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Original Article

Radical prostatectomy is associated with favorable outcomes in patients over 80 years old

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Abstract: Introduction/Background: Although surgery is less commonly selected as treatment for localized prostate cancer (PCa) as patients age, outcomes among older patients treated with radical prostatectomy remain unclear. The objective of this study was to compare survival across non-definitive therapy (NDT), radiotherapy, and radical prostatectomy (RP) among men older than 80 years old. Materials and Methods: Using the SEER-17 database, we identified patients ≥80 years at diagnosis with localized prostate cancer in 2000-2021 who were initially managed with NDT, radiotherapy, or RP. We compared overall (OS) and prostate cancer-specific survival (PCSS). Results: We identified 53,437 patients with PCa≥80 years including 35,728 (68.2%) who underwent NDT, 15,906 (30.4%) treated with radiotherapy, and 736 (1.4%) with RP. The median age was 83 years (IQR: 81-85) and median PSA at diagnosis was 10.7 ng/mL (IQR: 6.7-19.9). Median OS was 66, 102 and 116 months for patients managed with NDT, radiotherapy, and RP, respectively (OS-P<0.01, PCSS-P<0.01). Cox regression revealed that compared to NDT, radiotherapy (OS-baseline adjusted hazard ratio: 0.48, 95% CI: 0.45-0.51, P<0.01; PCSS-baHR: 0.44, 95% CI: 0.38-0.51, P<0.01) and RP were associated with higher OS and PCSS (OS-baHR: 0.33, 95% CI: 0.24-0.46, P<0.01; PCSS-baHR: 0.19, 95% CI: 0.08-0.42, P<0.01). Conclusion: These findings suggest that well-selected patients ≥80 years may experience favorable survival following RP.

Keywords: Prostate cancer, radical prostatectomy, radiotherapy, non-definitive therapy, elderly

Introduction

Prostate cancer (PCa) is the most commonly diagnosed cancer among men with an estimated 1.4 million diagnoses globally in 2020 [1]. The incidence of PCa increases with age from 1.8% at age 50-59 to 9.0% at age 70 and older [2]. However, the autopsy prevalence of PCa is considerably higher, and estimated to be 40% at age 60 and older to 60% at age 80 and older [3]. Elderly patients are also more likely to have more aggressive disease. Despite increased risks, competing causes of death are substantial in those ≥80 years, making the role of curative local therapy such as radiation and radical prostatectomy (RP) in this demographic unsettled. Current guidelines by the American Urological Association (AUA) limit the recommendation for curative therapy with RP or radiation therapy plus androgen deprivation therapy (ADT) for unfavorable intermediate and high risk prostate cancer to patients with an estimated life expectancy (LE) >10 years [4]. Given that the average LE in the United States is 76.1 years and 8.6 years for people aged 80 [5], prostatectomy is rarely untaken in this group [6, 7]. Nonetheless, there is limited evidence with which to counsel otherwise healthy individuals >80 years who wish to consider radical prostatectomy due to personal preference or a desire to avoid androgen deprivation therapy (ADT).

Determining the effect of PCa treatment may be particularly difficult due to selection biases

that may favor surgery in the healthiest subset of octogenarians. One study found that men older than 80 years old with high-risk PCa experienced a 2-fold higher survival rate after surgery or radiotherapy compared to those who received no treatment [8]. In contrast, Porcaro et al. reported that elderly patients were more likely to have high-risk disease and thus experience worse oncological outcomes after RP [9]. Functional outcomes are an additional consideration as elderly patients appear to have higher risks of urinary incontinence and erectile dysfunction following RP [7].

To our knowledge, no studies have compared outcomes across management strategies in elderly patients. Therefore, the objective of this study was to compare survival across management strategies, focusing on RP, radiotherapy and non-definitive therapy (NDT) in those ≥80. The hypothesis was that elderly patients receiving RP experience better survival compared to those receiving radiotherapy or NDT.

Methods

Data sources

We selected a cohort of patients at least 80-year-old at diagnosis with clinically localized prostate cancer from 2000-2021 from the Surveillance, Epidemiology, and End Results (SEER) 17 registries, which collects data from cancer registries in Alaskan Native Tumor Registry, Connecticut, Atlanta, rural Georgia, San Francisco - Oakland, San Jose - Monterey, Greater California, Hawaii, Iowa, Kentucky, Los Angeles, Louisiana, New Mexico, New Jersey, Seattle - Puget Sound, and Utah. Specifically, patients were limited to T1-T3, N0, M0 disease except for RP patients who could have N1 disease. SEER provides only the best available staging, so while patients could have either clinical or pathologic staging, RP patients would be more likely to have pathologic staging available. The rationale for this assumption is that patients who had RP likely had clinical N0 disease but converted to N1 following surgery. We extracted patient information using the SEER*Stat database and specific information on radiotherapy from SEER's Research Plus database.

Study variables

Study variables included age, race, T stage, PSA value (ng/mL), and treatment modality, which included NDT, radiotherapy, or RP. Patients who received both radiotherapy and RP were categorized based on the treatment they received first.

Statistical analysis

We first used descriptive statistics to compare all sociodemographic and clinical characteristics across management strategies. We also stratified patients by treatment including radiotherapy, RP, or NDT. If patients did not receive either radiotherapy or RP, they were categorized as NDT. To determine factors contributing to treatment selection, we implemented logistic regression using NDT vs. any treatment, radiotherapy vs. RP, and non-RP vs. RP. We primarily examined overall survival (OS) and prostate cancer-specific survival (PCSS) stratified by patient treatment. Given that 180 months approximately represented the 99th percentile for follow-up period for patients in the treatment group with the shortest median follow-up time, survival was cut off at 180 months across all groups. To examine short-term survival and safety of the treatments, we compared 36- and 60-month OS and PCSS rates as well. OS and PCSS were initially compared across treatment groups with the Kaplan-Meier method and log-rank test. Schoenfeld residuals tests indicated that survival functions were not proportional over time, violating the Cox proportional hazards assumption. Therefore, we incorporated time-varying covariates and adjusted for the aforementioned covariates into our Cox proportional hazards regression model using Stata/SE 18.0 [10]. Adjusted covariates included patient age, race, and PSA value.

Results

Patients undergoing RP experienced the highest OS and PCSS compared to those undergoing NDT and radiotherapy

The study cohort was composed of 53,437 patients with localized prostate cancer 80-year or older at diagnosis, 68.22% of whom underwent NDT with the remaining 30.37% and 1.41% undergoing radiotherapy and RP, respectively (**Table 1**). Patients managed with NDT had higher PSA levels with a median PSA of 11.9 (interquartile range: 7.0-24.1) relative to those receiving radiotherapy with a median PSA of 9.5 (IQR: 6.5-15.2) and RP with 8.2 (IQR:

Table 1. Patient characteristics for NDT, RP, and radiotherapy patients in raw sample

	NDT No. (%)	Radiotherapy No. (%)	RP No. (%)	*p*-value
N	35,728 (68.22)	15,906 (30.37)	736 (1.41)	
Median Age (years) (IQR)	83 (81-86)	82 (81-83)	81 (80-83)	<0.01*
Median PSA (ng/mL) (IQR)	11.9 (7.0-24.1)	9.5 (6.5-15.2)	8.2 (5.7-12.8)	<0.01*
T Stage				<0.01
T1	19,909 (55.72)	8,262 (51.94)	12 (1.63)	
T2	15,041 (42.10)	6,718 (42.24)	434 (58.97)	
T3	778 (2.18)	926 (5.82)	290 (39.40)	
PSA (ng/mL)				<0.01
≤10	7,174 (20.08)	5,266 (33.11)	226 (30.71)	
10<PSA≤20	4,651 (13.02)	3,056 (19.21)	89 (12.09)	
PSA>20	23,903 (66.90)	7,584 (47.68)	421 (57.20)	
Race				<0.01
Non-Hispanic White	26,704 (67.92)	12,063 (30.68)	550 (1.40)	
Non-Hispanic Black	3,218 (75.06)	1,034 (24.12)	35 (0.82)	
Hispanic	3,045 (68.81)	1,291 (29.18)	89 (2.01)	
Non-Hispanic Asian or Pacific Islander	2,180 (60.42)	1,375 (38.11)	53 (1.47)	
Non-Hispanic American Indian/Alaskan Native	118 (72.84)	40 (24.69)	4 (2.47)	
Unknown	463 (81.09)	103 (18.04)	5 (0.88)	

*Nonparametric equality-of-medians test.

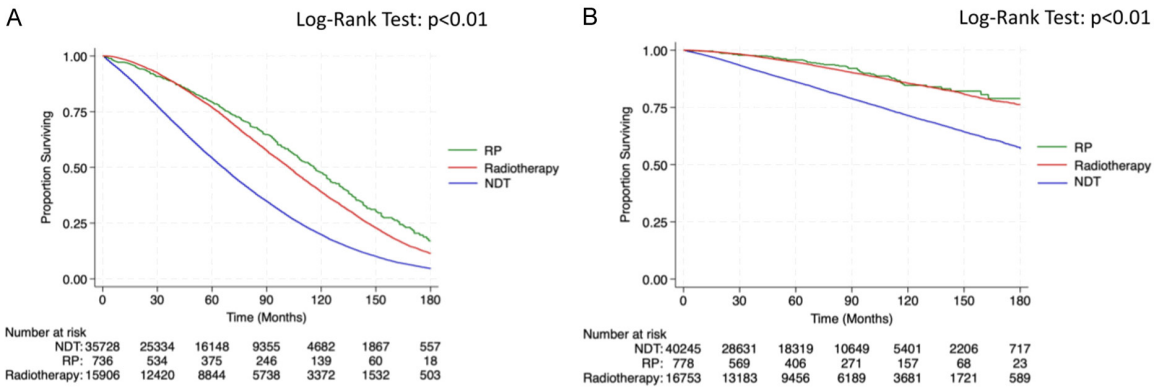

Figure 1. A. Overall survival of PCa patients older than age 80 who underwent NDT, RP, or radiotherapy. B. Prostate cancer-specific survival of PCa patients older than age 80 who underwent NDT, RP, or radiotherapy.

5.7-12.8). NDT had the highest proportion of patients with T1 disease at 55.7%, followed by radiotherapy at 51.9% and RP at 1.6%. Non-Hispanic Black patients more commonly received NDT at 75.1% and less frequently underwent radiotherapy (24.1%) or RP (0.8%). In comparison, 67.9%, 30.7%, and 1.4% of non-Hispanic White patients underwent NDT, radiotherapy, and RP, respectively (P<0.01, Pearson's chi-squared).

Median OS for patients undergoing RP was 116 (IQR: 69-163) months, followed by those undergoing radiotherapy at 102 months (IQR: 63-146) and then NDT at 66 months (IQR: 33-108). Differences in survival were confirmed by Kaplan-Meier analyses (**Figure 1**; P<0.01; log-rank test). Kaplan-Meier analysis for PCSS similarly demonstrated that RP patients observed the highest PCSS, followed by radiotherapy patients, and NDT patients (**Figure 1**; P<0.01; log-rank test). Patients across all three treatment modalities did not have median PCSS times available due to prostate cancer-specific mortality rates of less than 50% in 180 months. Regarding more short-term survival, 36-month

Table 2. Cox proportional hazards analysis of factors associated with overall survival

	Baseline HR (95% CI)	*p*-value	Baseline Adjusted HR (95% CI)	*p*-value
Age (years)	1.17 (1.17-1.18)	<0.01	1.12 (1.11-1.13)	<0.01
PSA (ng/mL)	1.02 (1.02-1.02)	<0.01	1.01 (1.01-1.01)	<0.01
T Stage				
T1	1.00 (Referent)		1.00 (Referent)	
T2	1.02 (0.99-1.06)	0.22	1.08 (1.02-1.14)	<0.01
T3	1.11 (1.00-1.23)	0.05	1.25 (1.08-1.43)	<0.01
Race				
Non-Hispanic White	1.00 (Referent)		1.00 (Referent)	
Non-Hispanic Black	1.24 (1.16-1.32)	<0.01	1.11 (1.01-1.22)	0.03
Hispanic	0.78 (0.73-0.84)	<0.01	0.78 (0.71-0.86)	<0.01
Non-Hispanic Asian or Pacific Islander	0.73 (0.68-0.80)	<0.01	0.74 (0.66-0.83)	<0.01
Non-Hispanic American Indian/Alaskan Native	0.82 (0.57-1.18)	0.29	0.94 (0.58-1.53)	0.80
Unknown	0.32 (0.23-0.43)	<0.01	0.25 (0.16-0.42)	<0.01
Treatment				
NDT	1.00 (Referent)		1.00 (Referent)	
Radiotherapy	0.34 (0.32-0.35)	<0.01	0.48 (0.45-0.51)	<0.01
RP	0.32 (0.26-0.40)	<0.01	0.33 (0.24-0.46)	<0.01

OS and PCSS rates were 73.9% and 93.0% for NDT, 90.7% and 97.9% for radiotherapy, and 90.5% and 98.1% for RP, respectively (OS: P<0.01; PCSS: P<0.01; log-rank test). Finally, 60-month OS and PCSS rates were 58.1% and 89.5% for NDT, 81.0% and 96.0% for radiotherapy, and 83.7% and 96.9% for RP, respectively (OS: P<0.01; PCSS: P<0.01; log-rank test).

Cox proportional hazards model adjusted for covariates indicated that patients undergoing RP continued to experience the highest OS and PCSS

Adjusted Cox proportional hazards model with time-varying covariates indicated that PSA (per 1 unit) was associated with decreased OS and PCSS (OS: baHR 1.01, 95% CI 1.01-1.01, P<0.01; PCSS: baHR 1.02, 95% CI 1.02-1.02, P<0.01; **Tables 2**, **3**, Supplementary Tables 1, 2). Compared to T1 disease, those with T2 and T3 observed worse OS and PCSS (T1 - OS: baHR 1.08, 95% CI 1.02-1.14, P<0.01; PCSS: baHR 1.16, 95% CI 1.03-1.30, P=0.01; T2 - OS: baHR 1.25, 95% CI 1.08-1.43, P<0.01; PCSS: baHR 1.95, 95% CI 1.53-2.49, P<0.01). Compared to non-Hispanic White race, non-Hispanic Black race was associated with worse adjusted OS but not PCSS (OS: baHR 1.11, 95% CI 1.01-1.22, P=0.03; PCSS: baHR 0.97, 95% CI 0.80-1.18, P=0.79). In comparison, Hispanic ethnicity was associated with improved adjusted OS but not PCSS, while non-Hispanic Asian or Pacific Islanders ethnicity was associated with better adjusted OS and PCSS (Hispanic - OS: baHR 0.78, 95% CI 0.71-0.86, P<0.01; PCSS: baHR 0.87, 95% CI 0.72-1.07, P=0.18; Asian/Pacific Islander - OS: baHR 0.74, 95% CI 0.66-0.83, P<0.01; PCSS: baHR 0.67, 95% CI 0.53-0.86, P<0.01).

Relative to NDT, radiotherapy was associated with significantly improved OS and PCSS (OS: baHR 0.48, 95% CI 0.45-0.51, P<0.01; PCSS: baHR 0.44, 95% CI 0.38-0.51, P<0.01; **Tables 2**, **3**, Supplementary Tables 1, 2). RP was associated with comparatively longer OS and PCSS (OS: baHR 0.33, 95% CI 0.24-0.46, P<0.01; PCSS: baHR 0.19, 95% CI 0.08-0.42, P<0.01). With each subsequent month, however, the relative OS and PCSS improvement for radiotherapy slightly decreased in magnitude (OS: time-varying covariate in aHR of 1.00, 95% CI 1.00-1.00, P<0.01; PCSS: TVC in aHR of 1.00, 95% CI 1.00-1.01, P<0.01). By comparison, the relative OS improvement for RP decreased in magnitude over time (TVC in aHR of 1.00, 95% CI 1.00-1.01, P=0.01), but the PCSS improvement did not change (TVC in aHR of 1.09, 95% CI 1.00-1.02, P=0.07).

Table 3. Cox proportional hazards analysis of factors associated with prostate cancer-specific survival

	Baseline HR (95% CI)	*p*-value	Baseline Adjusted HR (95% CI)	*p*-value
Age (years)	1.21 (1.20-1.23)	<0.01	1.12 (1.10-1.14)	<0.01
PSA (ng/mL)	1.03 (1.02-1.03)	<0.01	1.02 (1.02-1.02)	<0.01
T Stage				
T1	1.00 (Referent)		1.00 (Referent)	
T2	1.20 (1.10-1.30)	<0.01	1.16 (1.03-1.30)	0.01
T3	2.08 (1.74-2.48)	<0.01	1.95 (1.53-2.49)	<0.01
Race				
Non-Hispanic White	1.00 (Referent)		1.00 (Referent)	
Non-Hispanic Black	1.30 (1.15-1.48)	<0.01	0.97 (0.80-1.18)	0.79
Hispanic	0.94 (0.82-1.08)	0.39	0.87 (0.72-1.07)	0.18
Non-Hispanic Asian or Pacific Islander	0.71 (0.60-0.83)	<0.01	0.67 (0.53-0.86)	<0.01
Non-Hispanic American Indian/Alaskan Native	0.89 (0.46-1.71)	0.72	0.66 (0.25-1.70)	0.38
Unknown	0.24 (0.12-0.47)	<0.01	0.24 (0.07-0.79)	0.02
Treatment				
NDT	1.00 (Referent)		1.00 (Referent)	
Radiotherapy	0.30 (0.27-0.33)	<0.01	0.44 (0.38-0.51)	<0.01
RP	0.26 (0.16-0.43)	<0.01	0.19 (0.08-0.42)	<0.01

36-month Cox proportional hazards analysis indicated that compared to NDT patients, radiotherapy was associated with improved OS and PCSS (OS: baHR 0.28, 95% CI 0.23-0.33, P<0.01; PCSS: baHR 0.44, 95% CI 0.38-0.51, P<0.01; Supplementary Tables 3, 4). RP patients also observed higher OS and PCSS, although the value for OS was not statistically significant (OS: baHR 0.47, 95% CI 0.21-1.05, P=0.07; PCSS: baHR 0.19, 95% CI 0.08-0.42, P<0.01). 60-month Cox analysis demonstrated similar results regarding the improved OS and PCSS of radiotherapy and RP compared to NDT but no statistically significant values for OS and PCSS in RP (Radiotherapy - OS: baHR 0.36, 95% CI 0.32-0.41, P<0.01; PCSS: baHR 0.32, 95% CI 0.24-0.41, P<0.01; RP - OS: baHR 0.58, 95% CI 0.33-1.02, P=0.06; PCSS: baHR 0.24, 95% CI 0.05-1.18, P=0.08) (Supplementary Tables 5 and 6).

Compared to patients on NDT who had a median age of 83 (IQR: 81-86) and median PSA of 11.9 (IQR: 7.0-24.1), those receiving treatment such as radiotherapy or RP tended to be younger with a median age of 82 (IQR: 81-83) and have a lower median PSA at 9.5 (IQR: 6.5-15.1) (**Table 4**). A logistic regression model of NDT vs. any treatment indicated that lower age, lower PSA, and being non-Hispanic White or non-Hispanic Asian or Pacific Islander were associated with receiving treatment (**Table 5**). In another logistic regression model with radiotherapy vs. RP, younger age, lower PSA, and being non-Hispanic White, Hispanic, or non-Hispanic Asian or Pacific Islander were associated with undergoing RP as opposed to radiotherapy (**Table 6**). A final logistic regression model with non-RP vs. RP demonstrated that younger age, PSA, and being non-Hispanic White, Hispanic, or non-Hispanic American Indian/Alaskan Native were associated with being selected for RP as opposed to no RP (**Table 7**). Data on urinary and sexual function were not available for comparison.

Discussion

In this study examining patterns of treatment and PCa outcomes among patients ≥80 years old, we found that the smaller subset of patients who underwent RP experienced increased overall and prostate cancer-specific survival compared to patients treated with radiotherapy or NDT. This survival benefit, however, decreased with age. The findings of this study support the use of RP as a viable treatment in carefully selected patients >80 years.

Of the three treatment groups, RP patients experienced the highest OS and PCSS, followed by radiotherapy, and then NDT patients.

Table 4. Patient characteristics for NDT vs. any treatment (radiotherapy/RP)

	NDT No. (%)	Any Treatment No. (%)	*p*-value
N	35,728 (68.22)	16,642 (31.78)	
Median Age (years) (IQR)	83 (81-86)	82 (81-83)	<0.01
Median PSA (ng/mL) (IQR)	11.9 (7.0-24.1)	9.5 (6.5-15.1)	<0.01
T Stage			<0.01
T1	19,909 (55.72)	8,274 (49.72)	
T2	15,041 (42.10)	7,152 (42.98)	
T3	778 (2.18)	1,216 (7.31)	
PSA (ng/mL)			
≤10	7,174 (20.08)	5,492 (33.00)	<0.01
10<PSA≤20	4,651 (13.02)	3,145 (18.90)	
PSA>20	23,903 (66.90)	8,005 (48.10)	
Race			
Non-Hispanic White	26,704 (67.92)	12,613 (32.08)	<0.01
Non-Hispanic Black	3,218 (75.06)	1,069 (24.94)	
Hispanic	3,045 (68.81)	1,380 (31.19)	
Non-Hispanic Asian or Pacific Islander	2,180 (60.42)	1,428 (39.58)	
Non-Hispanic American Indian/Alaskan Native	118 (72.84)	44 (27.16)	
Unknown	463 (81.09)	108 (18.91)	

Table 5. Logistic regression model of NDT vs. any treatment (radiotherapy/RP)

	OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Age (years)	0.80 (0.80-0.81)	<0.01	0.81 (0.80-0.82)	<0.01
PSA (ng/mL)	0.98 (0.98-0.98)	<0.01	0.98 (0.98-0.98)	<0.01
T Stage				
T1	1.00 (Referent)		1.00 (Referent)	
T2	1.14 (1.10-1.19)	<0.01	1.09 (1.03-1.15)	<0.01
T3	3.76 (3.42-4.13)	<0.01	4.00 (3.47-4.60)	<0.01
Race				
Non-Hispanic White	1.00 (Referent)		1.00 (Referent)	
Non-Hispanic Black	0.70 (0.65-0.76)	<0.01	0.70 (0.64-0.78)	<0.01
Hispanic	0.96 (0.90-1.03)	0.23	0.86 (0.78-0.94)	<0.01
Non-Hispanic Asian or Pacific Islander	1.39 (1.29-1.49)	<0.01	1.38 (1.25-1.52)	<0.01
Non-Hispanic American Indian/Alaskan Native	0.79 (0.56-1.12)	0.18	0.80 (0.49-1.33)	0.39
Unknown	0.49 (0.40-0.61)	<0.01	0.48 (0.36-0.64)	<0.01

Importantly, these findings may reflect treatment selection bias, as Miccio et al. reported that patients selected for RP may be healthier than those on radiotherapy [11]. Due to the potential presence of confounding factors such as age, race, and PSA as well as time-varying factors, we implemented an adjusted Cox proportional hazards model with time-varying covariates, which still found the highest OS and PCSS among RP patients. The utility of RP in elderly PCa patients has frequently been questioned, as RP, like all surgical procedures, has increased risks among elderly patients [12]. While the vast majority of elderly patients currently do not receive RP, our study demonstrates that in spite of potentially higher-risk disease among elderly patients, well-selected individuals treated with surgery may experience favorable long-term survival. Similarly, Wang et al. found that elderly, high to very high-risk PCa patients who underwent RP had a higher survival than those who underwent external beam radiotherapy [13]. Studies have further reported that physicians tend to un-

Table 6. Logistic regression model of radiotherapy vs. RP

	OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Age (years)	0.94 (0.91-0.98)	<0.01	0.90 (0.85-0.95)	<0.01
PSA (ng/mL)	0.99 (0.98-1.00)	0.08	0.98 (0.97-0.99)	<0.01
T Stage				
T1	1.00 (Referent)		1.00 (Referent)	
T2	44.48 (25.04-79.00)	<0.01	132.41 (32.86-533.45)	<0.01
T3	215.62 (120.56-385.63)	<0.01	831.31 (205.12-3369.12)	<0.01
Race				
Non-Hispanic White	1.00 (Referent)		1.00 (Referent)	
Non-Hispanic Black	0.74 (0.52-1.05)	0.09	0.94 (0.52-1.70)	0.85
Hispanic	1.51 (1.20-1.91)	<0.01	1.29 (0.89-1.87)	0.18
Non-Hispanic Asian or Pacific Islander	0.85 (0.63-1.13)	0.25	0.81 (0.51-1.28)	0.36
Non-Hispanic American Indian/Alaskan Native	2.19 (0.78-6.15)	0.14	4.23 (1.04-17.26)	0.04
Unknown	1.06 (0.43-2.62)	0.89	1.27 (0.37-4.37)	0.70

Table 7. Logistic regression model of non-RP vs. RP

	OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Age (years)	0.82 (0.79-0.84)	<0.01	0.81 (0.77-0.85)	<0.01
PSA (ng/mL)	0.98 (0.97-0.99)	<0.01	0.97 (0.96-0.98)	<0.01
T Stage				
T1	1.00 (Referent)		1.00 (Referent)	
T2	46.65 (26.28-82.80)	<0.01	134.54 (33.41-541.81)	<0.01
T3	391.24 (219.19-698.32)	<0.01	1428.45 (352.83-5783.22)	<0.01
Race				
Non-Hispanic White	1.00 (Referent)		1.00 (Referent)	
Non-Hispanic Black	0.58 (0.41-0.82)	<0.01	0.73 (0.41-1.30)	0.29
Hispanic	1.45 (1.16-1.82)	<0.01	1.20 (0.84-1.73)	0.32
Non-Hispanic Asian or Pacific Islander	1.05 (0.79-1.39)	0.75	0.91 (0.58-1.44)	0.69
Non-Hispanic American Indian/Alaskan Native	1.79 (0.66-4.84)	0.25	2.75 (0.75-10.05)	0.13
Unknown	0.62 (0.26-1.50)	0.29	0.85 (0.26-2.78)	0.79

derestimate 10-year LE for their patients [7, 14-18], meaning that a significant percentage of elderly patients may not be recommended for appropriate curative treatment [7]. Mandel and colleagues similarly stated that age should not be the sole determining factor in determining RP for elderly patients [7]. Analysis of shorter-term, 36-month and 60-month OS and PCSS demonstrated similar results with RP patients having a higher OS and PCSS rate compared to NDT patients, supporting the overall safety of the procedure in well-selected elderly patients.

We found that older patients selected for RP tended to be towards the younger end of the cohort and have lower PSA levels, suggesting selection factors for more favorable life expectancy. However, RP patients were also more likely to have higher T stage disease. While many studies and organizations have advocated for prioritizing baseline health when deciding whether elderly patients should receive curative treatment, the ideal guidelines remain less clear [7, 19]. For elderly PCa patients seeking RP, the EAU suggests a LE of greater than 10 years, while the National Comprehensive Cancer Network recommends a LE of 10-20 years based on the risk group and the American Urological Association suggests a “reasonable” LE [7, 19-21]. RP is also an infrequent treatment for PCa patients older than 80, which is supported by our findings that only 0.9% of these patients underwent RP and may be useful for counseling patients on possible treatment modalities. There is evidence, however, that elderly, healthy patients with PCa often may be undertreated. Bratt and colleagues found that while high-risk PCa patients aged

75-80 with a Charlson Comorbidity Index of 0 had a 52% probability of a 10-year LE, only 10% received radiotherapy or RP [6]. These findings underscore that re-evaluation of patient risks, including the use of quantitative decision tools such as the Veterans Aging Cohort Study Charlson Comorbidity Index may be valuable to improve patient selection and decision-making [22].

It is important to note that the survival differences by treatment diminished with age, likely reflecting competing causes of death. This finding is consistent with the current body of literature, which has established that increased age is associated with factors such as more common causes of death and more postoperative complications [23, 24]. Thus, while patient age should not be the only or even deciding factor, it nevertheless remains an important component in assessing the appropriateness of RP in elderly patients. Additionally, physicians should note that RP has been associated with higher rates of erectile dysfunction and incontinence among elderly men, so the diminishing survival benefits of RP in elderly men should be weighed against the risks [7]. Overall, as opposed to selecting patient treatment solely based on patient age or even LE using current nomograms, we advocate for shared decision-making and a holistic approach for treatment selection involving factors such as patient goals for care as well as more objective measures such as patient comorbidities like prior studies have done [7].

To our knowledge, there have been no studies examining the time-varying effect of RP and radiotherapy on survival in elderly PCa patients along comparing their use in Black and White elderly men in population-level databases. Limitations of this study primarily included its retrospective design as well as limitations inherent to the SEER database. For example, SEER does not provide information on both clinical and pathologic staging but only offers the best available staging method. Given that pathologic staging would likely mostly be found in the RP group, N1 patients undergoing RP were not removed from the final analysis. However, the inclusion of N1 patients in RP group would lower the survival of RP group, thereby strengthening our findings on the increased OS and PCSS of RP patients relative to NDT. SEER also does not include information on androgen deprivation therapy (ADT) or hormonal therapy, so patients on ADT or hormonal therapy may be included in the non-definitive treatment modality. Furthermore, we do not know how many RP patients went on adjuvant or early salvage radiation therapy (SRT), and counseling patients about the risk of recurrence after attempted definitive therapy is important. Additionally, the sample size for RP patients was smaller than those of radiotherapy and NDT, largely because elderly patients are less likely to receive surgery [6, 7]. This small sample size is likely related to healthier elderly patients being selected for RP instead of NDT. Furthermore, the outcomes of this study were limited to OS and PCSS. However, patients may prioritize other attributes such as quality of life, so physicians should account for the findings of this study regarding the overall and prostate cancer-specific survival benefits of RP in elderly patients but ultimately defer to the patient based on their goals for care. Thus, future studies should examine other outcomes besides OS and PCSS such as clinical and metastatic progression and need for ADT. Lastly, the observational design of this study makes it a hypothesis-generating study that future studies should use to further investigate the benefits of RP in elderly patients.

Conclusion

Elderly PCa patients who received RP experienced a higher median OS compared to those on NDT. Patients who were younger and had lower PSA were more likely to receive curative treatment with radiotherapy or RP, suggesting that elderly patients who are selected for RP may observe high short-term and long-term OS. However, this survival benefit diminished as patients became older.

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Disclosure of conflict of interest

None.

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Supplementary Table 1. Cox proportional hazards analysis with time-varying covariates of factors associated with overall survival

	Baseline HR (95% CI)	*p*-value	Time-Varying Covariate in HR (95% CI)	*p*-value	Baseline Adjusted HR (95% CI)	*p*-value	Time-Varying Covariate in aHR (95% CI)	*p*-value
Age (years)	1.17 (1.17-1.18)	<0.01	1.00 (1.00-1.00)	<0.01	1.12 (1.11-1.13)	<0.01	1.00 (1.00-1.00)	<0.01
PSA (ng/mL)	1.02 (1.02-1.02)	<0.01	1.00 (1.00-1.00)	<0.01	1.01 (1.01-1.01)	<0.01	1.00 (1.00-1.00)	<0.01
T Stage								
T1	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
T2	1.02 (0.99-1.06)	0.22	1.00 (1.00-1.00)	0.87	1.08 (1.02-1.14)	<0.01	1.00 (1.00-1.00)	0.20
T3	1.11 (1.00-1.23)	0.05	1.00 (1.00-1.00)	0.43	1.25 (1.08-1.43)	<0.01	1.00 (1.00-1.00)	0.60
Race								
Non-Hispanic White	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Non-Hispanic Black	1.24 (1.16-1.32)	<0.01	1.00 (1.00-1.00)	<0.01	1.11 (1.01-1.22)	0.03	1.00 (1.00-1.00)	0.01
Hispanic	0.78 (0.73-0.84)	<0.01	1.00 (1.00-1.00)	0.02	0.78 (0.71-0.86)	<0.01	1.00 (1.00-1.00)	0.13
Non-Hispanic Asian or Pacific Islander	0.73 (0.68-0.80)	<0.01	1.00 (1.00-1.00)	0.76	0.74 (0.66-0.83)	<0.01	1.00 (1.00-1.00)	0.81
Non-Hispanic American Indian/Alaskan Native	0.82 (0.57-1.18)	0.29	1.00 (1.00-1.01)	0.17	0.94 (0.58-1.53)	0.80	1.00 (0.99-1.01)	0.64
Unknown	0.32 (0.23-0.43)	<0.01	1.00 (1.00-1.00)	0.61	0.25 (0.16-0.42)	<0.01	1.00 (1.00-1.01)	0.79
Treatment								
NDT	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Radiotherapy	0.34 (0.32-0.35)	<0.01	1.01 (1.01-1.01)	<0.01	0.48 (0.45-0.51)	<0.01	1.00 (1.00-1.01)	<0.01
RP	0.32 (0.26-0.40)	<0.01	1.01 (1.00-1.01)	<0.01	0.33 (0.24-0.46)	<0.01	1.00 (1.00-1.01)	0.01

Supplementary Table 2. Cox proportional hazards analysis with time-varying covariates of factors associated with prostate cancer-specific survival

	Baseline HR (95% CI)	*p*-value	Time-Varying Covariate in HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value	Time-Varying Covariate in aHR (95% CI)	*p*-value
Age (years)	1.21 (1.20-1.23)	<0.01	1.00 (1.00-1.00)	<0.01	1.12 (1.10-1.14)	<0.01	1.00 (1.00-1.00)	<0.01
PSA (ng/mL)	1.03 (1.02-1.03)	<0.01	1.00 (1.00-1.00)	<0.01	1.02 (1.02-1.02)	<0.01	1.00 (1.00-1.00)	<0.01
T Stage								
T1	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
T2	1.20 (1.10-1.30)	<0.01	1.00 (1.00-1.00)	0.23	1.16 (1.03-1.30)	0.01	1.00 (1.00-1.00)	0.21
T3	2.08 (1.74-2.48)	<0.01	1.00 (0.99-1.00)	0.14	1.95 (1.53-2.49)	<0.01	1.00 (0.99-1.00)	0.44
Race								
Non-Hispanic White	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Non-Hispanic Black	1.30 (1.15-1.48)	<0.01	1.00 (1.00-1.00)	0.72	0.97 (0.80-1.18)	0.79	1.00 (1.00-1.00)	0.94
Hispanic	0.94 (0.82-1.08)	0.39	1.00 (1.00-1.00)	0.41	0.87 (0.72-1.07)	0.18	1.00 (1.00-1.00)	0.71
Non-Hispanic Asian or Pacific Islander	0.71 (0.60-0.83)	<0.01	1.00 (1.00-1.00)	0.88	0.67 (0.53-0.86)	<0.01	1.00 (1.00-1.00)	0.61
Non-Hispanic American Indian/Alaskan Native	0.89 (0.46-1.71)	0.72	1.01 (1.00-1.02)	0.13	0.66 (0.25-1.70)	0.38	1.01 (1.00-1.02)	0.10
Unknown	0.24 (0.12-0.47)	<0.01	1.00 (1.00-1.01)	0.37	0.24 (0.07-0.79)	0.02	1.00 (0.98-1.01)	0.87
Treatment								
NDT	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Radiotherapy	0.30 (0.27-0.33)	<0.01	1.01 (1.00-1.01)	<0.01	0.44 (0.38-0.51)	<0.01	1.00 (1.00-1.01)	<0.01
RP	0.26 (0.16-0.43)	<0.01	1.01 (1.00-1.01)	0.04	0.19 (0.08-0.42)	<0.01	1.09 (1.00-1.02)	0.07

Supplementary Table 3. 36-month cox proportional hazards analysis with time-varying covariates of factors associated with overall survival

	HR at Baseline (95% CI)	*p*-value	Time-Varying Covariate in HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value	Time-Varying Covariate in aHR (95% CI)	*p*-value
Age (years)	1.21 (1.20-1.23)	<0.01	1.00 (1.00-1.00)	<0.01	1.13 (1.11-1.16)	<0.01	1.00 (1.00-1.00)	0.14
PSA (ng/mL)	1.02 (1.02-1.02)	<0.01	1.00 (1.00-1.00)	<0.01	1.01 (1.01-1.01)	<0.01	1.00 (1.00-1.00)	0.04
T Stage								
T1	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
T2	1.02 (0.94-1.11)	0.58	1.00 (1.00-1.00)	0.77	1.15 (1.02-1.30)	0.02	1.00 (0.99-1.00)	0.36
T3	0.92 (0.74-1.14)	0.52	1.01 (1.00-1.02)	0.04	1.01 (0.74-1.39)	0.93	1.01 (1.00-1.02)	0.13
Race								
Non-Hispanic White	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Non-Hispanic Black	1.29 (1.13-1.47)	<0.01	0.99 (0.99-1.00)	0.09	1.38 (1.14-1.68)	<0.01	0.99 (0.98-0.99)	<0.01
Hispanic	0.81 (0.69-0.94)	0.01	1.00 (0.99-1.01)	0.58	0.79 (0.63-1.00)	0.05	1.00 (0.99-1.01)	0.71
Non-Hispanic Asian or Pacific Islander	0.70 (0.58-0.83)	<0.01	1.01 (1.00-1.01)	0.11	0.77 (0.59-0.99)	0.04	1.00 (0.99-1.02)	0.39
Non-Hispanic American Indian/Alaskan Native	0.94 (0.46-1.93)	0.86	1.00 (0.97-1.04)	0.89	1.34 (0.55-3.23)	0.52	0.99 (0.95-1.03)	0.62
Unknown	0.34 (0.18-0.66)	<0.01	1.00 (0.97-1.03)	0.95	0.40 (0.13-1.20)	0.10	0.98 (0.93-1.03)	0.50
Treatment								
NDT	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Radiotherapy	0.17 (0.15-0.19)	<0.01	1.03 (1.03-1.04)	<0.01	0.28 (0.23-0.33)	<0.01	1.03 (1.02-1.03)	<0.01
RP	0.39 (0.24-0.63)	<0.01	1.00 (0.97-1.02)	0.78	0.47 (0.21-1.05)	0.07	0.99 (0.96-1.03)	0.75

Supplementary Table 4. 36-month cox proportional hazards analysis with time-varying covariates of factors associated with prostate cancer-specific survival

	HR at Baseline (95% CI)	*p*-value	Time-Varying Covariate in HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value	Time-Varying Covariate in aHR (95% CI)	*p*-value
Age (years)	1.21 (1.20-1.23)	<0.01	1.00 (1.00-1.00)	<0.01	1.12 (1.10-1.14)	<0.01	1.00 (1.00-1.00)	<0.01
PSA (ng/mL)	1.03 (1.02-1.03)	<0.01	1.00 (1.00-1.00)	<0.01	1.02 (1.02-1.02)	<0.01	1.00 (1.00-1.00)	<0.01
T Stage								
T1	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
T2	1.20 (1.10-1.30)	<0.01	1.00 (1.00-1.00)	0.23	1.16 (1.03-1.30)	0.01	1.00 (1.00-1.00)	0.21
T3	2.08 (1.74-2.48)	<0.01	1.00 (0.99-1.00)	0.14	1.95 (1.53)	2.49	1.00 (0.99-1.00)	0.44
Race								
Non-Hispanic White	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Non-Hispanic Black	1.30 (1.15-1.48)	<0.01	1.00 (1.00-1.00)	0.72	0.97 (0.80-1.18)	0.79	1.00 (1.00-1.00)	0.94
Hispanic	0.94 (0.82-1.08)	0.39	1.00 (1.00-1.00)	0.41	0.87 (0.72-1.07)	0.18	1.00 (1.00-1.00)	0.71
Non-Hispanic Asian or Pacific Islander	0.71 (0.60-0.83)	<0.01	1.00 (1.00-1.00)	0.88	0.67 (0.53-0.86)	<0.01	1.00 (1.00-1.00)	0.61
Non-Hispanic American Indian/Alaskan Native	0.89 (0.46-1.71)	0.72	1.01 (1.00-1.02)	0.13	0.66 (0.25-1.70)	0.38	1.01 (1.00-1.02)	0.10
Unknown	0.24 (0.12-0.47)	<0.01	1.00 (1.00-1.01)	0.37	0.24 (0.07-0.79)	0.02	1.00 (0.98-1.01)	0.87
Treatment								
NDT	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Radiotherapy	0.30 (0.27-0.33)	<0.01	1.01 (1.00-1.01)	<0.01	0.44 (0.38-0.51)	<0.01	1.00 (1.00-1.01)	<0.01
RP	0.26 (0.16-0.43)	<0.01	1.01 (1.00-1.01)	0.04	0.19 (0.08-0.42)	<0.01	1.01 (1.00-1.02)	0.07

Supplementary Table 5. 60-month cox proportional hazards analysis with time-varying covariates of factors associated with overall survival

	HR at Baseline (95% CI)	*p*-value	Time-Varying Covariate in HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value	Time-Varying Covariate in aHR (95% CI)	*p*-value
Age (years)	1.20 (1.19-1.21)	<0.01	1.00 (1.00-1.00)	<0.01	1.14 (1.12-1.15)	<0.01	1.00 (1.00-1.00)	<0.01
PSA (ng/mL)	1.02 (1.02-1.02)	<0.01	1.00 (1.00-1.00)	<0.01	1.01 (1.01-1.01)	<0.01	1.00 (1.00-1.00)	<0.01
T Stage								
T1	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
T2	1.03 (0.97-1.09)	0.37	1.00 (1.00-1.00)	0.92	0.36 (0.32-0.41)	<0.01	1.00 (1.00-1.00)	0.16
T3	1.01 (0.86-1.19)	0.86	1.00 (1.00-1.01)	0.21	0.58 (0.33-1.02)	0.06	1.00 (1.00-1.01)	0.14
Race								
Non-Hispanic White	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Non-Hispanic Black	1.19 (1.08-1.32)	<0.01	1.00 (1.00-1.00)	0.68	1.12 (0.97-1.30)	0.13	1.00 (0.99-1.00)	0.47
Hispanic	0.75 (0.67-0.85)	<0.01	1.00 (1.00-1.01)	0.17	0.71 (0.60-0.84)	<0.01	1.00 (1.00-1.00)	0.06
Non-Hispanic Asian or Pacific Islander	0.79 (0.69-0.91)	<0.01	1.00 (0.99-1.00)	0.31	0.88 (0.73-1.06)	0.18	1.00 (0.99-1.00)	0.09
Non-Hispanic American Indian/Alaskan Native	1.05 (0.61-1.80)	0.86	1.00 (0.98-1.01)	0.62	1.18 (0.59-2.34)	0.64	1.00 (0.98-1.02)	0.79
Unknown	0.32 (0.19-0.53)	<0.01	1.00 (0.99-1.02)	0.94	0.32 (0.13-0.76)	0.01	0.99 (0.97-1.02)	0.59
Treatment								
NDT	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Radiotherapy	0.22 (0.20-0.25)	<0.01	1.02 (1.02-1.02)	<0.01	0.36 (0.32-0.41)	<0.01	1.01 (1.01-1.02)	<0.01
RP	0.36 (0.24-0.52)	<0.01	1.00 (0.99-1.01)	0.72	0.58 (0.33-1.02)	0.06	0.99 (0.97-1.00)	0.13

Supplementary Table 6. 60-month cox proportional hazards analysis with time-varying covariates of factors associated with prostate cancer-specific survival

	HR at Baseline (95% CI)	*p*-value	Time-Varying Covariate in HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value	Time-Varying Covariate in aHR (95% CI)	*p*-value
Age (years)	1.24 (1.22-1.26)	<0.01	1.00 (1.00-1.00)	<0.01	1.14 (1.10-1.17)	<0.01	1.00 (1.00-1.00)	0.01
PSA (ng/mL)	1.03 (1.03-1.03)	<0.01	1.00 (1.00-1.00)	<0.01	1.02 (1.02-1.03)	<0.01	1.00 (1.00-1.00)	<0.01
T Stage								
T1	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
T2	1.21 (1.07-1.38)	<0.01	1.00 (1.00-1.00)	0.86	1.18 (0.98-1.42)	0.08	1.00 (1.00-1.01)	0.78
T3	1.85 (1.43-2.40)	<0.01	1.00 (1.00-1.01)	0.47	1.58 (1.09-2.31)	0.02	1.01 (1.00-1.02)	0.19
Race								
Non-Hispanic White	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Non-Hispanic Black	1.30 (1.08-1.56)	0.01	1.00 (0.99-1.01)	0.98	0.85 (0.62-1.16)	0.30	1.00 (1.00-1.01)	0.31
Hispanic	0.95 (0.77-1.17)	0.60	1.00 (0.99-1.01)	0.73	0.85 (0.62-1.17)	0.32	1.00 (0.99-1.01)	0.75
Non-Hispanic Asian or Pacific Islander	0.82 (0.64-1.06)	0.13	0.99 (0.99-1.00)	0.16	0.86 (0.59-1.26)	0.44	0.99 (0.98-1.00)	0.24
Non-Hispanic American Indian/Alaskan Native	1.42 (0.57-3.51)	0.45	0.99 (0.96-1.02)	0.56	1.03 (0.28-3.78)	0.96	1.00 (0.96-1.04)	1.00
Unknown	0.05 (0.01-0.24)	<0.01	1.05 (1.01-1.09)	0.01	0.01 (0.00-0.62)	0.03	1.07 (0.99-1.16)	0.08
Treatment								
NDT	1.00 (Referent)		1.00 (Referent)		1.00 (Referent)		1.00 (Referent)	
Radiotherapy	0.19 (0.16-0.23)	<0.01	1.02 (1.01-1.02)	<0.01	0.32 (0.24-0.41)	<0.01	1.01 (1.00-1.02)	<0.01
RP	0.25 (0.11-0.56)	<0.01	1.01 (0.98-1.03)	0.68	0.24 (0.05-1.18)	0.08	0.99 (0.95-1.04)	0.76