Cost Comparison of Androgen Deprivation Therapy and Radical Prostatectomy for Prostate Cancer

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〈Abstract〉

전립선암의 남성호르몬 박탈 치료와 근치적 전립선적출술의 비용 분석

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Purposes: 본 연구는 전립선암 환자의 의료비 지출을 평가하기 위해 남성호르몬 박탈 치료와 근치적 전립선적출술의 비용을 비교하였다.

Methods: 본 연구는 스마트 전립선암 데이터베이스(Smart Prostate Cancer Database)의 전립선암 환자 357명의 데이터와 청구데이터베이스에서 의료비 관련 데이터를 도출하였다. 근치적 전립선적출술과 남성호르몬 박탈 치료간 비교를 위해 독립표본 t검정을 실시하였다. 또한 남성호르몬 박탈 치료와 근치적 전립선적출술에 영향을 미치는 요인을 검증하기 위해 다중회귀 분석을 실시하였다.

Findings: 치료 후 1년까지 남성호르몬 박탈치료가 근치적 전립선적출술 보다 비용이 낮은 것으로 나타났으며, 치료 후 4년까지 낮게 유지되었다. 그러나 4년이 지나면 남성호르몬 박탈 치료의 누적의료비가 근치적 전립선적출술보다 더 유의미하게 높게 나타났다. 환자의 병기가 높거나 나이가 많은 경우 근치적 전립선적출술보다 남성호르몬 박탈 치료를 할 확률이 더 높았다.

Practical Implications: 본 연구는 조기 암 발견이 환자 뿐 아니라 국민건강보험공단의 의료비를 줄일 수 있다는 것을 보여 준다. 또한 의료비를 정확히 평가하기 위해서는 오랜 기간의 정보를 평가해야 하며, 이를 기반으로 평가 및 예측이 필요함을 증명하였다.

Keywords: 남성호르몬 박탈치료; 근치적 전립선적출술; 전립선암; 비용분석

Ⅰ. INTRODUCTION

Prostate cancer is the most common of newly diagnosed male cancers. The American Cancer Society estimated that prostate cancer accounted for 28% of male cancer cases in 2013[1]. In line with the increased incidence in the Western World, the rates of prostate cancer have continued to increase in Korea[2]. The age-standardized incidence rate per 100,000 of prostate cancer has been reported to be 7.2 in 2000 and 27.4 in 2011, with an annual percentage change of 12.8% in Korea. Additionally, the Health Insurance Review and Assessment Service (HIRA) reported that the total annual medical expenditure for prostate cancer increased from USD 63,108.72 in 2009 to USD 105,680.78 in 2013, corresponding to an annual growth rate of 14.67%. From the standpoint of national health economics, prostate cancer will become an important disease due to its increased incidence among men in the population.

There have been two representative treatment modalities aimed at improving the oncologic and functional outcomes of these patients. Radical prostatectomy (RP) is the standard treatment of localized or locally advanced prostate cancer[3]. Urologists consider RP as the gold standard treatment. However, some studies with RT or other treatment such as permanent prostate brachy-therapy (PPB) indicate similar biochemical control rates[3]. Therefore, it was complicated to choose the treatment for many patients[4]. In addition, Androgen deprivation therapy (ADT) constitutes a major standard in the treatment of advanced or relapsed prostate cancer[5]. The ADT initially was restricted to patients with metastatic and inoperable, locally advanced disease. Nowadays, the ADT has been used for neoadjuvant or adjuvant therapy for surgery and radiotherapy, for biochemical recurrence after surgery or radiation[6].

To determine the appropriate treatment modality, many factors should be taken into account, including oncologic outcomes and economic analyses.

As the incidence of prostate cancer increases, health care spending due to prostate cancer will increase. There are several studies comparing medical expenditures among the various treatment options within their own healthcare system [7-13]. Nguyen et al. (2007) compared the mean medical expenditures of brachytherapy, external radiation therapy and laparoscopic or robotic minimally invasive radical prostectomy (MIRP)[14]. This study reported that the mean medical expenditure of MIRP was $29,988 in 2002, $21,325 in 2003, $17,645 in 2004 and $16,762 in 2005 [15-17]. Although finding cost effective treatments for prostate cancer is important for both the patient and the government, there has been no research comparing ADT and RP.

Considering the situation in healthcare systems, drug pricing and the availability of drugs in South Korea, the elucidation of health economics in prostate cancer treatment in South Korea is necessary. Our study aimed to determine the medical expenditures, including out-of-pocket expenditures, for prostate cancer patients and compare them between ADT and RP treatment.

Ⅱ. Methodology

1. Subjects

This study used the medical expenditures of patients with prostate cancer in S hospital located in Seoul. Specifically, we compared ADT and RP treatment. This study was conducted using the Smart Prostate Cancer Database (SPC-DB), which is a prostate cancer registry developed in 2013 [18]. Initially, 2381 patients were identified with a prostate cancer diagnosis, using the ICD-10 code

C61, from April 1997 to February 2013. Among the 2381 patients with prostate cancer, we selected patients who were admitted to the hospital and received treatment between January 1, 2011, and December 31, 2011. In addition, we included patients with more than three hospital admissions by physicians comments. Among 464 patients, we identified 357 patients who had either ADT (n=155) or an RP (n=202).

2. Statistical analysis

We performed the analysis using the independent two-sample t-test to compare the difference between ADT and radical prostatectomy. Pearson x^2-test was used to identify independency in patient characteristics variables. Multivariable logistic regression analysis was conducted to identify determining factors for ADT and RP treatments. All statistical analyses were performed using SPSS, version 18.0.

3. Ethics statement

The prostate cancer patient data were de-identified, and the requirement for informed consent was waived. This study was approved by the institutional review board (IRB number: MC16RIMI0107).

Ⅲ. RESULTS

155 prostate cancer patients received ADT (43.4%), and 202 of the prostate cancer patients had an RP (56.6%) (Table 1). The majority of prostate cancer patients were 60-70 years old (n=290, 81.2%). Among patients who received ADT, the largest age group was 70-79 years old (n=89). Among patients who received an RP, the largest age group was 60-69 years old (n=106). The majority of the prostate cancer patients were

stage 2 or stage 3 (n=318, 89.1%). The most advanced cancer stage for the ADT patients was stage 3 (n=63), and the most advanced cancer stage for RP patients was stage 2 (n=150). Many of the patients received a maximum treatment of three years (n=272, 76.2%). The survival rate for the patients was 96.6%, corresponding to a mortality rate of 3.4%. When evaluating employment status, most patients were classified as unemployed, other or unknown (81.5%). When evaluating the highest education level achieved, most patients had less than a high school education (37%).

1. Characteristics of medical expenditures for prostate cancer

We compared the medical expenditures between ADT and radical prostatectomy. First, there was no significant difference in average hospital fees per patient. When evaluating out-of-pocket expenditures, there were significant differences between the ADT and RP treatments (p<0.05). Second, when comparing insurance payment benefits, there was no significant difference. When combining both the non-benefit insurance payment and the special doctor fee, there were significant difference between ADT and RP treatment (p<0.05, p< 0.001). Finally, between the ADT and RP treatment groups, there was a significant difference in both treatment and operating charges (p< 0.001). In addition, there was a significant difference in drug and injection charges (p< 0.001).

2. Cost comparison of ADT and RP depending on cancer stage

To compare the costs between ADT and RP when taking cancer stage into consideration, we focused

<Table 1> Patient characteristics

Characteristic	Items	ADT	RP treatment	Total (Percent)	p−Value (for x^2)
Age	〈60	5	33	38(10.6%)	〈0.001
	60~69	34	106	140(39.2%)	
	70~79	89	61	150(42.0%)	
	≥80	27	2	29(8.1%)	
Cancer Stage	Stage 1	13	3	16(4.5%)	〈0.001
	Stage 2	57	150	207(58.0%)	
	Stage 3	63	48	111(31.1%)	
	Stage 4	22	1	23(6.4%)	
Treatment period	First−year	45	65	110(30.8%)	0.001*
	Second−year	27	64	91(25.5%)	
	Third−year	31	40	71(19.9%)	
	Fourth−year	17	15	32(9.0%)	
	Over Fifth−year	35	18	53(14.8%)	
Survival	Yes	145	200	345(96.6%)	0.005
	No	10	2	12(3.4%)	
Job	White−collar worker	7	23	30(8.4)	〈0.001
	Blue−collar worker	6	30	36(10.1)	
	Unemployed/Other/Unknown	142	149	291(81.5)	
Education	Less than high school	55	77	132(37.0)	0.019*
	College education or higher	37	79	116(32.5)	
	Other/Unknown	63	46	109(30.5)	
Total (Percent)		155	202	357	

White−collar worker: Professional, manager and white−collar; Blue−collar worker: Service, production, sales, labor, transportation, agriculture/fisheries/animal husbandry/forestry
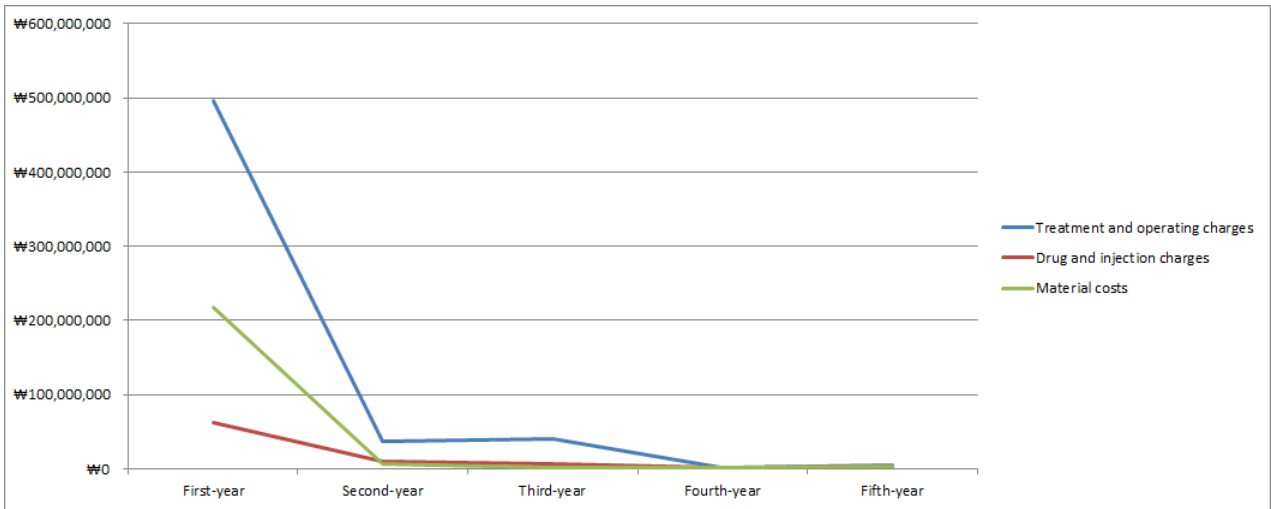* p 〈 0.05; ** p〈 0.01; *** p〈 0.001

<Table 2> Cost differences between ADT and RP

Perspective	Item	ADT	RP treatment	P−value
Payer	Covered expenditure	$1,643($2,922)	$1,487($2,066)	0.571
	Out−of−pocket expenditure	$667($2,737)	$1,656($3,590)	0.003*
Claim	Benefit insurance payment	$1,730($3,076)	$1,565($2,175)	0.571
	Non−benefit insurance payment	$477($2,336)	$1,270($3,401)	0.010*
	Special doctor fee	$103($397)	$308($444)	〈0.001
Cost item	Treatment and operating charges	$985($2,724)	$2,587($4,200)	〈0.001
	Drug and injection charges	$1,283($1,544)	$382($631)	〈0.001
	Material costs	$1,141($1,611)	$1,030($1,456)	0.504
	Medical checkup charge	$866($1,373)	$826($989)	0.759
	Patient's room charge and management cost	$389($1,911)	$351($632)	0.812
	Doctor's fee	$193($164)	$161($174)	0.072
Average hospital fee per patient		$2,310($5,282)	$3,143($4,847)	0.127

* p 〈 0.05; ** p〈 0.01; *** p〈 0.001, value: mean(SD)
The exchange rate for Koreanw on to the U.S. dollar is 1,108.11 won(annual average in 2011).

<Figure 3> Medical cost trend of RP
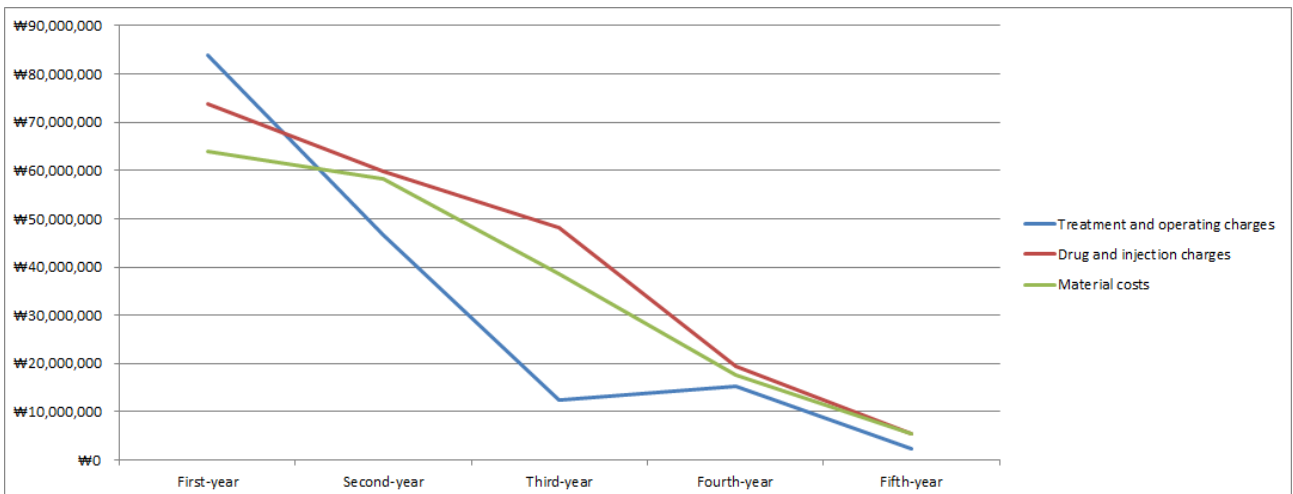

<Figure 1> Hospital fee trend depending on treatment period

(Left) Average hospital fee per patient depending on treatment period, (Right) accumulated average hospital fee per patient depending on treatment period

<Figure 2> Medical cost trend of ADT

<Table 3> Cost differences depending on cancer stage

Cancer Stage	Average hospital fee per patient		P-value	Covered expenditure		T-test	Out-of-pocket expenditure		P-value
	ADT	RP		ADT	RP		ADT	RP	
Stage 2	$1,454 (n =57)	$3,077 (n=150)	0⟨0.001	$1,150	$1,597	0.042*	$304	$1,480	⟨0.001
Stage 3	$3,279 (n =63)	$3,255 (n=48)	0.985	$2,135	$1,186	0.162	$1,145	$2,069	0.249

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.
The exchange rate for Korean won to the U.S. dollar is 1,108.11 won(annual average in 2011).

on the expenditures depending on both stage 2 and stage 3. In the case of stage 2, there was a significant difference in the average hospital fee per patient, covered expenditure and out-of-pocket expenditure ($p < 0.001$, $p < 0.05$, $p < 0.001$). In terms of the average hospital fee per patient, covered and out-of-pocket expenditures, the medical expenditures of ADT treatment were less expensive than RP. In the case of stage 3, although both ADT and RP treatment are expensive, there was no significant difference in the average hospital fee per patient or covered or out-of-pocket expenditures. When looking at covered expenditures, ADT was more expensive than RP. However, the out-of-pocket expenditures of ADT treatment were lower than those of RP.

3. Cost trends depending on treatment period

First, to find the cost trend, we created a graph showing expenditures depending on treatment period. In the ADT group, the medical expenditures of the second year were higher than those of any other period. However, the graph of medical expenditures shows a curve moving downward for each year. When looking at the average hospital fee per patient and the covered and out-of-pocket expenditures, there was a similar cost pattern. In the case of RP, the highest cost is in the first year. The medical expenditures

then decreased steadily after the second year. In the fifth year, the medical expenditures increased slightly(Figure 1.). Figure 1 expresses the accumulated average hospital fee per patient depending on treatment period. The medical expenditures of ADT were much lower than those of RP until the fourth year. After that, the medical expenditures of ADT were higher than those of RP.

Second, to find the three cost trend(treatment and operating charges, drug and injection charges, material costs), we created a graph showing expenditures depending on treatment period. Figure 2 expressed the medical cost trend of ADT, Figure 3 expressed the medical cost trend of RT. In case of RP, treatment and operating charges, drug and injection charges, material costs are related to the first treatment year. In case of ADT, treatment and operating charge decreased steadily until the third year, and increased until fourth year. Drug and injection charges is descending curve. Material costs is also descending curve.

4. Predictors associated with ADT and RP treatment

Table 4 presents the logistic regression analysis of factors that were associated with ADT and RP treatment. When comparing the probability that a patient received ADT compared to RP based on age, patients who were 70-79 years old were 7.668

<Table 4> Factors associated with ADT and RP

Variable	OR	β	95% CI	P-value
Age				
〈60	1			Ref
60~69	1.309	0.269	0.424 to4.040	.640
70~79	7.668	2.037	2.482 to23.685	〈0.001
≥80	67.499	4.212	10.871 to 419.104	〈0.001
Stage				
Stage 1	1			Ref
Stage 2	0.189	−1.666	0.046 to 0.775	.021*
Stage 3	0.558	−.584	0.133 to2.340	.425
Stage 4	11.440	2.437	0.943 to138.850	.056
Job				
White−collar worker	1			Ref
Blue−collar worker	0.222	−0.469	0.318 to1.230	.174
Un−employer/Other/Unknown	0.594	0.773	1.110 to4.228	.023*
Education				
Less than high school	1			Ref
College education or　higher	0.626	−1.506	0.050 to 0.987	.048*
Other/Unknown	2.167	−0.521	0.194 to1.821	.362

* p 〈 0.05; ** p〈 0.01; *** p〈 0.001, CI= confidence interval; OR= odds ratio
By logistic regression analysis: R^2 of Cox and Snell=0.353, R^2 of Nagelkerke = 0.474

times more likely to receive ADT than those below 60 years old (β =2.037, p〈 0.001). In addition, patients who were over the age of 80 were 67.499 times more likely to receive ADT than those below 60 years old (β =4.212, p〈 0.001). When comparing the probability that a patient received ADT compared to RP treatment based on cancer stage, patients with stage 2 cancer were 0.189 times less likely to receive ADT than those with stage 1 (β =−1.666, p〈 0.05).

When comparing the probability that a patient received ADT compared to RP based on employment, patients who were unemployed were 0.594 times more likely to receive ADT than those who were white collar workers (β =0.773, p〈 0.05). When comparing the probability that a patient received ADT compared to RP depending on their highest level of education, patients who had a college education or higher were 0.626 times less

likely to receive ADT than those who had less than a high school education (β =−1.506, p〈 0.05). However, employment, cancer stage and highest level of education were not consistent significant predictors of treatment with ADT or RP.

Ⅳ. DISCUSSION

There have been two representative treatment modalities aimed at improving the oncologic and functional outcomes of prostate cancer patients: RP and ADT. RP is the standard treatment of localized or locally advanced prostate cancer[5]. In addition, ADT constitutes a major cornerstone in the treatment of advanced or relapsed prostate cancer[6]. Our aim was to describe the medical expenditures, including out−of−pocket expenditures, for prostate cancer patients and to compare the expenditure patterns between ADT and RP. Based

on our findings, we drew the following conclusions.

First, we will compare the characteristics of medical expenditures based on payer. The average hospital fee per patient was similar between ADT and RP. However, out-of-pocket expenditures were different between the groups, with RP costing the patient US 1,655.94 more than ADT. In terms of claims, both non-benefit insurance payments and the special doctor fee of ADT treatment were less expensive than those of RP. In terms of cost, the treatment and operating charges of ADT were less expensive than those of RP. In contrast, the drug and injection charges of ADT were more expensive than those of RP.

Second, there were some interesting results depending on cancer stage. In the case of stage 2 cancers, there was a difference in all medical costs, including average hospital fee per patient and covered and out-of-pocket expenditures. On average, the hospital fee per patient, covered expenditures and out-of-pocket expenditures of ADT treatment were less expensive than those of RP. In the case of stage 3 cancers, both ADT and RP treatment were expensive although there was no difference in average hospital fee per patient, covered expenditures or out-of-pocket expenditures. Thus, early detection of cancer is important to both improve treatment and decrease cost. Because the higher the stage is, the higher is the total cost for therapy.

Third, we evaluated cost trends depending on treatment period (Figure 1). In the second year, the medical expenditures of ADT were higher than those of any other period. However, medical expenditures showed a downward curve over each year.

For RP, the highest cost was in the first year. According to the Figure 3, three cost of RP(treatment and operating charges, drug and injection charges, material costs) are related to the first treatment year. And the medical expenditures then decreased steadily after the second year. In addition, in the case of accumulated medical expenditures, RP was more expensive than ADT until the fourth year. However, after that, the medical expenditures of ADT were higher than those of RP due to drug and injection charges for ADT. According to the Figure 2, three cost of ADT decreased steadily until the third year or fourth year. We found that ADT is less expensive than RP in the short term. However, there are no large differences between RP and ADT in the long term.

Finally, we found that the older the patients were and the more advanced the cancer stage was, the more likely it was that the patient would be treated using ADT compared to RP. Thus, early detection of cancer is a key factor for both treatment and cost. Early detection of cancer has advantages for both cost and treatment outcomes for both the public corporation and the individual.

Although meaningful conclusions can be drawn from this study, there were also limitations. First, we only focused on stage 2 and stage 3 cancers to compare the cost between ADT and RP depending on cancer stage. Because there were few patients in both stage 1 and stage 4, we did not focus on them. Future studies should focus on all stages and need to evaluate a time series analysis of stage and duration of life. Second, this study focused on 2381 patients with prostate cancer with the ICD-10 code C61 from April 1997 to February 2013. Among 2381 patients, we selected prostate patients who were admitted to the hospital and received treatment between January 1, 2011, and December 31, 2011, and those who were admitted more than three times. We also included data from patients who died in 2011 or 2012, if they were admitted to the hospital more than three times and were admitted to the hospital and received treatment in 2011. Future studies should establish

exclusion criteria in detail. Third, this study only explored cost differences depending on the claim or payer. However, hospital revenue may be reflected in the medical cost. Future studies should focus on hospital revenue and its reflection on the cost. Fourth, there is medical expense insurance in South Korea. Many people have signed up for medical expense insurance. Thus, there could be a cost difference depending on the insurance status. Future studies need to consider the medical expense insurance. Fifth, there are studies that identify the relationship between medical costs and satisfaction[19]. Accordingly, we hope future studies will find a relationship between medical costs and satisfaction. Finally, we could not use lots of references related to medical cost for therapy of prostate cancer in discussion. There are some researches related medical cost[20]. However, there is little researches related medical cost for therapy of prostate cancer. Thus, more study related medical cost for therapy of prostate cancer is needed.

This study yielded valuable results. There are several studies comparing medical expenditures among the various treatment options within their own healthcare system [7-13]. Although finding cost effective treatments for prostate cancer is important for both the patient and the government, there has been no research comparing ADT and RP. This study is the first to compare the costs of ADT and RP for prostate cancer in South Korea. We hope that there will be a variety of follow-up studies. We propose that early detection of cancer may have both a cost and treatment advantage to both the public corporation and the individual. In addition.

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〈Abstract〉

Cost Comparison of Androgen Deprivation Therapy and Radical Prostatectomy for Prostate Cancer

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Purpose: To evaluate the medical expenditures for prostate cancer patients, including out-of-pocket costs, and compared the costs between androgen deprivation therapy and radical prostatectomy treatment.
Methodology: This study combined clinical data from 357 prostate cancer patients from the Smart Prostate Cancer Database and the medical expenditure data from the claims and cost databases. We used the independent two-sample t-tests to compare androgen deprivation therapy and radical prostatectomy. Multivariable logistic regression analysis was conducted to identify determining factors for androgen deprivation therapy and radical prostatectomy treatments.
Findings: The medical costs of androgen deprivation therapy treatment were much lower than radical prostatectomy treatment at the one year and remained lower until the fourth-year. However, after four years, the accumulated medical expenditures of androgen deprivation therapy become significantly higher than radical prostatectomy treatment. Patients with a higher cancer stage and older age had higher chances of being treated using androgen deprivation therapy treatment than radical prostatectomy treatment.
Practical Implications: Our results show that early detection of cancer reduces the treatment cost for both patients and insurance payers. It also demonstrates that cost comparisons should be conducted over long periods of time in order to most accurately assess the costs.

Keywords: Androgen deprivation therapy; Cost analysis; Health expenditures; Prostate cancer; Radical prostatectomy