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Trends in End-of-Life Resource Utilization and Costs among Prostate Cancer Patients from 2006 to 2015: A Nationwide Population-Based Study

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Purpose: The purpose of this study was to evaluate end-of-life resource utilization and costs for prostate cancer patients during the last year of life in Korea.

Materials and Methods: The study used the National Health Information Database (NHIS-2017-4-031) of the Korean National Health Insurance Service. Healthcare claim data for the years 2002 through 2015 were collected from the Korean National Health Insurance System. Among 83,173 prostate cancer patients, we enrolled 18,419 after excluding 1,082 who never claimed for the last year of life.

Results: From 2006 to 2015, there was a 3.2-fold increase the total number of prostate cancer decedents. The average cost of care during the last year of life increased over the 10-year period, from 14,420,000 Korean won to 20,300,000 Korean won, regardless of survival time. The cost of major treatments and medications, other than analgesics, was relatively high. Radiologic tests, opioids, pain control, and rehabilitation costs were relatively low. Multiple regression analysis identified age and living in rural area as negatively associated with prostate cancer care costs, whereas income level and a higher number of comorbidities were positively associated.

Conclusions: Expenditure of prostate cancer care during the last year of life varied according to patient characteristics. Average costs increased every year. However, the results suggest underutilization of support services, likely due to lack of al-

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ternative accommodation for terminal prostate cancer patients. Further examination of patterns of utilization of healthcare resources will allow policymakers to take a better approach to reducing the burden of prostate cancer care.

Keywords: Health care costs; Healthcare utilization; Prostatic neoplasms; Terminal care

INTRODUCTION

There has been an unprecedented rise in the number of cancer cases around the globe, and improved treatments have resulted in higher rates of survival than ever before [1]. Cancer is placing an increasing burden on healthcare systems and is a major expense for developed countries [2]. In contrast to the evidence base supporting clinical decision making at the time of a cancer diagnosis, there is limited understanding about what constitutes quality end-of-life care. In 2015, cancer was the number one leading cause of death in Korea; the total number of cancer-related deaths was 76,855, accounting for 27.9% of all deaths [3]. Therefore, the end-of-life period is of particular interest given the high volume of care and speculation about the quality of care provided; this is something that has wide-reaching clinical and economic consequences [2,4]. Previous research suggests that the year following diagnosis and the last year of life are the most resource- and cost-intensive periods of cancer treatment [5]. Chastek et al [6] showed that terminal cancer patients spent an average of US $74,212 during their last 6 months of life, which is considerably higher than the average Medicare beneficiary's expenditure (US $35,156) during the last year of life (both cost estimates are based on 2009 data) [7]. However, few studies have examined end-of-life medical costs for cancer patients, particularly those with prostate cancer (PCa), in Korea.

PCa is the fifth most common male cancer in Korea [8]. The incidence of PCa has increased consistently and the annual age-standardized mortality rates increased from 1983 to 2015 [3]. Thus, the economic burden of PCa in Korea has increased to levels similar to those in other developed countries. In the United States, the annual cost of PCa management totals several billion dollars [9]. Despite the increasing burden of PCa, there are few nationwide data concerning the economic burden of PCa on the Korean population. Moreover, there are

now multiple effective treatment strategies for PCa [10]. To date, there has been no comprehensive analysis of chronological changes focused on end-of-life resource utilization and costs related to end-of-life care for PCa. To secure reliable data, we used the Korean National Health Insurance (KNHI) database. Using this dataset, we assessed chronological trends in PCa care costs during the last year of life with respect to patient characteristics and treatment modalities, which in turn enabled us to identify patterns of health care utilization among Korean PCa patients.

MATERIALS AND METHODS

1. Data sources and patient identification

This study used data from the National Health Information Database (NHIS-2017-4-031) held by the Korean National Health Insurance Service (NHIS). The authors declare no conflict of interest with NHIS. Healthcare claim data for the years 2002 through 2015 were collected. Mostly based on a fee-for-service approach, KNHI claim data contain a specific disease code and all data necessary for reimbursement, including patient sociodemographic information (age, health insurance premiums, residential area, comorbid diseases, diagnostic tests, procedures, and prescriptions provided, and outcome [death]). This database is used extensively for epidemiological and health policy studies [11]. All patient data were anonymized. All patients with code C61 claims from 2002 to 2015 (indicating PCa according to the International Classification of Diseases, 10th edition, Clinical Modification) were screened.

Among 874,924 patients assigned code C61 from 2002 to 2015, 791,751 patient were excluded and 83,173 who had undergone primary treatments, such as surgery (radical prostatectomy, robot-assisted radical laparoscopic prostatectomy), androgen deprivation therapy (ADT), or radiotherapy (RT) for PCa for the first time since 2003 were enrolled. The 3,356 patients who

received primary treatment in 2002 were excluded because we could not confirm the date of the first primary treatment. We also excluded patients who only received second line ADT for PCa (n=232) and those lacking information regarding residential area (n=53). Finally, we excluded 1,082 patients who had never claimed for the last year of life, leaving 18,419 patients for analysis (Fig. 1).

2. Variables and outcomes

Patient sociodemographic parameters included age, income class, and residential area. Patients were divided into five categories according to age at diagnosis (<50, 50–64, 65–74, and ≥75 years). Based on income levels, patients were assigned to insurance premium categories "below the poverty line" (lowest) and "quintile" (I, II, III, IV, and V [highest]). KNHI contributions were used as a proxy measure for actual household income because contributions are based on income, property, and private auto taxes for each household [12]. Patients were grouped into three residential area categories, metropolitan, urban, and rural, according to Korean ZIP code. The Charlson comorbidity index (CCI), which is a single index of comorbidity burden developed to assess the relative risk of a patient's comorbid conditions on outcome after a critical illness, was used to group patients into four categories based on the index score: 0, 1–2, 3–4, and ≥5 (the most severe) [13]. Survival time was defined as the period from the date of cancer diagnosis to that of death or end of follow-up. The operational definition of time of diagnosis was the first day of admission for primary treatment. As for the last year of life, most of health service research on end-of-life cancer care costs calculated its costs per patient for each month and for the entire 6-month or 1-year period before death according to the amounts spent on all medical and pharmaceutical services [14,15]. And also, costs are presented, including both cancer-related costs and non-cancer ones because it is not easy to distinguish the two and is often claimed as cancer-related costs. Therefore, we defined end-of-life cancer care costs as the final 12 months of life in accordance with previous studies, and the mean medical cost during the last year of life was calculated by combining the medical claims for each individual [16]. All cost measures were calculated as combined insurer and co-payment amounts for each claim, and The hospital input price index (unit price per point of the relative value scales) was used to adjust for inflation during the study period. All cost estimates are reported in Korean won (KRW) (2015).

3. Statistical analyses

Descriptive analyses of demographics and end-of-life costs were performed for the following categories: age, residential area, insurance premium level, CCI, type of primary treatment at first diagnosis, survival time, and use of hospice facilities and the emergency department. Monthly costs before death, and those based on the year of death, were also calculated. Multiple linear regression analyses were performed to estimate the association between the mean cost of PCa during the last year of life and the decedent's demographic and clinical characteristics. All analyses were performed using SAS software ver. 9.4 (SAS Institute Inc., Cary, NC, USA). Two-sided p-values of 0.05 were considered significant.
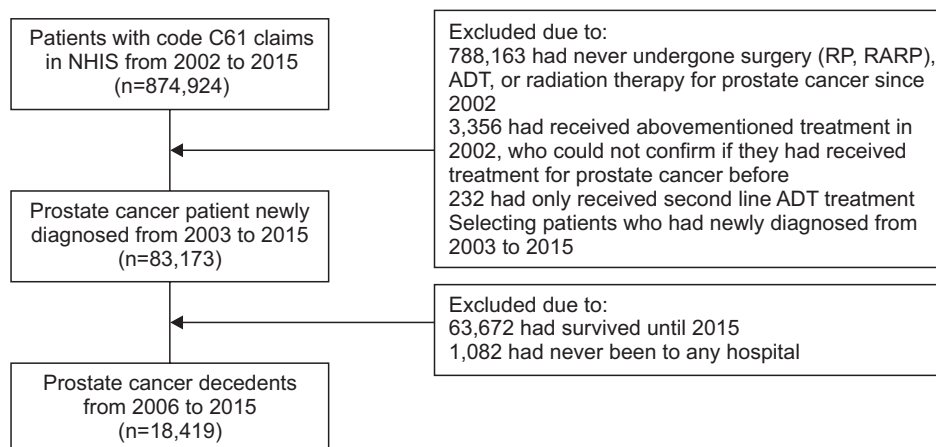
Fig. 1. Selection of study subjects. NHIS: National Health Insurance Service, RP: radical prostatectomy, RARP: robot-assisted laparoscopic radical prostatectomy, ADT: androgen deprivation therapy.

Table 1. Subject characteristics and cancer care costs during the last year of life

Characteristic	Subject	Total costs (10,000 KRW)	Insurer payment (10,000 KRW)	Out-of-pocket (10,000 KRW)
Total	18,419 (100.0)	1,852±1,452	1,634±1,317	207±197
Year of death				
2006	834 (4.5)	1,442±1,053	1,242±924	194±153
2007	1,107 (6.0)	1,677±1,215	1,467±1,090	205±161
2008	1,296 (7.0)	1,734±1,283	1,495±1,121	231±198
2009	1,506 (8.2)	1,816±1,416	1,561±1,234	249±228
2010	1,761 (9.6)	1,786±1,333	1,582±1,204	196±185
2011	1,993 (10.8)	1,880±1,485	1,673±1,356	196±194
2012	2,223 (12.1)	1,911±1,491	1,703±1,369	194±191
2013	2,540 (13.8)	1,918±1,523	1,702±1,389	201±197
2014	2,509 (13.6)	1,866±1,500	1,655±1,376	200±190
2015	2,650 (14.4)	2,030±1,607	1,800±1,465	217±220
Time before death (mo)				
1		272±380	243±349	28±45
2		265±449	237±410	28±52
3		202±360	179±328	22±41
4		156±287	138±262	17±34
5		139±250	122±224	16±34
6		124±213	109±191	14±29
7		113±208	99±187	13±28
8		109±188	95±168	13±25
9		99±184	86±164	12±28
10		92±168	80±151	11±23
11		90±163	78±145	11±25
12		84±149	73±133	11±23
Age (y)	77.2±8.3			
<65	1,264 (6.9)	2,817±1,802	2,575±1,684	238±187
65–74	5,010 (27.2)	2,130±1,505	1,905±1,375	216±190
75–84	8,746 (47.5)	1,730±1,336	1,511±1,193	205±201
≥85	3,399 (18.5)	1,400±1,261	1,200±1,109	189±198
Residential area				
Metropolitan	9,996 (54.3)	1,920±1,511	1,693±1,372	215±205
Urban	5,213 (28.3)	1,807±1,436	1,597±1,304	199±191
Rural	3,198 (17.4)	1,718±1,267	1,512±1,142	196±179
Unknown	12 (0.1)	1,248±715	1,106±663	129±80
Insurance premium, quintile				
Below poverty line (lowest)	1,725 (9.4)	1,861±1,358	1,804±1,317	53±131
I	2,027 (11.0)	1,747±1,476	1,536±1,338	199±193
II	1,722 (9.3)	1,762±1,381	1,544±1,250	205±175
III	2,300 (12.5)	1,817±1,390	1,595±1,268	212±170
IV	3,249 (17.6)	1,808±1,341	1,582±1,214	214±173
V (highest)	7,396 (40.2)	1,930±1,542	1,677±1,379	241±216
Charlson comorbidity index				
0	2,006 (10.9)	1,624±1,302	1,454±1,197	164±159
1–2	4,819 (26.2)	1,722±1,372	1,523±1,252	192±177
3–4	3,895 (21.1)	1,838±1,468	1,614±1,329	214±206
≥5	7,699 (41.8)	2,000±1,513	1,761±1,368	225±211

Table 1. Continued

Characteristic	Subject	Total costs (10,000 KRW)	Insurer payment (10,000 KRW)	Out-of-pocket (10,000 KRW)
Primary treatment at prostate cancer diagnosis				
Surgery only	1,483 (8.1)	2,087±1,896	1,812±1,713	263±273
Surgery+ADT	332 (1.8)	1,987±1,676	1,749±1,523	234±243
Surgery+RT	229 (1.2)	2,479±1,684	2,239±1,536	236±218
Surgery+ADT+RT	210 (1.1)	2,517±1,381	2,285±1,299	225±160
RT only	345 (1.9)	2,307±1,959	2,051±1,800	245±222
ADT only	12,645 (68.7)	1,656±1,296	1,449±1,160	195±190
ADT+RT	3,175 (17.2)	2,370±1,517	2,143±1,406	220±165
Survival time (y)	3.3±2.5			
<2	7,099 (38.5)	1,913±1,399	1,695±1,281	209±182
2–5	7,222 (39.2)	1,839±1,478	1,626±1,335	202±198
5–10	3,810 (20.7)	1,767±1,491	1,540±1,341	212±217
≥10	288 (1.6)	1,823±1,511	1,577±1,342	229±237
Hospice facility use				
Yes	8,047 (43.7)	1,931±1,443	1,713±1,314	209±188
No	10,372 (56.3)	1,788±1,455	1,573±1,316	202±198
Emergency department use	0.6±1.2			
Yes	5,473 (29.7)	2,412±1,655	2,145±1,513	260±217
No	12,946 (70.3)	1,613±1,284	1,418±1,159	182±178
Cancer care-related visit				
Yes	16,743 (90.9)	846±1,026	773±944	70±103
No	1,676 (9.1)	1,006±1,293	861±1,150	137±184

Values are presented as number (%) or mean±standard deviation.
KRW: Korean won, ADT: androgen deprivation therapy, RT: radiotherapy.

4. Ethics statement

The study protocol was approved by the Institutional Review Board of the Chungbuk University Hospital (CBNUH 2015-04-004-002). The requirement for informed consent was waived because the study was based on routinely collected administrative data.

RESULTS

Table 1 summarizes patient characteristics and medical costs during the last year of life. The mean age of the enrolled patients was 77.2 years. The number of PCa decedents in 2006 was 834. This showed a steady annual increase across the 10 years study period, with a 3.2-fold increase in the total of number observed in 2015. The average cost of PCa care during the last year of life increased over the 10-year period, from 14,420,000 KRW to 20,300,000 KRW (Fig 2). However, with support from the KNHI program, out-of-pocket expenditure remained stable. Individuals aged 75 years or older accounted for 66.0% of PCa decedents. We
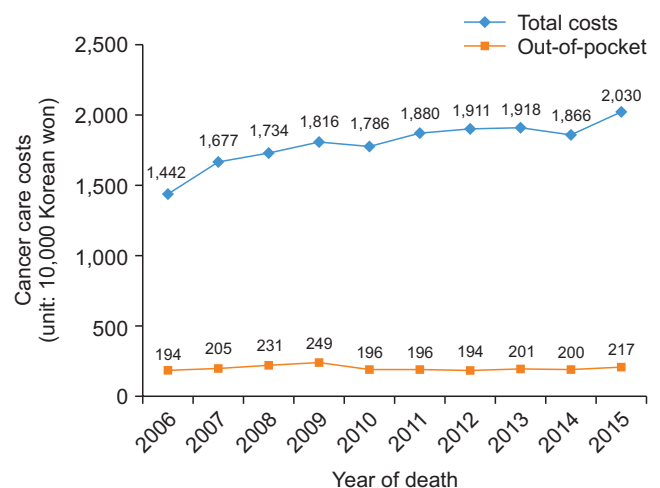

Fig. 2. Year of death and cancer care costs.

found that a pattern of decreasing expenditure on end-of-life resources with increasing age, particularly for the "oldest old" (aged≥85 years), was pervasive. There were 1,725 patients (9.4%) in the lowest income class (below the poverty line); however, the largest percent-

age (40.2%) was in the highest income class (group V). Patients in group V spent the most on care while those in group I spent the least. About half of patients (54.3%) lived in metropolitan areas, and 45.7% lived in urban or rural areas. Total medical expenditure by rural decedents was lower than that by urban and metropolitan counterparts. Because the study population comprised PCa decedents, most (n=11,594, 62.9%) scored ≥3 on the CCI, suggesting a relatively high level of comorbidity. Costs increased along with the CCI score. Of the subjects, 29.7% used the emergency department at least once during the last year of life; the mean number of visits was 0.6.

PCa care expenditure according to treatment and resource utilization during the last year of life is also presented in Table 1. Most patients (68.7%) received ADT only, which is the least expensive therapy. If patients received RT only, or RT combined with surgery or ADT, as the primary treatment after PCa diagnosis, expenditure was higher. PCa care costs increased steadily as death approached, from 840,000 KRW in the 12th month to 2,720,000 KRW in the month before death. Patients using hospice facilities (43.7%) had higher costs than those who did not. PCa decedents surviving less than 2 years had the highest costs (19,130,000 KRW), while those surviving for 5–10 years had the lowest (17,670,000 KRW). When stratified ac-

cording to survival period, the costs of PCa care per patient during the last year of life increased gradually in all subgroups over the 10-year period; the exception was patients surviving ≥10 years (Supplement Figure). Support from the KNHI program meant that out-of-pocket expenditure remained stable during the last of life.

Fig. 3 shows the costs of treatment according to age, income, and survival time. On average, the cost of major treatment was highest (26.0% of total costs), followed by other medications (22.3%), radiologic tests (5.3%), pain control (4.3%), opioid use (3.7%), and rehabilitation (1.1%). Costs associated with major treatment comprised a lower percentage of the total for older patients and for patients that survived longer. Expenditure associated with rehabilitation, which is a supportive care service, were very low (0.7%–1.4% of the total) for all subgroups.

Predictors of care expenditure during the last year of life are presented in Table 2. In our study cohort, older age was negatively associated with PCa care expenditure. Compared with patients living in metropolitan areas, those in urban and rural areas were more likely to have lower costs. Higher income, indicated by the insurance premium, was positively associated with PCa care costs. As would be expected, having a higher CCI score was associated with higher mean medical expen-
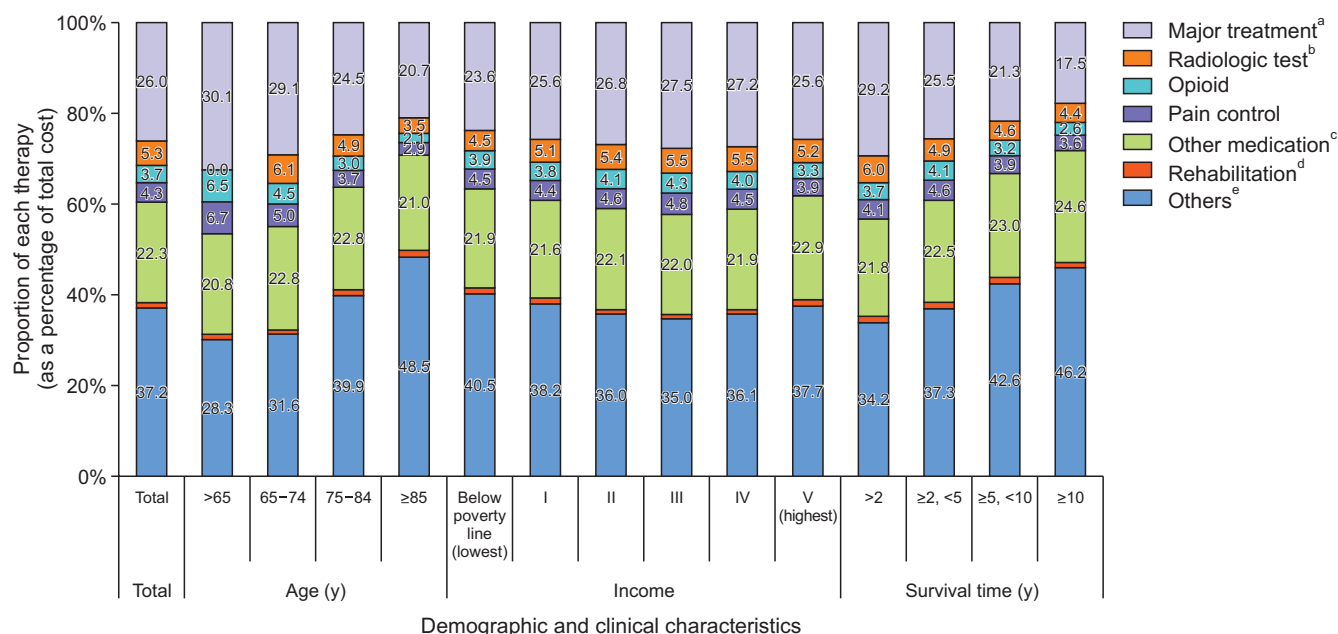
Fig. 3. Cost of each therapy according to age, income, and survival time. [a]Surgery, radiotherapy, and chemotherapy. [b]Radiologic special diagnostic tests included computed tomography (CT), magnetic resonance imaging, positron emission tomography/CT scan, ultrasonography, and densitometry. [c]Drugs other than opioids and analgesics. [d]Physiotherapy and psychotherapy. [e]Therapies other than those mentioned above.

Table 2. Factors affecting cancer care costs during the last year of life

Variable	Unadjusted		Adjusted	
	Coefficient	p-value	Coefficient	p-value
Age (y)				
<65				
65–74	-686.1	<0.0001	-254.0	<0.0001
75–84	-1,086.7	<0.0001	-417.1	<0.0001
≥85	-1,416.1	<0.0001	-522.3	<0.0001
Residential area				
Metropolitan				
Urban	-112.8	<0.0001	-49.0	0.002
Rural	-201.9	<0.0001	-151.3	<0.0001
Insurance premium, quintile				
Below poverty line (lowest)				
I	-114.5	0.016	84.3	0.006
II	-101.6	0.040	79.5	0.012
III	-46.0	0.320	96.5	0.001
IV	-55.0	0.204	71.1	0.011
V (highest)	66.6	0.086	173.4	<0.0001
Charlson comorbidity index				
0				
1–2	97.0	0.012	35.9	0.148
3–4	213.4	<0.0001	64.0	0.013
≥5	375.9	<0.0001	74.8	0.002
Survival time (y)				
<2				
2–5	-75.1	0.002	-3.1	0.844
5–10	-147.6	<0.0001	-25.8	0.195
≥10	-91.5	0.294	-41.1	0.474
Emergency department use				
Yes				
No	799.6	<0.0001	329.9	<0.0001
Healthcare utilization				
Inpatient days	9.5	<0.0001	9.4	<0.0001
Outpatient days	4.2	<0.0001	5.4	<0.0001
CT use	231.6	<0.0001	150.8	<0.0001
PET/CT use	94.6	<0.0001	37.7	<0.0001
MRI use	277.4	<0.0001	77.5	<0.0001
Year of death				
2006				
2007	233.3	<0.001	64.9	0.128
2008	290.1	<0.0001	25.5	0.538
2009	372.3	<0.0001	68.9	0.088
2010	341.9	<0.0001	26.8	0.496
2011	435.1	<0.0001	-121.3	0.002
2012	467.5	<0.0001	-104.4	0.007
2013	474.8	<0.0001	-50.5	0.184
2014	422.5	<0.0001	-73.5	0.055
2015	587.2	<0.0001	22.5	0.557

CT: computed tomography, PET: positron emission tomography, MRI: magnetic resonance imaging.

diture. Adjusted linear regression analyses revealed that survival time was not associated with PCa care costs. Use of the emergency department, longer hospital stay, and radiologic examinations during the last year of life resulted in relatively high costs. The unadjusted model showed that the year of death was positively associated with PCa care cost; however, the adjusted linear regression model revealed no significant association between year of death and medical expenditure.

DISCUSSION

To the best of our knowledge, this is the first study to investigate medical expenditure and resource utilization by Korean PCa decedents during the last year of life. The comprehensive analysis of end-of-life resource utilization and costs revealed the quality of health resource use and health system costs incurred by PCa patients approaching life's end. The main finding was that medical expenditure depends on decedent characteristics and demographics.

In concordance with a previous study [17], we found that medical costs during the last year of life decreased with age. This was driven by reduced utilization of hospital services [18]. Moreover, elderly populations tended to be cared for by palliative services rather than receive aggressive treatment [19]. When caring for elderly PCa patients, physicians usually select the least invasive treatment modality. Here, we found that the proportion of costs associated with major treatments was lower for older patients (Fig. 3). To sum up, decreasing expenditure with age is in large part due to less aggressive treatment.

Significant metropolitan/urban/rural disparities in terms of medical costs have been identified. Crouch et al [20], report that end-of-life Medicare costs for rural beneficiaries with breast, lung, or colorectal cancer are lower than those of urban beneficiaries. Kim and Park [21] noted that expenditure among urban adult Korean cancer patients was highest. Also, medical costs increased with insurance premium levels; this was due to high-income patients using inpatient and outpatient facilities more frequently than lower income patients [12]. However, medical expenditure by insurance premium level I and II patients were significantly lower than those by patients living below poverty line, indicating underutilization of health care services by the near-poor (indeed, in general there is a positive associa-

tion between income level and use of healthcare facilities). Medical expenditure increased with the number of comorbidities, as measured by the CCI. This result was reflected in the finding that the costs of non-PCa care-related visits were higher than those for PCa care-related visits (10,060,000 KRW *vs.* 8,460,000 KRW, respectively) (Table 1).

In our analysis, 29.7% of decedents visited the emergency department at least once during the last year of life. In 2009, Hwang et al [16] reported a slightly higher rate (35.1%) of emergency department use among all Korean cancer decedents. Most PCa decedents in Korea die from PCa (46.3%) itself or from another cancer (35.4%) [22]. Here, death from cardiovascular disease occurred in only 6.6% of the cohort. This proportion may affect cause the rate of visiting emergency room. We also found that costs increased sharply as death approached. A previous study also showed a similar trend; costs increased from $644 in the 12th month to $2,480 in the last month before death [16].

The most important findings of the current study were: (i) a marked increase in the number of PCa decedents over the 10-year period; and (ii) a gradual increase in medical costs over the 10-year period. The reason for the increasing number of PCa decedents is increased incidence of PCa. A previous study demonstrated that between 1999 and 2009, the age-standardized incidence of PCa showed an annual percentage change of 15.3% [3]. One cause of increased medical expenses was introduction of docetaxel chemotherapy. Two randomized large-scale clinical trials published in 2004 showed that docetaxel chemotherapy increased survival; therefore, it is now used as the standard therapy [23,24]. Most patients with terminal PCa have metastatic castration-resistant PCa (CRPC). Therefore, they have usually undergone docetaxel chemotherapy for as long as their general condition allows. Recently, several new treatments been developed for metastatic CRPC; these have the potential to increase of life care costs substantially [25]. These treatments include the potent second-generation androgen receptor inhibitor enzalutamide, the androgen synthesis inhibitor abiraterone, and the second-line chemotherapy agent cabazitaxel. Use of these medicines will increase PCa care costs. This is particularly true for patients in the subgroup with a survival time of less than 2 years as they tend to undergo active treatment until just before death. Since PCa in these patients is aggressive

and progressive, various treatments could be applied. Therefore, PCa decedents with a survival time of less than 2 years spent the highest amounts, and cost per patient during the last year of life increased most rapidly in this subgroup over the 10-year period (Fig. 3). However, more appropriate treatments for terminal cancer patients include supportive care, such as rehabilitation.

Immediately after diagnosis, approximately 70% of all PCa decedents received ADT alone as the primary treatment. These patients spent the least. Patients that underwent surgery, RT, or combination therapy paid more. This may be because those patients might suffer complications related to RT or surgery, including radiation-induced proctitis or cystitis and incontinence [26]. Here, we found that hospice use was relatively low (43.7%). By contrast, Bergman et al [27] reported that of 14,521 men with terminal PCa, 7,646 (53%) used a hospice for a median of 24 days. The other concern about PCa end-of-life care in Korea was that palliative services were relatively underutilized, even though they were associated with lower expenditure than hospital-based care [28]. Previous studies noted that rehabilitation and psychotherapy can make a meaningful contribution, even to those with terminal cancer [29,30]. However, patients in the current study spent 1.1% and 0% of their medical costs on rehabilitation and psychotherapy, respectively, indicating underutilization of such services in Korea.

This study has some limitations. Because data regarding clinical and pathologic stage are held in the KNHI database, analyses adjusted for stage could not be performed. Thus, analyses of treatment patterns and medical costs according to stage were precluded. However, stage can be deduced by the primary treatment type. In the case of localized PCa, patients can undergo RP or RT. In addition, we did not have information related to cause of death. Differences in utilization of medical resources might lead to differences in medical expenses related to cause of death. Furthermore, we used an administrative claims database that contains the cost of billed services only, not costs associated with loss of patient/caregiver productivity/wages, travel to/ from the place of treatment, over-the-counter medications, and other cancer-related expenses [6]. This may have led us to underestimate the economic burden. A more comprehensive study would be useful to study the end-of-life cancer care costs including analysis

the expenditures according to the cause of death. One strength of the present investigation was that the study population represents all PCa decedents in Korea during the time period of interest.

CONCLUSIONS

This study is a health service search that examines the trend for end of life medical care in a descriptive way among PCa patients in Korea. PCa care-related expenditure during the last year of life varied according to patient characteristic/demographics. Average PCa care costs increased every year from 2006 to 2015. However, the study results suggest underutilization of support services, most likely due to lack of alternative accommodation for patients with terminal PCa. Further study of patterns of utilization of healthcare resources will help provide evidence for policymakers that will enable them to reduce the burden of end-of-life care costs for PCa patients.

ACKNOWLEDGEMENTS

Conflict of Interest

The authors have nothing to disclose.

Author Contribution

Conceptualization: JHP, SJY, WJK. Data curation: JIC, HC. Formal analysis: YSH, SYK, JHP, SJY, DJP. Investigation: JSK, JYL, HTK, ESY, TGK. Methodology: YSH, SYK, JHP, SJY. Project administration: YSH, SYK, DJP, KM. Resources: SYK, JHP. Software: JHK, HSY, DJP. Supervision: SJY, JHP. Validation: ICC, HJK, HCC. Writing – original draft: YSH, SYK, DJP, KM. Writing – review & editing: YSH, SYK, JHP, SJY.

Supplementary Materials

Supplementary materials can be found *via* https://doi.org/10.5534/wjmh.200113.

Data Sharing Statement

The data required to reproduce these findings cannot be shared at this time due to technical and time limitations.

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