

Risk of hospitalisation after primary treatment for prostate cancer

Stephen B. Williams^{*,†}, Zhigang Duan[‡], Karim Chamie[§], Karen E. Hoffman[¶], Benjamin D. Smith^{‡,¶}, Jim C. Hu^{*,*}, Jay B. Shah^{*}, John W. Davis^{*} and Sharon H. Giordano^{‡,††}

^{*}Department of Urology, The University of Texas MD Anderson Cancer Center, Houston, [†]Division of Urology, The University of Texas Medical Branch, Galveston, [‡]Department of Health Services Research, The University of Texas MD Anderson Cancer Center, Houston, TX, [§]Department of Urology, University of California Los Angeles, Los Angeles, CA, [¶]Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, ^{**}Department of Urology, Weill-Cornell Medical College, New York, NY, and ^{††}Department of Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective

To compare the risk of hospitalisation and associated costs in patients after treatment for prostate cancer.

Patients and Methods

We identified 29 571 patients aged 66–75 years without significant comorbidity from the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database who were diagnosed with localised prostate cancer between 2004 and 2009. We compared the rates of all-cause and treatment-related hospitalisation that occurred within 365 days of the initiation of definitive therapy. We used multivariable logistic regression analysis to identify determinants associated with hospitalisation.

Results

Men who underwent radical prostatectomy (RP) rather than radiotherapy (RT) had lower odds of being hospitalised for any cause after therapy [odds ratio (OR) 0.80, 95% confidence interval (CI): 0.74–0.87]. Patients who underwent RP rather than RT had higher odds of being hospitalised for treatment-related complications (OR 1.15, 95% CI: 1.03–1.29). However, men who underwent external beam RT (EBRT)/

intensity modulated RT (IMRT) (OR 0.84, 95% CI: 0.72–0.99) had a 16% lower odds of hospitalisation from treatment-related complications than patients undergoing RP. Using propensity score-weighted analyses there was no significant difference in the odds of hospitalisation from treatment-related complications for men who underwent RP vs RT (OR 1.06, 95% CI: 0.92–1.21). Patients hospitalised for treatment-related complications after RT were costlier than patients who underwent RP (Mean \$18 381 vs \$13 203, $P < 0.001$).

Conclusions

With the exception of men who underwent EBRT/IMRT, there was no statistically significant difference in the odds of hospitalisation from treatment-related complications. Costs from hospitalisation after treatment were significantly higher for men undergoing RT than RP. Our findings are relevant in the context of penalties linked to hospital readmissions and bundled payment models.

Keywords

prostate cancer, treatments, hospitalisation, costs, utilisation, outcomes

Introduction

Prostate cancer remains the most commonly diagnosed solid organ tumour among men in the USA, with an estimated 220 800 new cases and 27 540 deaths in 2015 [1]. Broadly speaking, curative treatment options for prostate cancer include surgery and radiotherapy (RT) [2,3]. Driven by intensive PSA screening over the last quarter of a century, prostate cancer has witnessed a marked stage migration [4], toward a more indolent course in most newly diagnosed cases [5].

In recent years, there has been a concerted effort to maximise the value of healthcare delivery by improving the quality of

medical outcomes and by reducing unnecessary costs [6]. Prostate cancer represents a high-yield target for value-based reform given the preponderance of overtreatment, as well as the expensive technologies required for RT and surgery. Currently, the Centers for Medicare and Medicaid Services (CMS) has initiated a hospital readmission reduction programme in accordance with the Affordable Care Act to reduce payments to hospitals with excessive readmissions for the following procedures and diagnoses: acute myocardial infarction, congestive heart failure, pneumonia, chronic obstructive pulmonary disease, and elective total hip arthroplasty and total knee arthroplasty [7]. Similar payment

reductions may ensue for readmissions after treatment for common malignancies, including prostate cancer. Prior studies have rigorously assessed complications, interventions to treat complications, as well as the time interval to first complication among patients who underwent surgery or RT [8–10]. While studies often report 30- and 90-day readmission rates, CMS uses readmission 30-days following intervention when discerning payment reductions [7]. However, the use of relatively short readmission time intervals may inaccurately assess delayed hospitalisation rates after prostate cancer treatment [8]. In this context, the rate of hospitalisation after prostate cancer treatment and the associated costs in the general population is currently unknown. The objective of the present study was to assess the risk, predictors, and costs of hospitalisation after primary treatment for prostate cancer.

Patients and Methods

Data Sources

We used Surveillance, Epidemiology, and End Results (SEER)-Medicare data for analysis, which are composed of a linkage of population-based cancer registry data from 16 SEER areas with Medicare administrative data. The SEER programme covers ~26% of the USA population, and the Medicare programme provides benefits to 97% of Americans aged ≥ 65 years [11].

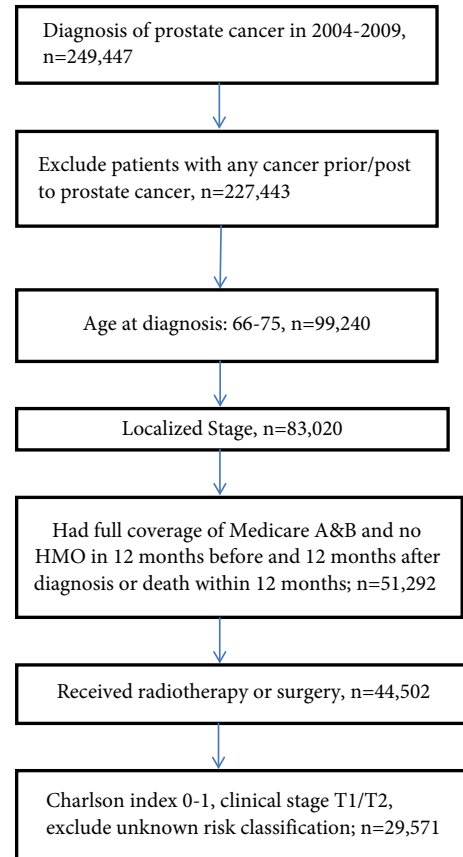
Study Population

Due to baseline differences between patient populations undergoing RT and surgery, we limited our analysis to only include patients expected to be candidates for either radical prostatectomy (RP) or RT based on age and limited comorbid medical conditions. From the SEER-Medicare linked database, we identified 29 571 patients who met the following criteria: age 65–75 years, Charlson Comorbidity Index (CCI) scores of 0 or 1, localised prostate cancer (clinical stage T1/T2), diagnosed with prostate cancer between 2004 and 2009, and treated with RP or RT. To ensure data completeness and to allow enough follow-up time to evaluate treatment and hospitalisation, we included only patients who had full medical insurance coverage provided by Medicare Part A and Part B during the 12 months before and after treatment and who were not Health Maintenance Organisation members. Patients who received both RP and RT were excluded from analysis (192 patients). Patients with a diagnosis of any other cancer before or after prostate cancer diagnosis were excluded (Fig. 1).

Study Variables

Patient demographics and tumour characteristics at the time of diagnosis were extracted from the SEER-Medicare Patient

Fig. 1 Flow chart of study cohort selection. HMO, Health Maintenance Organisation.



Entitlement and Diagnosis Summary File (PEDSF). Patient treatment information was extracted from Medicare claims files for durable medical equipment (DME), physician (NCH), inpatient service (MEDPAR), and outpatient service files (OUTPAT).

The primary exposure was the treatment received within 6 months after diagnosis, identified using International Classification of Diseases 9th edition (ICD-9) procedure codes and Current Procedural Terminology (CPT) codes in Table S1. The primary outcome of interest was the rate of hospitalisations within 12 months following initiation of treatment. Hospitalisation for the index RP was not considered as part of the outcome.

For descriptive purposes, patients were classified into two, mutually exclusive categories based on the treatment received within this initial period: RP (open, minimally invasive or perineal) and RT (external beam, brachytherapy or both) with or without androgen-deprivation therapy (ADT, luteinising hormone-releasing hormone agonist or orchidectomy) (Table S1). CPT-4 code 55899 (unspecified male genitourinary procedure) may sometimes be used with an

open RP administrative code to specify minimally invasive RP with robotic assistance for private health plans, but Medicare does not recognise this coding schema, and very few men had this combination of codes; therefore, this was not used to identify minimally invasive RP.

We obtained the age, race, geographic region, census variables (urban/rural, education, poverty level), diagnosis year, and stage (T1/T2) from the PEDSF file. Treatment variables including RP, RT, and ADT use were determined from Medicare claims. Comorbidity was assessed using the Klabunde modification of the CCI during the year before diagnosis [12]. The Klabunde modification uses comorbid conditions identified by the CCI and incorporates the diagnostic and procedure data contained in Medicare physician (Part B) claims. Variables were categorised as in Table 1.

Statistical Analysis

We evaluated the rate of hospitalisation for any cause as well as hospitalisation for treatment-related complications that

occurred within 12 months of treatment initiation. Prior adjusted analyses where sensitivity analyses performed excluded patients with pre-existing conditions have demonstrated similar results. Based on prior studies [13], we derived our definition for recording hospitalisation for treatment-related complication vs any cause. Conditions listed in the Table S2 that were not present in the Medicare claims during the 12 months preceding treatment were deemed treatment-related complications. We calculated and compared the hospitalisation rates from a treatment-related complication for patients who underwent RT and RP. The most common reasons for hospitalisation from a treatment-related complication (categorised as urinary, gastrointestinal, etc.) were identified. Total cost of hospitalisation for all-cause and treatment-related hospitalisations were calculated as the sum of the Medicare reimbursement, the amount that was made by a primary payer other than Medicare, the total of all claims passed through for the stay, and patients' deductible and Part A co-insurance.

The rates of hospitalisation and 95% CIs were calculated and compared between the two treatment groups. We used

Table 1 Characteristics of patients with prostate cancer according to treatment regimen.

Characteristic	Categories	Total, N	RT, n (%)	RP, n (%)	P
Year of diagnosis	2004	5 150	3 785 (17.8)	1 365 (16.5)	<0.001
	2005	4 855	3 592 (16.9)	1 263 (15.3)	
	2006	5 152	3 773 (17.7)	1 379 (16.7)	
	2007	5 276	3 770 (17.7)	1 506 (18.2)	
	2008	4 792	3 352 (15.7)	1 440 (17.4)	
	2009	4 346	3 029 (14.2)	1 317 (15.9)	
Age, years	66–70	16 058	10 150 (47.7)	5 908 (71.4)	<0.001
	71–75	13 513	11 151 (52.3)	2 362 (28.6)	
CCI score	0	22 169	15 543 (73.0)	6 626 (80.1)	<0.001
	1	7 402	5 758 (27.0)	1 644 (19.9)	
Race/ethnicity	White	23 605	16 805 (78.9)	6 800 (82.2)	<0.001
	Black	2 758	2 232 (10.5)	526 (6.4)	
	Hispanic	1 742	1 205 (5.7)	537 (6.5)	
	Other	1 466	1 059 (5.0)	407 (4.9)	
Marital status	Unmarried	4 939	3 789 (17.8)	1 150 (13.9)	<0.001
	Married	22 005	15 453 (72.6)	6 552 (79.2)	
	Unknown	2 627	2 059 (9.7)	568 (6.9)	
Education: % of persons in census tract with <12 years education	≥24.5	7 393	5 649 (26.5)	1 744 (21.1)	<0.001
	14.3–24.5	7 368	5 399 (25.4)	1 969 (23.8)	
	8.0–14.3	7 320	5 273 (24.8)	2 047 (24.8)	
% of tract residents living below the poverty level	0–8.0	7 490	4 980 (23.4)	2 510 (30.4)	<0.001
	≥13.9	7 419	5 523 (25.9)	1 896 (22.9)	
	7.3–13.9	7 458	5 329 (25.0)	2 129 (25.7)	
	3.9–7.3	7 321	5 124 (24.1)	2 197 (26.6)	
SEER region	0–3.9	7 373	5 325 (25.0)	2 048 (24.8)	<0.001
	Midwest	3 397	2 420 (11.4)	977 (11.8)	
	Northeast	5 988	4 897 (23.0)	1 091 (13.2)	
	South	8 512	6 521 (30.6)	1 991 (24.1)	
	West	11 674	7 463 (35.0)	4 211 (50.9)	
Residence	Urban	26 105	18 749 (88.0)	7 356 (89.0)	0.021
	Rural	3 466	2 552 (12.0)	914 (11.0)	
Clinical stage	T1	18 022	13 276 (62.3)	4 746 (57.4)	<0.001
	T2	11 549	8 025 (37.7)	3 524 (42.6)	
Gleason Score	≤6	14 075	10 564 (49.6)	3 511 (42.5)	<0.001
	7	11 808	7 754 (36.4)	4 054 (49.0)	
	>8	3 304	2 669 (12.5)	635 (7.7)	
	Unknown	384	314 (1.5)	70 (0.8)	

summary statistics to describe demographic information and disease characteristics between the two treatment groups; differences were evaluated with the chi-squared test for categorical variables and *t*-test for continuous variables. We used logistic regression models adjusted for patients' demographics, comorbidities, and tumour characteristics to compare the odds of hospitalisation between patient groups. We used the Hosmer–Lemeshow test to check the goodness-of-fit of the models. We also performed a sensitivity analysis by logistic regression analysis with probability weighting, as the inverse of propensity score of treatment estimated from a generalised logit model. The variables used were age, race, geographic region, census variables (urban/rural, education, poverty level), comorbidity, diagnosis year, stage (T1/T2), marital status, and Gleason score (Table S3). A $P < 0.05$ was considered statistically significant. The SAS software program version 9.4 (SAS Institute, Cary, NC, USA) was used to perform all data management and statistical analyses. This study was deemed exempt by the Institutional Review Board at the University of Texas MD Anderson Center.

Results

Of the 29 571 patients who were included in the analysis, 21 301 patients received RT and 8 270 patients underwent RP within 6 months of cancer diagnosis. ADT was used in over a third of patients who underwent RT (7 892, 37.1%). The demographics of our study population are summarised in Table 1. The 1 510 patients excluded from analyses of the hospitalisation with treatment-related complications were because they had pre-existing conditions.

Patients were more frequently hospitalised for any condition within 365 days following RT than RP (15.9% vs 12.7%, $P < 0.001$). However, there was no significant difference in hospitalisation from treatment-related complications between the treatment groups (6.3% vs 6.5%, $P = 0.523$) (Table 2).

The most common diagnosis categories associated with hospitalisation from treatment-related complications in decreasing order were: genitourinary (36.9%), respiratory (23.4%), gastrointestinal (18.9%), cardiac (15.8%), heterologous blood transfusions (15.7%), vascular (4.0%), and wound complications (0.9%). There was no significant difference between primary therapy and treatment-related complications requiring hospitalisation: RP (6.4%), minimally invasive RP (6.5%), brachytherapy (6.1%), combined external beam RT (EBRT)/brachytherapy (6.1%) and EBRT/intensity modulated RT (IMRT) (6.6%) (unadjusted $P = 0.704$).

In multivariable analysis, patients who underwent RP rather than RT had lower odds of being hospitalised for any cause after therapy [odds ratio (OR) 0.80, 95% CI: 0.74–0.87] (Table 3). Higher odds of hospitalisation were also found among older men (aged 71–75 vs 66–70 years; OR 1.10, 95% CI: 1.03–1.18), unmarried (vs married; OR 1.10, 95% CI: 1.01–1.20), among men with a comorbidity (vs none; OR 1.47, 95% CI: 1.37–1.58), Gleason score 8 (vs ≤ 6 ; OR 1.23, 95% CI: 1.11–1.36), and in those diagnosed in the West (vs Midwest; OR 1.27, 95% CI: 1.13–1.43). In propensity score-weighted analysis, the difference was similar for risk of overall hospitalisation after RP vs RT (OR 0.75, 95% CI: 0.68–0.82). When compared with RP, brachytherapy (OR 1.41, 95% CI: 1.26–1.58) and combined EBRT/brachytherapy (OR 1.44, 95% CI: 1.29–1.60) had higher odds of hospitalisation after treatment, while patients who underwent EBRT/IMRT were not significantly different (OR 1.04, 95% CI: 0.93–1.17).

In multivariable analysis, patients who underwent RP rather than RT had higher odds of being hospitalised for treatment-related complications (OR 1.15, 95% CI: 1.03–1.29). Higher odds of treatment-related complications were seen among older men (71–75 vs 66–70 years; OR 1.14, 95% CI: 1.03–1.26); Black race (vs White; OR 1.36, 95% CI: 1.16–1.60), and those with a comorbid condition (vs none; OR 1.58, 95% CI:

Table 2 Rates of hospitalisation according to treatment type.

Variable	Total	Treatment			P**		
		RT (n = 21 301)	RP (n = 8 270)				
a.							
Hospitalisation any cause*, n (%)	4 441 (15.0)	3 393 (15.9)	1 048 (12.7)		<0.001		
Hospitalisation with treatment-related complication*, n (%)	1 769 (6.3)	1 257 (6.3)	512 (6.5)		0.523		
Variable	Total	Surgical treatment		RT treatment		P**	
		RP (n = 4 544)	MIRP (n = 3 726)	EBRT/IMRT (n = 7 809)	Brachytherapy (n = 5 978)		EBRT/IMRT/brachytherapy (n = 7 514)
b.							
Hospitalisation any cause*, n (%)	4 441 (15.0)	583 (12.8)	465 (12.5)	1 077 (13.8)	1 030 (17.2)	1 286 (17.1)	<0.001
Hospitalisation with treatment-related complication*, N (%)	1 769 (6.3)	279 (6.4)	233 (6.5)	439 (6.1)	350 (6.1)	468 (6.6)	0.704

MIRP, minimally invasive RP; *Hospitalisation defined as readmission within 365 days of initial treatment; **P value from chi-square test for overall difference among treatments.

Table 3 Multivariate logistic regression analysis for significant predictors of any hospitalisation within 365 days of initial treatment.*

Characteristic	Categories	OR (95% CI)	P
Treatment subtypes	RT	1.00	
	RP	0.80 (0.74–0.87)	<0.001
Year of diagnosis	2004	1.00	
	2005	0.93 (0.83–1.03)	0.154
	2006	0.91 (0.82–1.02)	0.092
	2007	0.86 (0.78–0.96)	0.007
	2008	0.83 (0.74–0.92)	0.001
	2009	0.77 (0.68–0.86)	<0.001
Age, years	66–70	1.00	
	71–75	1.10 (1.03–1.18)	0.004
CCI score	0	1.00	
	1	1.47 (1.37–1.58)	<0.001
Race/ethnicity	White	1.00	
	Hispanic	0.87 (0.75–1.01)	0.070
	Black	1.07 (0.95–1.20)	0.2281
	Other	0.73 (0.62–0.86)	<0.001
Marital status	Married	1.00	
	Unmarried	1.10 (1.01–1.20)	0.027
	Unknown	0.98 (0.87–1.10)	0.672
SEER region	Midwest	1.00	
	Northeast	1.12 (0.99–1.27)	0.068
	South	1.00 (0.88–1.12)	0.960
	West	1.27 (1.14–1.43)	<0.001
Residence	Rural	1.00	
	Urban	0.79 (0.71–0.88)	<0.001
Clinical stage	T1	1.00	
	T2	1.05 (0.99–1.13)	0.126
Gleason score	≤6	1.00	
	7	1.04 (0.97–1.11)	<0.332
	>8	1.23 (1.11–1.36)	<0.001
	Unknown	1.08 (0.82–1.42)	0.594

*Adjusted for education, poverty.

1.43–1.76) (Table 4). Using propensity score-weighted analyses, there was no statistically significant difference in the incidence of hospitalisation from treatment-related complications for men who underwent RP vs RT (OR 1.04, 95% CI: 0.91–1.19). Compared with RP, the incidence of treatment-related complications were not significantly different for brachytherapy (OR 0.94, 95% CI: 0.80–1.11) and combined EBRT/brachytherapy (OR 0.91, 95% CI: 0.77–1.07). However, patients who underwent EBRT/IMRT (OR 0.84, 95% CI: 0.72–0.99) had a 16% lower odds of hospitalisation from treatment-related complications than patients undergoing RP.

For costs, we found that patients who underwent RT had greater healthcare expenditures for any cause hospitalisation when compared with patients undergoing RP (mean \$16 465 vs \$13 597, $P < 0.001$). Similarly, patients hospitalised for treatment-related complications after RT were costlier than RP patients (mean \$18 381 vs \$13 205, $P < 0.001$) (Table 5).

Discussion

Treatment options for clinically significant prostate cancer may include RP, EBRT, and brachytherapy with active surveillance reserved for men diagnosed with indolent disease

Table 4 Logistic regression analysis for significant predictors of hospitalisation with treatment-related complication within 365 days of initial treatment.*

Characteristic	Categories	OR (95% CI)	P
Treatment subtypes	RT	1.00	
	RP	1.15 (1.03–1.29)	0.014
Year of diagnosis	2004	1.00	
	2005	0.94 (0.80–1.11)	0.445
	2006	1.02 (0.87–1.19)	0.843
	2007	0.89 (0.75–1.05)	0.155
	2008	0.90 (0.76–1.07)	0.231
	2009	0.93 (0.78–1.10)	0.370
Age, years	66–70	1.00	
	71–75	1.14 (1.03–1.26)	0.009
CCI	0	1.00	
	1	1.58 (1.43–1.76)	<0.001
Race/ethnicity	White	1.00	
	Hispanic	1.14 (0.92–1.40)	0.237
	Black	1.36 (1.16–1.60)	<0.001
	Other	1.02 (0.82–1.29)	0.842
Marital status	Married	1.00	
	Unmarried	1.12 (0.98–1.27)	0.089
	Unknown	1.16 (0.98–1.37)	0.088
SEER region	Midwest	1.00	
	Northeast	1.10 (0.91–1.33)	0.333
	South	1.11 (0.93–1.32)	0.266
	West	1.08 (0.91–1.29)	0.378
Residence	Rural	1.00	
	Urban	0.87 (0.74–1.03)	0.098
Clinical stage	T1	1.00	
	T2	1.02 (0.92–1.13)	0.743
Gleason score	≤6	1.00	
	7	1.04 (0.94–1.16)	0.422
	>8	1.24 (1.07–1.45)	0.006
	Unknown	1.20 (0.80–1.79)	0.375

*Adjusted for education, poverty.

Table 5 Associated mean Medicare costs of hospitalisation according to treatment type.

Variable	Treatment cost, \$		P* *
	RT	RP	
Hospitalisation any cause*, n (%)	16 465	13 597	<0.001
Hospitalisation with treatment-related complication*, n (%)	18 381	13 203	<0.001

*Hospitalisation defined as readmission within 365 days of initial treatment; **P from t-test for overall difference among treatments.

[2,3]. Prior research has shown varying complication rates and need for additional procedures after each treatment method [9]. In recent years, there has been a concerted effort to maximise the value of healthcare delivery by improving the quality of medical outcomes through decreased readmissions and reducing unnecessary costs [7]. In the present study, of the 29 571 patients undergoing RP or RT as their primary treatment for prostate cancer, with the exception of EBRT/IMRT, there was no statistically significant difference in the odds of hospitalisation from treatment-related complications. Moreover, costs from hospitalisation after treatment were

significantly higher for men undergoing RT than RP. We provide one of the first population-based analyses to further discern determinants costs of hospitalisation after primary treatment for prostate cancer.

Our present study has several important findings. First, in a cohort of men who would theoretically be candidates for either RP or RT because of age and good overall health, we found men who underwent RT more likely to be hospitalised for any reason. Prior studies have shown that men with advanced age and increased comorbidities were more likely to have complications after treatment for prostate cancer [14]. This is attributed to the variation in patient demographics undergoing RT compared with RP, those undergoing RT are often more unwell and more likely to have other competing risks for hospitalisation [14–16]. Our present results are relevant given the fact that we limited our cohort to those without significant comorbidities or advanced age. In addition, we were able to show that men without significant comorbidities and more recent year of RP were less likely to be hospitalised, which is consistent with prior reports [14]. Furthermore, tumour biology was a significant determinant of risk of overall and treatment-related hospitalisation. While we cannot conclude a cause and effect, there was an association between tumour biology and hospitalisation risk. Taking these patient factors into account and as suggested by current guidelines, physicians should incorporate life expectancy and competing risks when counselling patients on appropriate treatments.

Second, we found geographic variability in hospitalisation after primary treatment for prostate cancer. Specifically, men treated in rural areas and in the West were more likely to be hospitalised after primary treatment. While significantly different, the absolute differences observed were small and the comparative rates of hospitalisation were close. Our geographic variability observed is consistent with other prior reports about costs of treatment where regional differences are not due to differences in the prices of medical services, levels of illness or the socio-demographic characteristics of a region, but rather secondary to a greater quantity of medical services delivered including greater propensity for readmission after treatments in high cost areas [17]. Quality of care may not necessarily be better in regions of higher utilisation, and may in fact be significantly worse than quality of care in areas that use fewer resources [18]. The culture in medical communities is an important determinant of the quantity of medical care delivered [18], and may be the rate-limiting step when attempting to attenuate regional variation in hospitalisation after treatment for prostate cancer.

Third, in multivariable analyses we found that men treated with RP were more likely to be hospitalised due to a treatment-related complication than men treated with RT. Our present findings are consistent with prior reports

suggesting complications related to therapy following RP occur sooner than that of RT patients [19]. However, while we identified a statistically significant difference in likelihood of hospitalisation after treatment, the absolute difference was very small and may not be clinically relevant. Moreover, we attempted to provide a comparable group of men to discern potential differences in risk of treatment-related complications requiring hospitalisation. There may be other confounding variables that we are unable to control and further determinants needed to be discerned about hospitalisation risk. In the present study, propensity score-weighted analyses identified no significant difference in treatment-related hospitalisation except that patients who underwent EBRT/IMRT had 16% lower odds of treatment-related hospitalisation than patients undergoing RP. These findings support prior studies confirming a decreased side-effect profile associated with three-dimensional conformal RT and IMRT [20]. To our knowledge, this is the first comparative effectiveness study to discern risk of hospitalisation after primary treatment with RP or RT for prostate cancer. Other studies have critically assessed complications and additional procedures following either surgery or RT [9,10]. However, because patients treated with RT were older and more comorbid, selection bias limits the strength of conclusions that can be drawn from those studies.

Lastly, RT patients had higher attributable costs overall and related to complications when hospitalised when compared with RP patients. Recently, Wallis *et al.* [9] examined rates of interventions to manage complications after RT or RP using SEER-Medicare data within the same time period as the present study. While they did not evaluate associated costs, RT patients had significantly higher rates of urological procedures and anal-rectal procedures after RT. Our present analysis included diagnosis and procedure codes that further support the likelihood of increased complications requiring intervention, hospitalisations, and the associated increased costs after RT. These increased costs associated with RT should be balanced with individual risks of complication-related hospitalisation associated with certain types of RT such as EBRT/IMRT. These findings are important in the current healthcare climate, with an ever increasing demand for comparative effectiveness research discerning high quality cost-effective care over the entire care cycle [6]. In the hospital readmission reduction programme, the CMS currently uses 30-day readmission rates as a benchmark [7]. With payment penalties for increased readmissions in the setting of bundled payments and increased pressures to improve the value of care across the entire care cycle, there will be an increased need for comparative effectiveness research [21,22]. Critical assessment of hospitalisation risks for disease and treatments that may occur at greater than 30 or even 90 days are imperative to understanding how best to allocate resources appropriately.

While our present findings are policy relevant, they must be interpreted in the context of the study design. First, SEER-Medicare is limited to men aged ≥ 65 years and our results may not be generalisable to younger men diagnosed with prostate cancer. Second, neither SEER nor Medicare explicitly identifies those men who are being treated with robot-assisted RP. However, patients who undergo minimally invasive RP are more likely to have undergone robot-assisted surgery, which was increasing during the study period [23]. Third, we excluded PSA values in the present study due to preliminary evaluation of SEER data uncovered problems with the quality and interpretation of the PSA value [24]. While this questions the validity of large datasets, prior studies have suggested the limited impact PSA may have on disease risk stratification with patients having similar tumour characteristics as those with complete data [25]. Fourth, claims data are primarily designed to provide billing information and may not accurately capture all clinical information [13]. However, prior studies have shown a high degree of correlation between use of Medicare claims to detect complications after RP [26]. Fifth, our present results may not reflect long-term risk of hospitalisation after either treatment. Side-effects after RT treatment may take many years to become clinically apparent. However, recent long-term outcomes research have shown similar incidence of certain treatment-related complications [27]. Lastly, while we attempted to control for known predictors for hospitalisation, the findings are hypothesis-generating and there may be omitted variable bias. While we used the CCI, there may have been differences in health between the RP and RT groups that were not reflected in the CCI scores. However, observational studies reflect practice patterns and when compared with results from well-conducted randomised controlled trials they do not appear to overestimate treatment effects nor differ qualitatively [28,29].

Conclusions

With the exception of men who underwent EBRT/IMRT, there was no statistically significant difference in the odds of hospitalisations from treatment-related complications. Costs from hospitalisations after treatment were significantly higher for men undergoing RT compared with RP. Our present findings are relevant in the context of penalties linked to hospital readmissions and bundled payment models.

Acknowledgements

This work was supported by The University of Texas MD Anderson Center for Radiation Oncology Research (CROR) seed-grant awarded to Stephen B. Williams, M.D. and the Duncan Family Institute. Dr Williams is a Comparative Effectiveness Research on Cancer in Texas (CERCIT) Scholar. Drs Giordano and Smith are supported by CPRIT RP140020. Dr Smith receives research funding from Varian Medical Systems, but this funding was not used to support the present

study. This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the Applied Research Program, National Cancer Institute (NCI); the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumour registries in the creation of the SEER-Medicare database.

Conflict of interests

All authors have no conflicts of interest.

References

- 1 Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin* 2015; 65: 5–29
- 2 Mohler JL, Kantoff PW, Armstrong AJ et al. Prostate cancer, version 2.2014. *J Natl Compr Canc Netw* 2014; 12: 686–718
- 3 Heidenreich A, Aus G, Bolla M et al. EAU guidelines on prostate cancer. *Eur Urol* 2008; 53: 68–80
- 4 Makarov DV, Trock BJ, Humphreys EB et al. Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partin tables) based on cases from 2000 to 2005. *Urology* 2007; 69: 1095–101
- 5 Lu-Yao GL, Albertsen PC, Moore DF et al. Outcomes of localized prostate cancer following conservative management. *JAMA* 2009; 302: 1202–9
- 6 Porter ME. A strategy for health care reform – toward a value-based system. *N Engl J Med* 2009; 361: 109–12
- 7 Joynt KE, Jha AK. A path forward on Medicare readmissions. *N Engl J Med* 2013; 368: 1175–7
- 8 Nam RK, Cheung P, Herschorn S et al. Incidence of complications other than urinary incontinence or erectile dysfunction after radical prostatectomy or radiotherapy for prostate cancer: a population-based cohort study. *Lancet Oncol* 2014; 15: 223–31
- 9 Wallis CJ, Mahar A, Cheung P et al. New rates of interventions to manage complications of modern prostate cancer treatment in older men. *Eur Urol* 2016; 69: 933–41
- 10 Potosky AL, Davis WW, Hoffman RM et al. Five-year outcomes after prostatectomy or radiotherapy for prostate cancer: the prostate cancer outcomes study. *J Natl Cancer Inst* 2004; 96: 1358–67
- 11 Warren JL, Klabunde CN, Schrag D, Bach PB, Riley GF. Overview of the SEER-Medicare data: content, research applications, and generalizability to the United States elderly population. *Med Care* 2002; 40: IV-3-18
- 12 Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. *J Clin Epidemiol* 2000; 53: 1258–67
- 13 Hu JC, Gu X, Lipsitz SR et al. Comparative effectiveness of minimally invasive vs open radical prostatectomy. *JAMA* 2009; 302: 1557–64
- 14 Alibhai SM, Leach M, Warde P. Major 30-day complications after radical radiotherapy: a population-based analysis and comparison with surgery. *Cancer* 2009; 115: 293–302
- 15 Barry MJ, Albertsen PC, Bagshaw MA et al. Outcomes for men with clinically nonmetastatic prostate carcinoma managed with radical prostatectomy, external beam radiotherapy, or expectant management: a retrospective analysis. *Cancer* 2001; 91: 2302–14
- 16 Yan Y, Carvalhal GF, Catalona WJ, Young JD. Primary treatment choices for men with clinically localized prostate carcinoma detected by screening. *Cancer* 2000; 88: 1122–30

- 17 Fisher ES, Bynum JP, Skinner JS. Slowing the growth of health care costs – lessons from regional variation. *N Engl J Med* 2009; 360: 849–52
- 18 Fowler FJ Jr, Gallagher PM, Anthony DL, Larsen K, Skinner JS. Relationship between regional per capita Medicare expenditures and patient perceptions of quality of care. *JAMA* 2008; 299: 2406–12
- 19 Sanda MG, Dunn RL, Michalski J *et al.* Quality of life and satisfaction with outcome among prostate-cancer survivors. *N Engl J Med* 2008 Mar; 20: 1250–61
- 20 Zelefsky MJ, Levin EJ, Hunt M *et al.* Incidence of late rectal and urinary toxicities after three-dimensional conformal radiotherapy and intensity-modulated radiotherapy for localized prostate cancer. *Int J Radiat Oncol Biol Phys* 2008; 70: 1124–9
- 21 Porter ME. What is value in health care? *N Engl J Med* 2010; 363: 2477–81
- 22 National Cancer Policy Forum, Board on Health Care Services, Institute of Medicine, National Academies of Sciences, Engineering, and Medicine. *Appropriate Use of Advanced Technologies for Radiation Therapy and Surgery in Oncology: Workshop Summary*. Washington DC, USA; National Academies Press, 2016
- 23 Williams SB, Prasad SM, Weinberg AC *et al.* Trends in the care of radical prostatectomy in the United States from 2003 to 2006. *BJU Int* 2011; 108: 49–55
- 24 Sun M, Trinh QD. A Surveillance, Epidemiology and End Results (SEER) database malfunction: perceptions, pitfalls and verities. *BJU Int* 2016; 117: 551–2
- 25 Elliott SP, Johnson DP, Jarosek SL, Konety BR, Adejoro OO, Virnig BA. Bias due to missing SEER data in D’Amico risk stratification of prostate cancer. *J Urol* 2012; 187: 2026–31
- 26 Lawthers AG, McCarthy EP, Davis RB, Peterson LE, Palmer RH, Iezzoni LI. Identification of in-hospital complications from claims data. Is it valid? *Med Care* 2000; 38: 785–95
- 27 Resnick MJ, Koyama T, Fan KH *et al.* Long-term functional outcomes after treatment for localized prostate cancer. *N Engl J Med* 2013; 368: 436–45
- 28 Lewis JH, Kilgore ML, Goldman DP *et al.* Participation of patients 65 years of age or older in cancer clinical trials. *J Clin Oncol* 2003; 21: 1383–9
- 29 Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials: race-, sex-, and age-based disparities. *JAMA* 2004; 291: 2720–6

Correspondence: Stephen B. Williams, The University of Texas Medical Branch, Division of Urology 301 University Blvd, Galveston, TX 77555, USA.

e-mail: stbwilli@utmb.edu

Abbreviations: ADT, androgen-deprivation therapy; CCI, Charlson Comorbidity Index; CMS, Centers for Medicare and Medicaid Services; CPT, Current Procedural Terminology; ICD-9, International Classification of Diseases 9th edition; OR odds ratio; PEDSF, Patient Entitlement and Diagnosis Summary File; RP, radical prostatectomy; (EB)(IM)RT, (external beam) (intensity modulated) radiotherapy; SEER, Surveillance, Epidemiology, and End Results.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1 International Classification of Diseases-9 (ICD-9) and Healthcare Common Procedure Coding System (HCPCS) codes for primary treatments for prostate cancer.

Table S2 ICD-9 codes for complications related to primary treatments for prostate cancer.

Table S3 Characteristics of patients with prostate cancer excluding those patients with pre-existing complications according to treatment regimen.