The Prognosis of Radical Prostatectomy, External Beam Radiotherapy plus Brachytherapy, and External Beam Radiotherapy Alone for Patients above 70 Years with Very High-Risk Prostate Cancer: A Population-Matched Study

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Keywords

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Abstract

Objective: The aim of this study was to evaluate the survival outcomes of radical prostatectomy (RP), external beam radiotherapy plus brachytherapy (EBRT + BT), and EBRT alone among elderly men (aged 70 years and above) with very high-risk (VHR) prostate cancer (PCa). **Methods:** We identified elderly men diagnosed with VHR PCa between 2004 and 2015 in the Surveillance, Epidemiology, and End Results database. The propensity score-matching method was adopted to balance the covariates and generate new cohorts. Kaplan-Meier and Cox analyses were conducted to build up survival curves and evaluate the overall survival (OS) and PCa-specific survival (PCSS) outcomes. **Results:** A total of 9,818 patients were identified. Of them, 5,839 were in the EBRT group, 725 in the EBRT + BT group, and 3,254 in the RP group. The survival curves of the overall cohort showed that

RP was associated with the best OS, followed by EBRT + BT and EBRT ($p < 0.001$). As for the PCSS, RP shared similar outcomes with EBRT + BT (hazard ratio [HR]: 1.25 [0.93–1.69], $p = 0.175$). EBRT was associated with significantly worse PCSS than both RP (HR: 1.88, 95% confidence interval [95% CI] [1.64–2.15], $p < 0.001$) and EBRT + BT (HR: 1.48, 95% CI [1.19–1.85], $p = 0.002$). In the matched cohorts, RP presented better OS (HR: 1.41, 95% CI [1.07–1.86], $p = 0.041$) and similar PCSS with EBRT + BT (HR: 1.50, 95% CI [0.91–2.47], $p = 0.12$). RP was associated with significantly better OS and PCSS outcomes than EBRT alone (OS HR: 1.58, 95% CI [1.59–2.12], $p < 0.001$; PCSS HR: 2.08 [1.60–2.72], $p < 0.001$). EBRT + BT also had significantly better OS and PCSS outcomes than EBRT alone (OS HR: 1.33, 95% CI [1.11–1.60], $p < 0.001$; PCSS HR: 1.57 [1.13–2.19], $p = 0.003$). **Conclusions:** For patients above 70 years with VHR PCa, RP was associated with better OS and similar PCSS than EBRT + BT. Both RP and EBRT + BT have better OS and PCSS than EBRT alone.

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Introduction

Prostate cancer (PCa) ranks first in the common malignancy among elderly men and is in the second position in male cancer-related deaths [1]. It poses a serious threat to patient's lives and health [2, 3]. Among all nonmetastatic PCa, very high-risk (VHR) PCa is particularly aggressive and associated with the worst prognosis for the patients. According to the guideline of the National Comprehensive Cancer Network, VHR PCa was defined as T3b–4, grade group 5, or >4 core positive grade group 4–5 [4]. Due to its aggressive characteristics and the tendency to relapse, it has brought certain challenges to the treatment of patients with VHR PCa, especially for elderly men.

Currently, the common radical treatments for non-metastatic PCa include radical prostatectomy (RP), external beam radiotherapy (EBRT), and interstitial brachytherapy (BT) [4]. Their benefits are still inclusive in patients with diseases of different stages. Even though no specific conclusion has been drawn on whether the combination of EBRT + BT had superior survival outcomes than EBRT alone [5–7], this combination is still expected to provide some extra benefits for PCa patients [8–12]. In previous studies, it was reported that RP was associated with similar or better survival outcomes than EBRT + BT for men with high-risk PCa [13–15].

As age is an important factor that influences the choice of treatments and prognoses [16], the outcomes of treatments in all age patients might not be suitable for elderly men, especially the surgical method. Considering the life expectancy and physical conditions of men aging 70 and older, the advantages of RP might not be as obvious as it was in other age-groups. In our study, we aimed to evaluate the survival outcomes of RP, EBRT + BT, and EBRT alone in elderly patients over 70 with VHR PCa.

Materials and Methods

Data Source

All of the data in this study were derived from the Surveillance, Epidemiology, and End Results (SEER) database. Elderly patients (70 years and older) diagnosed with nonmetastatic (T1–4NxM0) VHR PCa from January 1, 2004, to December 31, 2015, were retrospectively identified.

Inclusion and Exclusion Criteria

Patients were considered eligible if they met the following criteria: (1) patients were diagnosed with VHR PCa according to the guideline of the National Comprehensive Cancer Network. (2) Patients were over 70 at the time of diagnosis. (3) The main treatments were RP, EBRT + BT, and EBRT alone, regardless of the antiandro-

gen therapy. The following criteria were used for data exclusion: (1) multiple tumors; (2) important information such as PSA, GS, TNM stages, and follow-up time was incomplete or missing; and (3) the survival status at the end of the follow-up was unclear.

Variables and Main Outcomes

We collected basic patient's characteristic from the database. The variables included age at diagnosis, race (white, black, and other races), marital status (married, unmarried, and divorced or separated), the T stage (T1, T2a–b, T2c–3a, and T3b–4), the N stage (N0, N1, and Nx), the PSA level (<4.0 ng/mL, 4.0–10.0 ng/mL, 10.0–20.0 ng/mL, 20.0–40.0 ng/mL, and >40.0 ng/mL), the Gleason score (≤ 7 , 8, and 9–10), the living status (alive or dead), and the cancer-specific living status (alive, dead for other reasons, and dead for PCa). The overall survival (OS) and PCa-specific survival (PCSS) were regarded as main outcomes.

Statistical Analysis

The χ^2 test was adopted to assess the differences among RP, EBRT, and EBRT + BT groups. Propensity score matching was conducted to balance the covariates and generated new matched cohorts. Kaplan-Meier and Cox analyses were performed in both overall and matched cohorts. The effects on survival and prognoses were evaluated by the hazard ratio (HR) with 95% confidence interval (95% CI). All of the statistical operations above were conducted with the software SPSS 25 and Graph Prism 7.0. $p < 0.05$ was considered statistically significant.

Results

Patient Characteristics

A total of 9,818 patients with VHR PCa were identified. The median age was 74 (72–77) years old. Of them, 3,254 were in the RP group, 5,839 patients were in the EBRT group, and 725 in the EBRT + BT group. The median survival time of the overall cohort was 56.2 (30.6–87.8) months. After propensity score matching, 1,377 patients were left in either the RP or EBRT group in the comparison of RP versus EBRT, 725 patients were in either group in EBRT + BT versus EBRT. In RP versus EBRT + BT group, 334 patients were in the RP group and 408 were in the EBRT + BT group. The baseline characteristics of included patients in the overall cohort and matched cohort were presented in Tables 1 and 2, respectively.

Survival Outcomes

Survival Outcomes of the Overall Cohort

The OS curve of the overall cohort revealed that RP was associated with the best OS among all therapies, followed by EBRT + BT and EBRT. Significant differences were detected among 3 groups. With RP as the reference, the HRs of EBRT + BT and EBRT were 1.54 (95% CI [1.30–1.82], $p < 0.001$) and 2.18 (95% CI [2.02–2.35], $p <$

Table 1. Baseline characteristics of included patients in the overall cohort

Characteristics	Total	RP	EBRT + BT	EBRT	<i>p</i> value
<i>N</i>	9,818	3,254	725	5,839	
Age, years					
Median (IQR)	74 (72–77)	74 (71–74)	75 (72–78)	76 (73–79)	
Age, <i>n</i> (%)					
70–75 years	5,983 (60.9)	2,707 (83.2)	407 (56.1)	2,869 (49.1)	<0.001
76–80 years	2,550 (26)	468 (14.4)	227 (31.3)	1,855 (31.8)	
>80 years	1,285 (13.1)	79 (2.4)	91 (12.6)	1,115 (19.1)	
Race, <i>n</i> (%)					
White	8,119 (82.7)	2,779 (85.4)	595 (82.1)	4,745 (81.3)	<0.001
Black	853 (8.7)	211 (6.5)	45 (6.2)	597 (10.2)	
Others	754 (7.7)	244 (7.5)	79 (10.9)	431 (7.4)	
Unclear	92 (0.9)	20 (0.6)	6 (0.8)	66 (1.1)	
Marriage, <i>n</i> (%)					
Married	7,224 (73.6)	2,562 (78.7)	538 (74.2)	4,124 (70.6)	<0.001
Unmarried	638 (6.5)	194 (6)	42 (5.8)	402 (6.9)	
Separated	1,351 (13.8)	350 (10.8)	98 (13.5)	903 (15.5)	
Unclear	605 (6.2)	148 (4.5)	47 (6.5)	410 (7)	
T stage, <i>n</i> (%)					
T1	2,636 (26.8)	3 (0.1)	305 (42.1)	2,328 (39.9)	<0.001
T2a–b	2,288 (23.3)	242 (7.4)	225 (31)	1,821 (31.2)	
T2c–3a	1,902 (19.4)	966 (29.7)	105 (14.5)	831 (14.2)	
T3b–4	2,992 (30.5)	2,043 (62.8)	90 (12.4)	859 (14.7)	
N stage, <i>n</i> (%)					
N0	9,069 (92.4)	2,811 (86.4)	707 (97.5)	5,551 (95.1)	<0.001
N1	640 (6.5)	436 (13.4)	9 (1.2)	195 (3.3)	
Nx	109 (1.1)	7 (0.2)	9 (1.2)	93 (1.6)	
PSA, <i>n</i> (%)					
<4.0 ng/mL	696 (7.1)	264 (8.1)	53 (7.3)	379 (6.5)	<0.001
4.0–10.0 ng/mL	4,673 (47.6)	1,837 (56.5)	355 (49)	2,481 (42.5)	
10.0–20.0 ng/mL	2,615 (26.6)	819 (25.2)	183 (25.2)	1,613 (27.6)	
20.0–40.0 ng/mL	1,116 (11.4)	237 (7.3)	85 (11.7)	794 (13.6)	
>40.0 ng/mL	718 (7.3)	97 (3)	49 (6.8)	572 (9.8)	
GS, <i>n</i> (%)					
≤7	1,325 (13.5)	993 (30.5)	32 (4.4)	300 (5.1)	<0.001
8	703 (7.2)	415 (12.8)	26 (3.6)	262 (4.5)	
9–10	7,790	1,846	667 (92)	5,277 (90.4)	
Survival time, months					
Median (IQR)	56.2 (30.6–87.8)	56 (30–89)	70 (40–99)	55 (30–85)	

IQR, interquartile range; GS, Gleason score; PSA, prostate-specific antigen; RP, radical prostatectomy; EBRT, external beam radiotherapy; EBRT + BT, external beam radiotherapy + brachytherapy.

0.001), respectively. In contrast with EBRT alone, the addition of BT apparently increased the survival outcomes (HR: 0.71, 95% CI [0.63–0.80], $p < 0.001$). These results are shown in Figure 1a.

As for the PCSS results of the overall cohort, there was no significant difference between RP and EBRT + BT (HR: 1.25 [0.93–1.69], $p = 0.175$). EBRT was associated with worse PCSS outcomes than either RP (HR: 1.88 [1.64–2.15], $p < 0.001$) or EBRT + BT (HR: 1.48 [1.19–1.85], $p = 0.002$).

It was reported in our study that the 5-year PCSS of RP, EBRT + BT, and EBRT were 95.2% (95.98%–94.42%), 94% (95.96%–92.04%), and 90.9% (91.88%–89.92%), separately. As for the 10-year PCSS, 86.2% (88.36%–84.04%) was for RP, 84.7% (88.62%–80.78%) for EBRT + RT, and 77.6% (79.56%–75.64%) for EBRT. As for the survival time, the respective survival months of RP, EBRT + BT, and EBRT were 143.08 ± 1.48 months, 140.31 ± 3.44 months, and 134.4 ± 1.51 months, individually.

Table 2. Baseline characteristics of patients in propensity score-matched cohorts

Characteristics	RP	EBRT + BT	<i>p</i> value	RP	EBRT	<i>p</i> value	EBRT + BT	EBRT	<i>p</i> value
<i>N</i>	334	408		1,377	1,377		725	725	
Age, years									
Median (IQR)	75 (72–78)	74 (72–77)		73 (71–75)	72 (71–74)		75 (73–78)	75 (73–78)	
Age, <i>n</i> (%)									
70–75 years	208 (62.3)	228 (55.9)	0.158	963 (69.9)	964 (70)	0.673	407 (56.1)	426 (58.8)	0.600
76–80 years	92 (27.5)	124 (30.4)		356 (25.9)	346 (25.1)		227 (31.3)	213 (29.4)	
>80 years	34 (10.2)	56 (13.7)		58 (4.2)	67 (4.9)		91 (12.6)	86 (11.9)	
Race, <i>n</i> (%)									
White	293 (87.7)	349 (85.5)	0.671	1,188 (86.3)	1,199 (87.1)	0.185	595 (82.1)	591 (81.5)	0.795
Black	12 (3.6)	19 (4.7)		87 (6.3)	86 (6.2)		45 (6.2)	54 (7.4)	
Others	26 (7.8)	38 (9.3)		89 (6.5)	88 (6.4)		79 (10.9)	75 (10.3)	
Unclear	3 (0.9)	2 (0.5)		13 (0.9)	4 (0.3)		6 (0.8)	5 (0.7)	
Marriage, <i>n</i> (%)									
Married	252 (75.4)	310 (76)	0.524	1,078 (78.3)	1,076 (78.1)	0.813	538 (74.2)	532 (73.4)	0.984
Unmarried	19 (5.7)	23 (5.6)		83 (6)	82 (6)		42 (5.8)	42 (5.8)	
Separated	36 (10.8)	52 (12.7)		172 (12.5)	166 (12.1)		98 (13.5)	102 (14.1)	
Unclear	27 (8.1)	23 (5.6)		44 (3.2)	53 (3.8)		47 (6.5)	49 (6.8)	
T stage, <i>n</i> (%)									
T1	5 (1.5)	17 (4.2)	0.059	17 (1.2)	5 (0.4)		305 (42.1)	322 (44.4)	0.355
T2a–b	145 (43.4)	198 (48.5)		258 (18.7)	264 (19.2)		225 (31)	197 (27.2)	
T2c–3a	88 (26.3)	104 (25.5)		468 (34)	484 (35.1)		105 (14.5)	119 (16.4)	
T3b–4	96 (28.7)	89 (21.8)		634 (46)	624 (45.3)		90 (12.4)	87 (12)	
N stage, <i>n</i> (%)									
N0	321 (96.1)	395 (96.8)	0.606	1,277 (92.7)	1,277 (92.7)	0.077	707 (97.5)	701 (96.7)	0.621
N1	10 (3)	8 (2)		92 (6.4)	98 (7.1)		9 (1.2)	11 (1.5)	
Nx	3 (0.9)	5 (1.2)		9 (0.9)	2 (0.1)		9 (1.2)	13 (1.8)	
PSA, <i>n</i> (%)									
<4.0 ng/mL	34 (10.2)	32 (7.8)	0.691	109 (7.9)	99 (7.2)	0.969	53 (7.3)	50 (6.9)	0.841
4.0–10.0 ng/mL	167 (50)	198 (48.5)		652 (47.3)	656 (47.6)		355 (49)	358 (49.4)	
10.0–20.0 ng/mL	81 (24.3)	106 (26)		361 (26.2)	366 (26.6)		183 (25.2)	174 (24)	
20.0–40.0 ng/mL	32 (9.6)	48 (11.8)		174 (12.6)	176 (12.8)		85 (11.7)	98 (13.5)	
>40.0 ng/mL	20 (6)	24 (5.9)		81 (5.9)	80 (5.8)		49 (6.8)	45 (6.2)	
GS, <i>n</i> (%)									
≤7	41 (12.3)	32 (7.8)	0.119	259 (18.8)	259 (18.8)	0.914	32 (4.4)	34 (4.7)	0.960
8	22 (6.6)	25 (6.1)		162 (11.8)	155 (11.3)		26 (3.6)	25 (3.4)	
9–10	271 (81.1)	351 (86)		956 (69.4)	963 (69.9)		667 (92)	666 (91.9)	
Survival time, months									
Median (IQR)	67 (37–99)	55 (30–92)		60 (33–93)	55 (32–85)		70 (39–99)	53 (29–82)	

EBRT, external beam radiotherapy; EBRT + BT, external beam radiotherapy + brachytherapy; RP, radical prostatectomy; IQR, interquartile range; PSA, prostate-specific antigen; GS, Gleason score.

Survival Outcomes of the Matched Cohort

In the matched cohort of RP versus EBRT + BT, RP was associated with significantly better OS than EBRT + BT (HR: 1.41, 95% CI [1.07–1.86], $p = 0.041$, Fig. 2a1) but shared similar PCSS with EBRT + BT (HR: 1.50, 95% CI [0.91–2.47], $p = 0.12$, Fig. 2a2). The mean survival time of RP and EBRT + BT were 142.67 ± 5.18 and 137.13 ± 4.67 months.

In the matched cohort of RP versus EBRT, the survival curves revealed that RP had significantly better OS and

PCSS than EBRT (OS HR: 1.85 [1.59–2.12], $p < 0.001$, Fig. 2b1; PCSS HR: 2.08 (1.60–2.72), $p < 0.001$, Fig. 2b2). The mean survival time of RP and EBRT were 144.578 ± 2.45 and 135.06 ± 2.89 months.

In the comparison of EBRT + BT versus EBRT alone, EBRT + BT had remarkably better OS, as well as PCSS, than EBRT (OS HR: 1.33 [1.11–1.60], $p < 0.0001$, Fig. 2c1; PCSS HR: 1.57, 95% CI [1.13–2.19], $p = 0.003$, Fig. 2c1). The mean survival time of EBRT + BT and EBRT were 140.31 ± 3.44 and 133.75 ± 4.41 months.

Fig. 1. OS and PCSS curves of RP, EBRT alone, and EBRT + BT for patients aging 70 years and older with VHR PCa in the overall cohort. **a** The OS curve of RP, EBRT + BT, and EBRT alone in the overall cohort. **b** The PCSS curve of RP, EBRT + BT, and EBRT alone in the overall cohort. RP, radical prostatectomy; EBRT, external beam radiotherapy; EBRT + BT, external beam radiotherapy + brachytherapy; VHR, very high-risk; PCa, prostate cancer; PCSS, prostate cancer-specific survival; OS, overall survival.

Multivariate Cox Analysis for OS and PCSS

The results of Cox analyses of both OS and PCSS among the overall cohorts were presented in Table 3. With RP as the reference, the HRs and 95% CIs of OS of EBRT + BT and EBRT were 1.41 (1.19–1.66) and 1.80 (1.62–2.01), individually. The HRs and 95% CIs of PCSS of EBRT + BT and EBRT alone were 1.22 (1.03–1.88) and 1.81 (1.57–2.29), respectively.

The Cox results of both OS and PCSS among the matched cohorts were also shown in Table 3. With RP as the reference, the adjusted HR and 95% CI of EBRT + BT were 1.37 (1.02–1.84) in OS and 1.51 (0.88–2.59) in PCSS. The adjusted HR and 95% CI of OS and PCSS of EBRT were 1.89 (1.61–2.22) and 2.17 (1.63–2.90), respectively. In the contrast between EBRT + BT and EBRT alone, with EBRT + BT as the reference, the adjusted HR and 95% CI of EBRT for OS and PCSS were 1.35 (1.12–1.62) and 1.61 (1.15–2.25), individually.

Discussion

Risk stratification in patients with newly diagnosed PCa allows physicians to choose the optimal treatment strategy for each patient [17–19]. However, even within the same group of patients with high-risk PCa, there remains significant heterogeneity in outcomes [20–22]. While most high-risk patients respond favorably to local

definitive therapy, a subgroup of patients may yet progress to worse conditions and succumb to their cancer [20, 23, 24]. Elderly men with VHR PCa are those who need special consideration to choose their treatments. Offering optimal therapies to these patients is important and somewhat challenging. Although several studies had compared the prognosis of these therapies in patients with high-risk diseases, few studies had evaluated their survival differences in elderly men with VHR PCa. In our study, we assessed the OS and PCSS of patients over 70 with VHR PCa after RP, EBRT + BT, or EBRT. The analyzed results revealed that RP was associated with better OS and similar PCSS than EBRT + BT. Both RP and EBRT + BT had significantly better OS and PCSS than EBRT alone.

In the comparison of RP and EBRT + BT, several studies have analyzed the survival outcomes of patients in different PCa groups. Berg et al. [14] included young (≤ 65 years) and healthy men with localized high-risk PCa in his study. They reported that EBRT + BT was associated with a higher risk of all-cause mortality compared with RP with an HR and 95 % CI of 1.22 (1.05–1.43). Ennis et al. [13] analyzed the survival outcomes of patients of all age-groups with localized high-risk PCa. They found no statistically significant difference between RP and EBRT + BT. Our analyzed results showed the better OS and similar PCSS of RP than EBRT + BT in elderly men with VHR PCa. Our results showed that age did not seem to have enough influence on the survival outcomes. Muralidhar et al. [25] re-

Fig. 2. OS and PCSS curves of RP, EBRT alone, and EBRT + BT for patients aging 70 and older with VHR PCa in the matched cohorts. **a1** The OS curve of RP and EBRT + BT in the matched cohort. **a2** The PCSS curve of RP and EBRT + BT in the matched cohort. **b1** The OS curve of RP and EBRT in the matched cohort. **b2** The PCSS curve of RP and EBRT in the matched cohort. **c1** The OS

curve of EBRT + BT and EBRT alone in the matched cohort. **c2** The PCSS curve of EBRT + BT and EBRT alone in the matched cohort. RP, radical prostatectomy; EBRT, external beam radiotherapy; EBRT + BT, external beam radiotherapy + brachytherapy; VHR, very high-risk; PCa, prostate cancer; PCSS, prostate cancer-specific survival; OS, overall survival.

Table 3. Multivariate Cox analysis for PCSS

	OS			Cancer-specific survival		
	HR	95% CI	<i>p</i> value	HR	95% CI	<i>p</i> value
HRs (95% CIs)						
RP	1		Ref	1		Ref
EBRT + BT	1.41	(1.19–1.66)	<0.001	1.22	(1.03–1.88)	0.033
EBRT	1.80	(1.62–2.01)	<0.001	1.81	(1.57–2.29)	<0.001
Adjusted HRs (95% CIs)						
EBRT + BT	1		Ref			0.006
EBRT	1.35	(1.12–1.62)	0.002	1.61	(1.15–2.25)	
Adjusted HRs (95% CIs)						
RP	1		Ref	1		Ref
EBRT + BT	1.37	(1.02–1.84)	0.036	1.51	(0.88–2.59)	0.135
Adjusted HRs (95% CIs)						
RP	1		Ref	1		Ref
EBRT	1.89	(1.61–2.22)	<0.001	2.17	(1.63–2.90)	<0.001

EBRT, external beam radiotherapy; EBRT + BT, external beam radiotherapy + brachytherapy; RP, radical prostatectomy; HR, hazard ratio; Ref, reference; 95% CI, 95% confidence interval; PCSS, prostate cancer-specific survival; OS, overall survival.

ported that the 5-year OS and PCSS of multimodality surgical therapy were equivalent to EBRT + BT in men with Gleason score of 9–10 PCa. In their analysis, they found that there was no significant correlation between the patient's age (65 and above vs. <65) and treatment modality. Of course, there are different opinions. Yin et al. [26] analyzed prognostic effects of surgery, EBRT, and EBRT + BT in high-risk localized PCa. They found that EBRT + BT had a significantly better PCSS than surgery or EBRT alone in all age-group patients. EBRT ± BT was associated with superior CSS than surgical therapy in patients above 65 years. Therefore, the prognosis of RP, EBRT + BT, and EBRT for elderly men with VHR PCa should be reevaluated carefully by high-quality studies in the future.

As for the contrast between RP and EBRT, the results in our study revealed the RP's advantages over EBRT in both OS and PCSS. This finding was consistent with several former retrospective studies. Zelefsky et al. [27] reported that RP had a lower risk of metastatic progression and PCa-specific death than EBRT among patients with high-risk disease. The 8-year probability of freedom from metastatic progression was 97% for RP patients and 93% for EBRT patients. Boorjian et al. [28] analyzed 1,238 patients with localized HR/VHR PCa who underwent RP and 609 patients receiving EBRT. The 10-year PCSS rate was 92% and 88%, respectively ($p = 0.06$). Bandini et al. [29] revealed that the 10-year PCa-specific mortality in the RP and EBRT group were 4.3% and 6.1%, respectively, among old patients (>75 years) with localized PCa.

The prognosis of EBRT + BT versus EBRT alone seemed to be inconclusive. Some studies reported the addition of BT did not provide enough survival benefit than EBRT alone [5, 11]. Several trials revealed that EBRT + BT was associated with a better biochemical recurrence-free survival benefit than EBRT alone [9, 30–32]. Wedde et al. [33] analyzed the 10-year PCSS and OS in high-risk patients treated with EBRT plus high-dose-rate BT compared to EBRT alone. It was reported that EBRT and high-dose-rate BT was found to give a 3.6-fold decrease in PCa-specific mortality and a 1.6-fold decrease in overall mortality. It was likely that the addition of BT offered improved local control over EBRT, which may prevent a “second wave” of metastases [34]. These probably explain the identification of a significant association between EBRT + BT and improved prognostic outcomes.

Even though our study analyzed a large sample of patients, certain limitations still existed in our study. The limitations were as follows: (1) our study was a retrospective analysis, where some confounders and risk biases were unavoidable. It may make a difference and cause interferences with the results. (2) Even though we targeted men aged 70 years and older in our study, the large percentage were in 70–75 years old subgroup and only a small proportion of patients were in ≥80 years subgroup. Therefore, our results might not be suitable for all patients aging 70 and above. (3) Limited by the data characteristic, we only analyzed the survival outcomes. Many other important outcomes were not analyzed, such as biochemical re-

currence-free survival. (4) Even though we found surgical therapy was associated with superior survival outcomes, this result does not apply to all patients over 70 years. Because the patients in the RP treatment had been selected. Only the patients with good health conditions preoperatively (such as no serious chronic diseases, good food intake and proper body mass index, and better tumor condition). Therefore, our analyzed results might be only suitable for these selected patients. (5) Our study only focused on the analysis of prognostic survival, some additional important clinical outcomes were not taken into account, such as adverse events and quality of life.

Conclusion

For men over 70 with VHR PCa, RP and EBRT + BT had similar PCSS outcomes. Both RP and EBRT + BT were associated with better OS and PCSS than EBRT alone. However, with the limitations of our study, high-quality studies are needed for future evaluations.

Statement of Ethics

Ethics approval and consent to participate: all data are derived from the SEER database that is open-access for public. All patient labels have been removed in the database. Therefore, this study was exempted for the ethics approval.

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Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author Contributions

Pan Song, Mengxuan Shu, and Qiang Dong conceived of the presented idea, conducted all statistical analyses, wrote the manuscript, and approved the final manuscript. Luchen Yang, Xiaoyu Di, Peiwen Liu, Zhenghuan Liu, and Jing Zhou participated in data curation, visualization, writing review, and editing during the process of review and approved the final version of the manuscript.

Data Availability Statement

The data for constructing model were obtained from the SEER database.

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