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The trajectory of patients who die from metastatic prostate cancer: a population-based study

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Objectives

To describe health service use, symptom and survival characteristics in metastatic prostate cancer (mPCa) in order to outline usual care practices and identify future opportunities to improve the quality of care in this patient group.

Patients and Methods

This population cohort study, conducted in Victoria, Australia, used 10 years (2000–2010) of linked hospital discharge, emergency visit, and death registration data, to track patients from their first inpatient admission with mPCa until death. Descriptive statistics on inpatient health service use, symptoms, procedures, survival, and place of death are presented.

Results

In all, 4436 patients survived a median (interquartile range [IQR]) of 4 (1, 12) months from their first multiday admission with mPCa. They had a median (IQR) of 3 (1, 9) admissions, 1 (0, 2) emergency department presentation, and 35 (18, 63) days admitted to hospital. Lower urinary tract symptoms were common (50%), and 21% underwent lower urinary tract procedures, whilst 48% had blood product transfusions. In the last month of life, 3685 (83%) had at least one indicator of aggressive end-of-life care, including 48% with more than one acute hospital admission, and 55% staying ≥14 days. Hospital-based palliative care was accessed by 2657 (60%), occurring a median (IQR) of 30 (11, 74) days before death. In all, 23% died in the community, whilst 77% died in hospital, of whom 55% died in an acute hospital bed.

Conclusion

Half of all decedents first admitted for a multiday stay with mPCa survived <4 months thereafter. They had a marked symptom burden, underwent multiple procedures and had multiple admissions. In all, 40% of patients did not receive any hospital-based palliative care. Several opportunities exist to improve the timely transition to palliative care services with mPCa. These data form a benchmark against which future improvements to palliative care integration may be measured.

Keywords

end-of-life care, procedures, symptoms, #PCSM, #ProstateCancer, #uroonc

Introduction

Prostate cancer presents a significant challenge of mortality and morbidity for men diagnosed with this disease, their family caregivers, and for the healthcare system. Globally, it is the most common cancer in men, accounting for 1.6 million cases per year [1], and is the second leading cause of cancer death in the USA and Australia [2,3]. Men with metastatic prostate cancer (mPCa) report multiple symptoms related to disease progression, and a rapid deterioration in quality of life during the advanced stages of their illness [4]. Of note, 60% of all healthcare expenditure attributable to prostate cancer occurs in the last 6 months of life [5].

While 10–20% of men with prostate cancer present with metastatic disease, many others will later develop metastases despite treatment with surgery or radiotherapy [6]. Novel methods of detecting early metastatic disease [7]

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means that there will be marked variation in the illness trajectories experienced by this patient cohort. While overall mPCa has a known high prevalence and substantial morbidity, little attention has been given to the palliative care needs of this population. There are limited data describing the illness trajectory of patients with mPCa at the end of life [8–10], including access to the palliative care received. Where evidence exists it is restricted to single-site cohort studies with small sample sizes [8–10]. These studies suggest interventional procedure rates of 19–25% in the final years of life, most commonly involving nephrostomy tubes, Foley catheters and TURP [8,9], with about half of men (52%) requiring multiple interventions. Population-based data of opioid use across a range of cancers reveals that those with prostate cancer have a higher likelihood of opioid prescription (odds ratio 2.60) than other cancers [11]. Understanding use of intensive treatments at the end of life is receiving increasing focus in the international oncology literature [12], but is yet to be described in detail for men with prostate cancer.

Since 2010 a series of randomised trials have described the benefits of palliative care integration across a range of cancers. Such benefits include: improved quality of life, symptom relief, family support, and greater realisation of preferences for care at the end of life [13–16]. However, genitourinary cancers, including prostate cancer, are often underrepresented in these early palliative care trials [17–19], and the specific timing of palliative care integration for this group of patients is yet to be defined.

The present study aimed to describe health service use, symptom, and survival characteristics in men with mPCa at the end of life. Documenting the whole illness trajectory will outline current usual care practices and enable the identification of future opportunities to improve the quality of care in this patient cohort.

Patients and Methods

Setting

Victoria, Australia has a population of 5.6 million [20]. All residents of Australia have universal access to publicly funded medical care provided in both community settings and in public hospitals. For ~51% of Australians, this public coverage is complemented by private health insurance, which allows access to private hospitals [21]. Palliative care is also publicly funded, can be delivered concurrently with cancer treatments, and is available across settings including in acute hospitals, community settings, and in specialised inpatient palliative care units.

The present study was approved by the Monash University Human Research Ethics Committee [CF11/0628] and all data were de-identified, ensuring protection of patient privacy.

Data Sources

All hospital and emergency department data in the State are compiled by individual hospitals and maintained by the Victorian State Department of Health [22–24]. The two datasets contain demographic and clinical information on each episode of patient care; their quality is maintained using an independent audit programme [25,26]. Diagnostic information, including symptoms, is coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Australian Modification (ICD-10-AM) [27], and procedural information according to the Australian Classification of Health Interventions (ACHI), 7th edition. Death certificate data are maintained by the Registry of Births, Deaths and Marriages [24].

These three datasets (hospital, emergency department and Registry of Births, Deaths and Marriages) undergo data linkage at the Victorian Department of Health [28]. Linkage staffs assess data quality by a series of internal logic checks and manual review of randomly selected case groups. Notably, these data report patient contacts with hospital sectors but do not include community based care contacts.

Identification of mPCa Cases

Cases with mPCa were identified based on their first admission containing both primary prostate cancer (C61) and any metastatic extension (C77.0–C79.88). Patients were presumed to have mPCa from that admission onwards. We included only cases with mPCa who had their initial mPCa admission on or after 1 January 2003 and who died before or on 30 June 2010. A 30-month clearance or 'lookback' period was selected during which potential cases with previous admissions for mPCa were excluded to ensure selection of only cases with a first mPCA admission. This timeframe was applied consistently across the included years of data, chosen based upon clinical opinion, and confirmed within the data, with 93% of patients with mPCa in our data who had a period between their initial mPCa admission and death of ≤30 months. Only patients that resided within Victoria or a border region that fell under the Victorian hospital system were included.

Description of Outcome Variables

Sociodemographic and Clinical Characteristics

Demographic and clinical characteristics were obtained from the hospital discharge data, including age group, sex, cancer diagnosis, marital status, private health insurance, country of birth, and area of residence. The relative disadvantage of their area of residence was classified using the Socio-Economic Indexes for Areas (SEIFA) index of relative socio-economic disadvantage [29]. The SEIFA score

was divided into quintiles based on the Victorian population and border regions that access the Victorian hospital system. The remoteness classification of the area of residence was based on the Australian Statistical Geography standard [30].

Cancer and Treatment-related Symptoms and Procedures

Relevant tumour-related diagnoses, symptoms, and procedures, were selected based upon clinical relevance (J.P., J.M.), a review of the literature, and the most common ICD-10-AM and ACHI codes present during the mPCa admissions. This approach was employed in order to maximise face validity (expert opinion and literature review) and completeness ('bottom up' enumeration based on data). Major comorbidities were coded using the Quan version of the Charlson Comorbidity Index [31].

Palliative Care Utilisation

Two indicators of access to hospital-based palliative care were defined. The first involved use of a palliative care or hospice bed, whereby the patient was principally under the care of a specialist inpatient palliative care service. The second was when the patient, cared for by a primary hospital care team, received a consultation from the specialist hospital-based palliative care services. The timing of access to palliative care (as above) was defined based on the number of days between the initiation of a palliative care approach to care and death.

Quality of End-of-life Care

Aggressiveness of care, as adopted from Earle et al. [32] with information available in our datasets, was defined by the following parameters in the last 30 days of life: more than one emergency department presentation, more than one hospital admission, length of stay >14 days, intensive care unit admission, and inpatient chemotherapy administration within 14 days of death.

Site of Death

Site of death was based on a combination of hospital and death certificate data in order to classify it into three mutually exclusive groups: outside hospital that is, in the community; in an inpatient hospice/palliative care bed; and in an acute care hospital bed.

Statistical Analysis

The illness period being described began at the time of first admission with a diagnosis of metastatic palliative care to the date of death. Care characteristics or variables were extracted for every admission from the initial mPCa admission onwards. Patients were classified as having a characteristic if the data indicated its presence during any admission from their initial mPCa admission to death, inclusive. Medians, interquartile ranges (IQRs) and percentages were used to describe the distribution of these variables.

Stata 13.1, 2013 (Stata Corporation, College Station, TX, USA) was used for all statistical analyses.

Results

Sample

There were a total of 8039 patients who died with prostate cancer in the state of Victoria during the study timeframe, including 6890 (86%) who were included in the hospital admission records, and an additional 1149 (14%) who were never admitted. We examined the whole care trajectory of 4436 eligible cases with mPCA who died and were diagnosed with a first metastasis in the period of interest. In all, 66% (n = 2941) were aged ≥75 years and 64% were born in Australia (Table 1). At the first hospitalisation for mPCa, sites of metastases were: bone (n = 3734, 84%), lymph nodes (n = 475, 11%), liver (n = 375, 8%), lung (n = 361, 8%), and 19% (n = 860) had more than one metastatic site (Table 2).

Symptom Burden

The burden of symptoms experienced by patients increased over the illness course, including symptoms related to local problems caused by the cancer, such as LUTS (which increased cumulatively from 25% to 50% from first admission with mPCA to death), and also for systemic symptoms such as confusion, which affected 17% over the illness course (Table 2).

Medical Interventions/Procedures

The most frequent diagnostic imaging service performed for the inpatient population was CT (n = 2127, 48%), whilst 21% had procedures to address lower urinary tract problems, and 48% had a transfusion of blood products over the course of their trajectory from first mPCa to death (Table 3).

Survival

The median survival after first hospitalisation of any duration, from same-day to multiday with mPCa was 4 months, with 75% of patients (n = 3252) surviving ≥30 days and 25% (n = 1109) surviving >12 months. This short median survival reflects our sampling frame, which included only those patients who died during the sampling timeframe. In all, 20%

Table 1 Description of the mPCA sample (*N* = 4436).

Characteristic	*N* (%)
Age at presentation, years	
<65	399 (9)
65–74	1096 (25)
≥75	2941 (66)
Country of birth	
Australia	2831 (64)
Other, English speaking	451 (10)
Other, not English speaking	1154 (26)
Remoteness classification (home residence)	
Major city	2159 (49)
Inner regional	1574 (35)
Outer regional	527 (12)
Remote/very remote	161 (4)
Missing	15 (<1)
SEIFA index of economic disadvantage	
Most disadvantaged: 1st quintile	356 (8)
2nd quintile	488 (11)
3rd quintile	756 (17)
4th quintile	954 (22)
Least disadvantaged: 5th quintile	1881 (42)
Marital status	
Single	1073 (24)
Partnered	3363 (76)
Private hospital use, any	2362 (53)
Survival characteristics	
Months from first inpatient admission to death, median (IQR)	4 (1, 12)
Death in first admission	890 (20)

of patients (n = 890) died during their first admission with mPCa.

Patterns of Care and Quality of End-of-life Care

Between the first hospitalisation with mPCa and death, patients had a median of three admissions, spent a total of 35 days in hospital, with each admission a median of 8 days in length (Table 4). While 61% had an emergency department presentation, this was a median of one presentation per patient.

In the final month of life, 48% had more than one acute hospitalisation, and 7% had more than one emergency department presentation (Table 5). In all, 60% accessed palliative care within a median of 1 month prior to death, and for 64%, this access was in the final admission before death. Most patients (77%) died in hospital.

Discussion

The present study details the healthcare use of a large cohort of patients with mPCa and describes their quality of end-of-life care within a universal access health system including palliative care services. We have demonstrated that this patient group have frequent hospitalisations at the end of life, and overall, are hospitalised for nearly one-third of the time (35 days) between their first admissions with mPCa until death (a period of median 116 days). Based upon the quality of end-of-life care indicators, our data indicate that patients with mPCa have high rates of more than one acute hospitalisation (48%), and of >14 days in hospital (55%) in the final month of life. These findings are associated with poorer quality of end-of-life care, and, as such, demonstrate opportunities to improve care in this patient group [26].

The present study reveals that access to palliative care is not universal (60%) and, for the majority (64%), occurs late. These data mirror the findings of others. In a study by Roeland et al. [33] of 83 022 elderly patients across a range of cancers, including prostate cancer, 77% were not referred to palliative care until the last 4 weeks of life, suggesting that palliative care involvement is not yet a standard of care in this disease. Interestingly Roeland et al. [33] noted that health system factors affect palliative care service delivery, with an increased likelihood of a palliative care consultation in geographical regions with decreased numbers of regional acute care hospital beds. Meanwhile, others have reported that race appears to impact upon the quality of end-of-life care received amongst patients with prostate cancer [34]. These findings highlight the complex social and health systems that palliative care works within, where a myriad of factors including socio-cultural, resource, health system, and health professional practices may all influence referral to, or engagement with palliative care.

The recognition of need for palliative care, or the recognition of end-stage disease appears to be a critical step in timely and appropriate access to palliative care. In a large Danish study of 11 062 patients, physician recognition of the terminal phase of illness occurred at a median of 55 days before death, but for those with prostate cancer this recognition occurred earlier, at a median of 76 days before death [35]. This indicates the potential for early recognition of the end-stage of illness in prostate cancer, a finding also noted by William et al. [36], who suggested that patients with prostate cancer typically follow a different illness course at the end of life to people with other cancers. They suggested that patients with prostate cancer typically followed a slow deterioration with worsening performance status, increasing dependency and frailty over many months [36]. They described this patient cohort as frequently requiring increasing nursing care but not necessarily intensive medical or procedural input [36,37].

Furthermore, in a USA cohort of 3026 men with mPCa, Golan et al. [38] reported that higher rates of interventions, such as more frequent PSA testing and imaging, were not associated with observed survival benefits or improvements in the quality of care at the end of life. Thus, healthcare resources at this time may be better directed towards earlier palliative care input, which has been associated with significant improvements in symptoms, which are known to accompany the proposed prostate illness course of gradual deterioration to death. Studies of consecutive patients with

Table 2 Burden and characterisation of disease and symptoms for men with mPCA (*N* = 4436).

Disease-related complications	At first admission with mPCa, *n* (%)	Across illness course from first admission with mPCa until death, *n* (%)
Sites of metastases		
Bone	3734 (84)	3967 (89)
Brain and CNS	135 (3)	351 (8)
Lymph nodes	475 (11)	712 (16)
Liver	375 (8)	704 (16)
Lung and pleura	361 (8)	612 (14)
Other	410 (9)	718 (16)
>1 metastatic site	860 (19)	1773 (40)
>2 metastatic sites	255 (6)	790 (18)
Charlson comorbidity		
No comorbidity present	3214 (72)	2170 (49)
At least one* present	1222 (28)	2266 (51)
LUTS, including obstructive, incontinence, haematuria symptoms	1089 (25)	2207 (50)
Metabolic, nutrition and endocrine complications, including diabetes, dehydration, electrolyte imbalances	784 (18)	1914 (43)
Blood-related complications, including anaemia, thrombocytopaenia	850 (19)	2173 (49)
Skeletal-related complications, including fractures and cord compression	452 (10)	940 (21)
Psychological symptoms, including mood disorders	131 (3)	411 (9)
Most frequent specific symptoms and complications		
Renal failure	700 (16)	1305 (29)
Constipation	548 (12)	1408 (32)
Nausea and vomiting	295 (7)	929 (21)
Faecal incontinence	150 (3)	410 (9)
Anorexia or severe weight loss	170 (4)	454 (10)
Pain	318 (7)	939 (21)
Fever	86 (2)	400 (9)
Fatigue	93 (2)	314 (7)
Confusion, delirium, restlessness	260 (6)	747 (17)
Infections including pulmonary, urinary	883 (20)	**2296 (52)**
Rash and skin changes	122 (3)	426 (10)
Total number of complications, median (IQR)	1 (0, 3)	5 (3, 8)
≤1 complication	2468 (56)	623 (14)
2–3 complications	997 (22)	949 (21)
≥4 complications	971 (22)	2864 (65)

*Symptoms <5% not reported. *Acute myocardial infarction, congestive heart failure, peripheral vascular disease, cerebral vascular accident, dementia, pulmonary disease, connective tissue disorder, peptic ulcer, liver disease/severe liver disease, diabetes with or without complications, paraplegia, renal disease, HIV. Bold text represents major group of disease-related complications.*

prostate cancer presenting for outpatient consultation in the USA (55 patients) and Spain (605 patients), found significant rates of urinary problems as well as high levels of pain and fatigue, the latter two symptoms closely associated with poor quality of life [39,40]. Both these symptoms improved significantly following palliative care consultation [39]. These findings of others, and data from our present study demonstrate that patients with mPCa have significant symptom burden, and may benefit from palliative care input.

However, despite evidence that the terminal trajectory can be recognised earlier than for other cancers, in the present study, timely palliative care referrals were still not always enacted. Despite a series of studies demonstrating benefits of early palliative care, including improved end-of-life care, it appears such practice is not standardised, and many patients with mPCa have indicators of poor quality end-of-life care. While variation in practice may result from both individual clinician and 'system' level factors, as is the case with other areas of management [41], the present study demonstrates the need for guidelines to help standardise pathways to engagement with palliative care in a timely manner.

Attempts have been made to develop a standardised set of patient-reported outcomes for patients with mPCa with a focus on symptoms of cancer and side-effects of treatment [42]. We advocate that benchmarks for palliative care engagement at standardised time-points should be added to the patient-reported outcome set. We propose that the standardised time for palliative care referral should be at first multiday admission with mPCa [43], as a minimum requirement, and should occur earlier if particular needs are identified. This time-point would be readily identifiable, and, based upon these data, represents a time of high health service use and poor prognosis. Access to palliative care at, or prior to, this standardised time allows for benchmarking against such a standard. As such, the data from the present study may serve as an historical benchmark against which

Table 3 Interventional procedures for men with mPCa (*N* = 4436).

Imaging and Interventional procedures	At first admission with mPCa, *n* (%)	Across illness course from first admission with mPCa until death, *n* (%)
Inpatient diagnostic Imaging, any*	1663 (37)	2640 (60)
Ultrasonography	93 (2)	178 (4)
X-ray	50 (1)	114 (3)
CT	1213 (27)	2127 (48)
MRI	310 (7)	687 (15)
Whole body nuclear medicine imaging study	750 (17)	1087 (25)
Biopsy, any site	366 (8)	638 (14)
Local interventional procedures	648 (15)	1183 (27)
Upper urinary tract: including ureteric catheterisation, nephrostomy tube or ureteric stent insertion	178 (4)	366 (8)
Lower urinary tract: including urinary (Foley) catheter insertion, suprapubic catheterisation, TURP	483 (11)	945 (21)
Blood/blood-product transfusions	810 (18)	2124 (48)
Internal fracture fixation	64 (1)	150 (3)
Inpatient administration of antineoplastic agents	869 (20)	1670 (38)
Inpatient administration of radiotherapy	300 (7)	692 (16)
Any interventional procedure	2299 (52)	3239 (73)
Two or more interventional procedure	489 (11)	1983 (45)

**Within hospital only.*

Table 4 Acute inpatient hospital use for men with mPCa (*N* = 4436).

Variable	Value
Admissions	
Total admissions, median (IQR)	3 (1, 9)
Total same-day admissions, median (IQR)	1 (0, 5)
Same-day admission at presentation, *n* (%)	1106 (25)
Intensive care use, *n* (%)	271 (6)
Emergency department use, *n* (%)	2715 (61)
Emergency department presentation, median (IQR)	1 (0, 2)
Length of stay characteristics	
Total bed days, median (IQR)	35 (18, 63)
Total bed days per admission, median (IQR)	8 (4, 16)

Emergency department presentation only counted once for people who are transferred between emergency departments; multiple episodes of care are counted as one admission including cross-hospital transfer.

Table 5 Quality end-of-life care indicators for men with mPCa (*N* = 4436).

	N (%)
Aggressiveness of Care	
>1 emergency department presentation in the last 30 days of life	311 (7)
>1 acute hospital admission in the last 30 days of life	2124 (48)
Length of stay ≥14 days in last 30 days of life	2451 (55)
Intensive care admission in last 30 days of life	90 (2)
Chemotherapy in last 14 days of life	527 (12)
At least one indicator of aggressive end-of-life care	3685 (83)
≥2 indicators of aggressive end-of-life care	1464 (33)
Access to palliative care	
No palliative care referral	1779 (40)
Hospital-based palliative care referral	2657 (60)
Palliative care hospice bed, *n* (%)	1744 (39)
Total bed days per palliative care admission, median (IQR)	11 (5, 22)
Timing of palliative care (*N* = 2657)	
Time (months) from first inpatient admission to referral, median (IQR)	2 (0, 10)
Time (months) from referral to death, median (IQR)	1 (0.4, 2.5)
Number of prior medical encounters before palliative care, median (IQR)	4 (2, 9)
First access in final admission, *n* (%)	1700 (64)
Place of death	
Outside hospital	1009 (23)
In-hospital	3427 (77)
Acute bed	1884 (55)
Palliative care or hospice bed	1428 (42)
Other	115 (3)

future improvements in patterns of palliative care access may be mapped.

The present study has a series of limitations, including, that it is based on inpatient hospital-based data only, with outpatient and community care, including community palliative care, not captured. As such, the patients included in the present study were those with mPCA who required admission. Although we know a majority (86%) of all men who died with mPCa care were admitted to hospital at least once, our sample likely represents the higher acuity patients. Furthermore, the data capture is of a time interval that preceded a series of landmark publications detailing benefits of palliative care, which may have resulted in practice change. Such potential practice changes would not be reflected in the data within the present study. Similarly, our present data did not contain information on hormone-sensitive disease or refractory state, so we are not able to ascertain the impact of these factors on symptoms or health service use. Nonetheless, the large State-wide, population-based dataset within a universal health system has enabled the documentation of the whole illness period from hospital admission until death, demonstrating State-wide patterns of all hospital care including end-of-life care.

Patients with mPCa spend a substantial time in hospital in their last months, including half having two or more acute care hospitalisations in the final 30 days of life. Most die in hospital and most have at least one indicator of poor quality end-of-life care. These data reveal opportunities for improvement in end-of-life care for patients with mPCa, including standardisation of access to and engagement of palliative care. By standardising palliative care engagement at a designated time, benchmarks can be developed to map and improve the quality of end-of-life care for patients with prostate cancer. We propose future population studies detailing access to and use of palliative care based on these standardised times of engagement, to contribute to the growing body of evidence highlighting the benefit of early palliative care integration.

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Conflicts of Interest

None declared.

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Abbreviations: ACHI, Australian Classification of Health Interventions; ICD-10-AM, International Statistical Classification of Diseases and Related Health Problems 10th RevisionAustralian Modification; IQR, interquartile range; mPCa, metastatic prostate cancer; SEIFA, Socio-Economic Indexes for Areas.