented with a more advanced stage IV disease. Patients who receive palliative hormonal therapy benefit from this type of treatment as the cancer is sensitive to hormonal therapy.[10]

The second highest number of patients (20.5%) was lost to follow-up, possibly due to a lack of transport, the patient was asymptomatic or did not understand the need for treatment, or the patient passed away and the family failed to inform the Department of Oncology. To improve patient follow-up, the Department of Oncology is sending out letters to all the patients who miss appointments.

Impact of age and risk group on initial treatment

In all the age groups the largest number of patients (between 34.8% and 45.2%) received palliative hormonal therapy due to metastatic disease or high risk classification.

Low risk patients were more likely to be lost to follow-up (39.1%), possibly as their symptoms were not advanced enough for them to return for further treatment. Treatment wise, most patients in this risk group (32.6%) were monitored through active surveillance/watchful waiting to ensure that the prostate cancer did not progress into a more advanced stage.

The highest percentage of patients in the intermediate risk group received radical prostatectomies (31.7%) followed by local radiation (22.0%), since the tumours were still localised. The aim of these therapies is local control.

Patients in the high risk group were mostly treated with palliative hormonal therapy (45.9%), as it is an effective treatment for patients who have advanced prostate cancer.

Controversies

Different institutions use different values to determine risk groups. For example, the ranges used by the NCCN differ from those of the D'Amico classifications.[6]

There is controversy surrounding the use of PSA as a means to screen people for prostate cancer, as screening of PSA may reveal patients who would have survived without treatment.[3] Although PSA-based screening allows for early identification of prostate cancer there are some disadvantages, which include, false positive tests (e.g. elevated PSA level due to hyperplasia of the prostate gland or prostatisis[11]) and unnecessary treatment which can lead to further complications.[12] The current guide is that screening has to consist of a combination of a rectal evaluation of the prostate and a PSA test.

In South Africa, patients do not necessarily go to the health care facilities closest to where they live. This is influenced by where they work or where they find a clinic or hospital where they can be helped. They also occasionally give incorrect details regarding their place of residence, especially if they do not have a permanent place of residence. As a result, the geographic location of patients with prostate cancer in South Africa is not necessarily correct.

Recommendations

A large number of the patients were found to be lost to follow-up. We recommend that if the patients are faced with transport problems, they should inform the oncology clinic. During the counselling of new patients, emphasis should be placed on the importance of follow-up visits.

We recommend education of the public, so that people in the community can understand the prevalence of the disease, the symptoms and effect of the cancer, and that it is treatable if detected early. It is important to ensure that local clinic staff is knowledgeable in the disease. During general visits for hypertension and diabetes, for example, questioning regarding prostate-related symptoms should become part of the evaluation. Health care workers should also encourage patients over the age of 50 years to be screened for prostate cancer. Pamphlets can aid in creating awareness of early symptom complexes as well as the procedures that need to be followed if a patient experiences symptoms.

It is recommended that similar studies be conducted in other provinces in South Africa so that a general profile of patients with prostate cancer can be gathered nationwide. The risk group stratification of patients in the different provinces will indicate whether screening is available and, if so, whether it is effective. For example, if most of South Africa's provinces have the largest number of patients in the high risk group, it will indicate that screening is not done or is ineffective. If this is the case, then the problem of screening can be addressed.

Conclusion

In this study it was found that 45.7% of the patients, treated for prostate cancer at the Universitas Annex Department of Oncology during 2008 to 2010, were between 65 and 75 years of age, 72.8% were in the black race group and 37.0% were from the Motheo district municipality of the Free State.

In this study population, the majority of patients (82.5%) were in the high risk group while 9.3% were in the low risk group, and 8.3% in the intermediate risk group. In each age group, most of the patients had a Gleason score of 8 to 10, PSA level > 20 ng/ml, and a T stage ≥ T3. This placed the majority of patients in each age group in the high risk group, which means that these patients are at a higher risk of developing metastatic prostate cancer.

Acknowledgements – The Department of Oncology for allowing the researchers to perform the study. The filing staff at the Oncology Department: Mr Ishmael Kopi, Mrs Charlene Pretorius and Mr Efraim Modifenyane. Mrs Theanette Mulder, medical writer, School of Medicine, University of the Free State, for technical and editorial preparation of the manuscript.

Conflict of interest – The authors declare that they have no financial or personal relationship(s) which may have inappropriately influenced them in writing this paper.

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Received: 27-06-2014 Accepted: 26-11-2014