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Survival rates with external beam radiation therapy in newly diagnosed elderly metastatic prostate cancer patients

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Abstract

Background: The survival benefit of primary external beam radiation therapy (EBRT) has never been formally tested in elderly men who were newly diagnosed with metastatic prostate cancer (mPCa). We hypothesized that elderly patients may not benefit of EBRT to the extent as younger newly diagnosed mPCa patients, due to shorter life expectancy.

Methods: We relied on Surveillance, Epidemiology and End Results (2004–2016) to identify elderly newly diagnosed mPCa patients, aged >75 years. Kaplan–Meier, univariable and multivariable Cox regression models, as well as Competing Risks Regression models tested the effect of EBRT versus no EBRT on overall mortality (OM) and cancer-specific mortality (CSM).

Results: Of 6556 patients, 1105 received EBRT (16.9%). M1b stage was predominant in both EBRT ($n = 823$; 74.5%) and no EBRT ($n = 3908$; 71.7%, $p = 0.06$) groups, followed by M1c ($n = 211$; 19.1% vs. $n = 1042$; 19.1%, $p = 1$) and M1a ($n = 29$; 2.6% vs. $n = 268$; 4.9%, $p < 0.01$). Median overall survival (OS) was 23 months for EBRT and 23 months for no EBRT (hazard ratio [HR]: 0.97, $p = 0.6$). Similarly, median cancer-specific survival (CSS) was 29 months for EBRT versus 30 months for no EBRT (HR: 1.04, $p = 0.4$). After additional multivariable adjustment, EBRT was not associated with lower OM or lower CSM in the entire cohort, as well as after stratification for M1b and M1c substages.

Conclusions: In elderly men who were newly diagnosed with mPCa, EBRT does not affect OS or CSS. In consequence, our findings question the added value of local EBRT in elderly newly diagnosed mPCa patients.

KEYWORDS

cancer-specific survival, EBRT, elderly, local treatment, overall survival

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1 | INTRODUCTION

The current National Comprehensive Cancer Network (NCCN) and European Association of Urology (EAU) guidelines recommend local treatment including external beam radiation therapy (EBRT) in primary newly diagnosed, low volume metastatic prostate cancer (mPCa) patients, regardless of patient age.[1,2] These recommendations are predominately based on the STAMPEDE trial that enrolled 2061 patients.[3] Of those, only 12.5% were aged 73 years or older. In consequence, data supporting the use of EBRT in elderly (75 years and older) are not excessively robust. The uncertainty about EBRT benefits in elderly patients is further compounded by the HORRAD trial that failed to confirm the survival benefit of EBRT, not only in elderly but in all newly diagnosed mPCa patients.[4] Five recent retrospective large-scale or institutional studies also addressed EBRT in newly diagnosed mPCa patients.[5–10] However, stratification between elderly versus others was not made. In consequence, there is uncertainty about the added benefit of EBRT to systematic therapy in elderly men who were newly diagnosed with mPCa.[11]

To address this uncertainty, we tested whether EBRT is associated with lower overall survival (OS) and/or lowers cancer-specific mortality (CSM) in elderly men (>75 years) who were newly diagnosed with mPCa. The rationale for using the >75 years of age cut-off was based on the United States Social Security Life Tables that indicate less than 10-year life expectancy in those individuals, even when mPCa does not represent a competing cause of mortality. We tested our hypothesis within the Surveillance, Epidemiology and End Results (SEER) database 2004–2016.

2 | MATERIALS AND METHODS

2.1 | Study population

The current SEER database samples approximately 35% of the United States population and approximates it in demographic composition and cancer incidence. Within SEER database (2004–2016), we identified patients >75 years old with newly diagnosed metastatic, histologically confirmed adenocarcinoma of the prostate (International Classification of Disease for Oncology [ICD-O-3] code 8140 site code C61.9). Autopsy cases or cases based on death certificates and non-primary prostate cancers were excluded. Elderly patients were defined as those aged >75 years. The predictor of interest consisted of EBRT versus no EBRT. Stratification of overall mortality (OM) and CSM was performed according to M1 substages, in accordance with TNM classification[12]: M1a versus M1b versus M1c versus M1x. These selection criteria resulted in a cohort of 6,556 elderly men who were newly diagnosed with mPCa patients.

2.2 | Statistical analyses

Descriptive statistics included frequencies and proportions for categorical variables. Means, medians, and interquartile ranges (IQR) were reported for continuously coded variables. The χ^2 tested the statistical significance in proportions' differences. The *t* test and Kruskal–Wallis test examined the statistical significance of means' and distributions' differences.

Kaplan–Meier and univariable, as well as multivariable Cox regression models after adjustment for covariates (PSA [prostate-specific antigen], age, Grade Group at biopsy, cT-stage, cN-stage, and race/ethnicity) tested the effect of EBRT in elderly men who were newly diagnosed with mPCa patients on OM and CSM.

Finally, to adjust for the potential confounding effect of other cause mortality (OCM) we also relied on competing risks regression (CRR). Here, the endpoint of interest consisted of CSM after adjustment for OCM. Additionally, propensity score matching was performed for comparisons between EBRT versus no EBRT. 1:4 matching relied on exact matching for age at diagnosis, PSA, M-stage (M1a vs. M1b vs. M1c vs. M1x) T-stage (T1-2 vs. T3-4), cN-stage (cN0 vs. cN1 vs. cNx), and Grade Groups (I vs. II vs. III, IV vs. V vs. unknown). Additional multivariable adjustment was performed for administration of chemotherapy and race/ethnicity.[13,14] All tests were two-sided with a level of significance set at $p < 0.05$ and R software environment for statistical computing and graphics (version 3.4.3) was used for all analyses.

3 | RESULTS

3.1 | Descriptive characteristics of the study population

Of 6556 elderly men who were newly diagnosed with mPCa (Tables 1), 1105 received EBRT (16.9%) versus 5451 no EBRT (83.1%). Median age at diagnosis was 81 years (IQR: 78–84) for EBRT versus 82 years (IQR: 78–85) for no EBRT ($p < 0.01$). Moreover, median PSA was 81.5 ng/ml (IQR: 22.6–98.0) in the EBRT versus 98 ng/ml (IQR: 29.5–98.0) in the no EBRT group ($p < 0.01$). M1b stage predominated in both EBRT ($n = 823$; 74.5%) and no EBRT ($n = 3908$; 71.7%, $p = 0.06$) groups, followed by M1c ($n = 211$; 19.1% vs. $n = 1042$; 19.1%, $p = 1$) and M1a ($n = 29$; 2.6% vs. $n = 268$; 4.9%, $p < 0.01$). No clinically meaningful or significant differences were recorded for cT-stage, cN-stage, Grade Group at biopsy or chemotherapy administration or regional differences. Median follow up was 15 months in EBRT versus 18 months in the no EBRT group ($p < 0.01$).

3.2 | OM and cancer-specific mortality in the overall cohort

In the overall cohort, Kaplan–Meier analyses revealed no clinically meaningful or statistically significant differences in OS or CSS values between EBRT versus no EBRT in elderly men who were newly diagnosed with mPCa. Median OS (Figure 1A) was 23 months for EBRT and 23 months for no EBRT patients (hazard ratio [HR]: 0.97,

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TABLE 1 Descriptive characteristics of 6556 elderly men who were newly diagnosed with metastatic prostate cancer patients, stratified according to external beam radiotherapy (EBRT) versus no EBRT, identified within the Surveillance, Epidemiology, and End Results database from 2004 to 2016

Variable		Overall *n* = 6556	EBRT *n* = 1105 (16.9%)	No EBRT *n* = 5451 (83.1%)	*p* value
Age at diagnosis	Median (IQR)	82 (78–85)	81 (78–84)	82 (78–85)	<0.001
Year of diagnosis	Median (IQR)	2011 (2007–2014)	2011 (2007–2014)	2010 (2007–2014)	<0.001
Follow up in months	Median (IQR)	17 (7–34)	15 (7–32)	18 (7–35)	0.039
PSA in ng/ml	Median (IQR)	96.8 (28.2–98.0)	81.5 (22.6–98.0)	98.0 (29.5–98.0)	<0.001
Race/ethnicity	Caucasian	4648 (70.9)	814 (73.7)	3834 (70.3)	0.040
	AA	805 (12.3)	108 (9.8)	697 (12.8)	
	Hispanic	640 (9.8)	110 (10)	530 (9.7)	
	Asian	402 (6.1)	66 (6)	336 (6.2)	
M stage	M1a	297 (4.5)	29 (2.6)	268 (4.9)	<0.01
	M1b	4731 (72.2)	823 (74.5)	3908 (71.7)	
	M1c	1253 (19.1)	211 (19.1)	1042 (19.1)	
	M1x	275 (4.2)	42 (3.8)	233 (4.3)	
cT stage	cT1-2	3775 (57.6)	593 (53.7)	3182 (58.4)	<0.01
	cT3-4	1346 (20.5)	233 (21.1)	1113 (20.4)	
	cTx	1435 (21.9)	279 (25.2)	1156 (21.2)	
cN stage	cN0	3671 (56.0)	648 (58.6)	3023 (55.5)	0.1
	cN1	1214 (18.5)	199 (18)	1015 (18.6)	
	cNx	1671 (25.5)	258 (23.3)	1413 (25.9)	
Grade Group at biopsy	I	187 (2.9)	31 (2.8)	156 (2.9)	<0.001
	II	362 (5.5)	50 (4.5)	312 (5.7)	
	III	492 (7.5)	85 (7.7)	407 (7.5)	
	IV	1173 (17.9)	173 (15.7)	1000 (18.3)	
	V	1633 (24.9)	337 (30.5)	1296 (23.8)	
	Unknown	187 (2.9)	31 (2.8)	156 (2.9)	
Chemotherapy	Yes	278 (4.2)	67 (6.1)	211 (3.9)	<0.01
	No/Unknown	6278 (95.8)	1038 (93.9)	5240 (96.1)	
Region	West	3633 (55.4)	607 (54.9)	3026 (55.5)	0.9
	Midwest	768 (11.7)	136 (12.3)	632 (11.6)	
	North-East	965 (14.7)	167 (15.1)	798 (14.6)	
	South	1190 (18.2)	195 (17.6)	995 (18.3)	

Abbreviations: AA, African-American; IQR, interquartile range; PSA, prostate-specific antigen.

confidence interval [CI]: 0.90–1.06, $p = 0.6$). Similarly, median CSS (Figure 1B) was 29 months for EBRT versus 30 months for no EBRT (HR: 1.04, CI: 0.95–1.14, $p = 0.4$).

After multivariable adjustment for Cox regression models predicting OM (Table 2), EBRT was unrelated to OM (HR: 1.04, $p = 0.3$). In multivariable Cox regression models addressing CSM, EBRT was associated with higher CSM, relative to no EBRT (HR: 1.11, CI: 1.02–1.22, $p = 0.02$).

3.3 | OM and cancer-specific mortality according to M1b and M1c substages

Kaplan–Meier plots demonstrated that in subgroup analyses according to M1 substages (M1b and M1c), EBRT was also unrelated to OS or CSS (Figures 2–3). In M1b patients regarding OS, median OS was 24 months after EBRT and 24 months after no EBRT (HR: 0.98, CI: 0.90–1.08, $p = 0.7$) in Kaplan–Meier plots. In M1b patients

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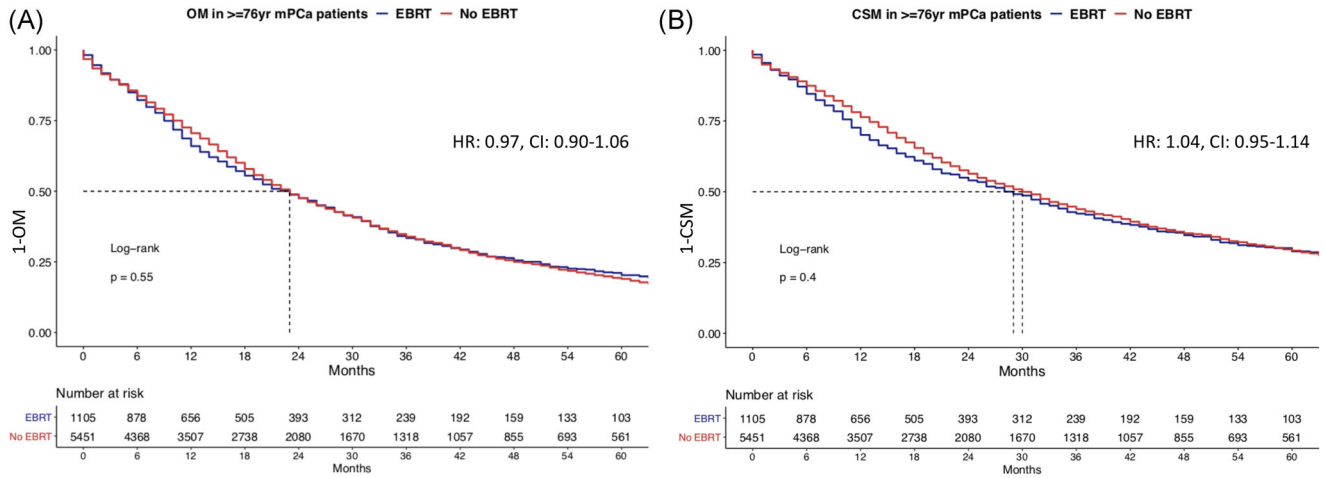

FIGURE 1 Kaplan–Meier plot illustrating (A) overall mortality (OM) and (B) cancer-specific mortality (CSM) in the overall cohort of elderly men who were newly diagnosed with metastatic prostate cancer, comparing external beam radiation therapy (EBRT) versus no EBRT. CI, confidence interval; HR, hazard ratio; mPCa, metastatic prostate cancer [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Univariable and multivariable Cox regression models in elderly men who were newly diagnosed with metastatic prostate cancer predicting overall mortality (OM) and cancer-specific mortality (CSM)

	OM				CSM			
	Univariable		Multivariable		Univariable		Multivariable	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value
No EBRT	Ref	-	-	-	Ref	-	-	-
EBRT	0.97 (0.90–1.06)	0.6	1.04 (0.96–1.13)	0.3	1.04 (0.95–1.14)	0.4	1.11 (1.02–1.22)	0.02
Age	1.06 (1.05–1.06)	<0.001	1.05 (1.04–1.06)	<0.001	1.05 (1.04–1.06)	<0.001	1.04 (1.04–1.05)	<0.001
PSA	1.00 (1.00–1.01)	<0.001	1.00 (1.00–1.00)	<0.001	1.01 (1.00–1.01)	<0.001	1.00 (1.00–1.01)	<0.001
Grade Group I	Ref	-	-	-	Ref	-	-	-
Grade Group II-III	1.18 (0.85–1.65)	0.3	0.97 (0.69–1.36)	0.9	1.13 (0.76–1.67)	0.6	0.93 (0.63–1.39)	0.7
Grade Group IV-V	1.43 (1.05–1.95)	0.02	1.11 (0.82–1.52)	0.5	1.50 (1.05–2.16)	0.03	1.17 (0.81–1.70)	0.4
Grade Group unknown	1.74 (1.29–2.36)	<0.01	1.28 (0.94–1.74)	0.1	1.80 (1.26–2.58)	<0.01	1.32 (0.91–1.91)	0.1
cT1 stage	Ref	-	-	-	Ref	-	-	-
cT2	1.02 (0.94–1.10)	0.6	0.95 (0.88–1.03)	0.3	1.00 (0.91–1.10)	1	0.94 (0.86–1.03)	0.2
cT3	1.08 (0.96–1.21)	0.2	1.03 (0.92–1.16)	0.6	1.11 (0.97–1.27)	0.1	1.04 (0.91–1.19)	0.5
cT4	1.52 (1.38–1.68)	<0.001	1.35 (1.22–1.49)	<0.001	1.59 (1.42–1.78)	<0.001	1.39 (1.24–1.57)	<0.001
cTx	1.40 (1.28–1.53)	<0.001	1.19 (1.09–1.31)	<0.001	1.45 (1.31–1.60)	<0.001	1.22 (1.09–1.36)	<0.01
cN0 stage	Ref	-	-	-	Ref	-	-	-
cN1	1.09 (1.01–1.18)	0.035	1.03 (0.95–1.11)	0.5	1.12 (1.02–1.22)	0.02	1.03 (0.94–1.13)	0.6
cNx	1.19 (1.11–1.27)	<0.001	1.03 (0.96–1.11)	0.4	1.20 (1.11–1.29)	<0.001	1.03 (0.95–1.12)	0.5
Caucasian	Ref	-	-	-	Ref	-	-	-
African American	1.05 (0.96–1.15)	0.3	1.06 (0.97–1.16)	0.2	1.05 (0.95–1.16)	0.4	1.04 (0.94–1.16)	0.4
Hispanic	0.86 (0.77–0.95)	<0.01	0.86 (0.78–0.96)	<0.01	0.91 (0.81–1.03)	0.1	0.91 (0.81–1.02)	0.1
Asian	0.68 (0.60–0.78)	<0.001	0.68 (0.59–0.77)	<0.001	0.68 (0.58–0.79)	<0.001	0.67 (0.57–0.78)	<0.001

Abbreviations: CI, confidence interval; EBRT, external beam radiation therapy; HR, hazard ratio; PSA, prostate-specific antigen.

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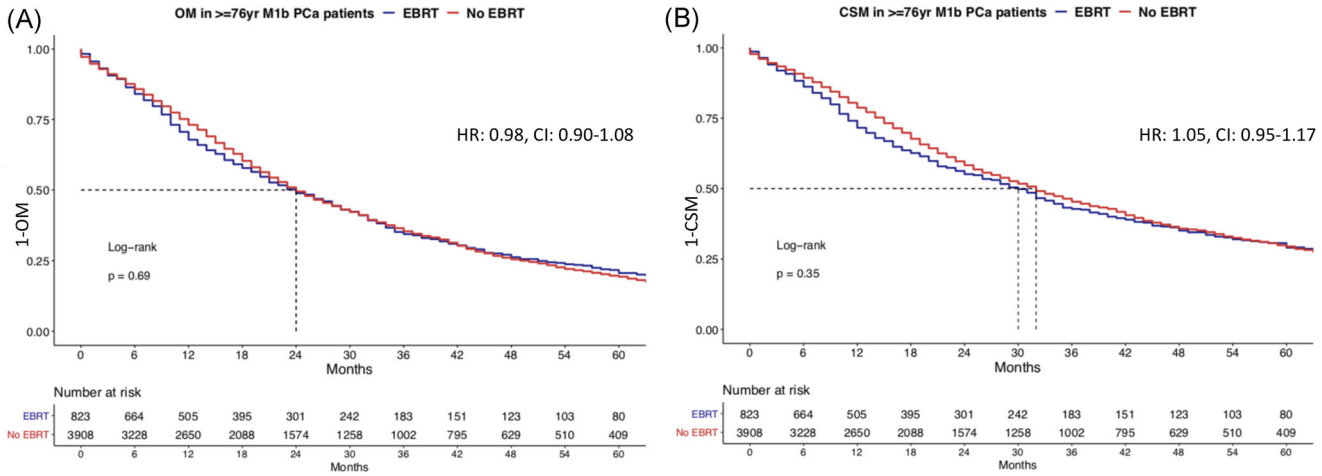

FIGURE 2 Kaplan-Meier plot illustrating (A) overall mortality (OM) and (B) cancer-specific mortality (CSM) in elderly men who were newly diagnosed with M1b prostate cancer, comparing external beam radiation therapy (EBRT) versus no EBRT. CI, confidence interval; HR, hazard ratio; mPCa, metastatic prostate cancer [Color figure can be viewed at wileyonlinelibrary.com]

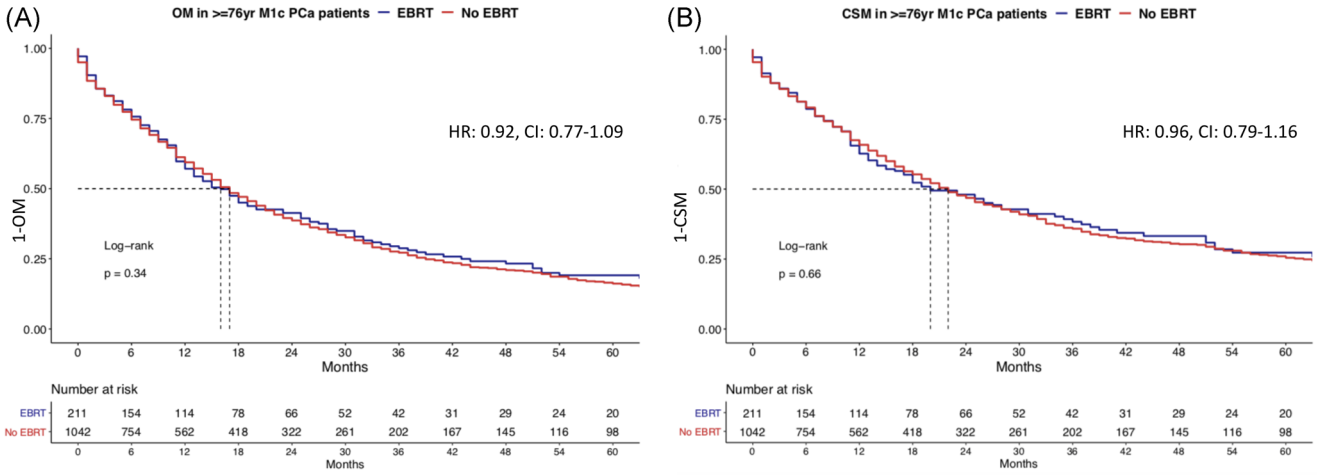

FIGURE 3 Kaplan–Meier plot illustrating (A) overall mortality (OM) and (B) cancer-specific mortality (CSM) in elderly men who were newly diagnosed with M1c prostate cancer, comparing external beam radiation therapy (EBRT) versus EBRT. CI, confidence interval; HR, hazard ratio, mPCa, metastatic prostate cancer [Color figure can be viewed at wileyonlinelibrary.com]

regarding CSS, median CSS was 30 months after EBRT versus 32 months after no EBRT (HR: 1.05, CI: 0.95–1.17, $p = 0.4$) in Kaplan–Meier plots.

After multivariable Cox regression addressing OM in M1b substage, EBRT failed to demonstrate statistical significance (HR: 1.04, $p = 0.4$). In multivariable Cox regression models addressing CSM in M1b substage, EBRT was associated with higher CSM (HR: 1.12, CI 1.00–1.24, $p = 0.04$).

In M1c patients regarding OS, median OS was 16 months after EBRT versus 17 months after no EBRT (HR: 0.92, CI: 0.77–1.09, $p = 0.3$). In M1c patients regarding CSS, median CSS was 20 months after EBRT versus 22 months after no EBRT (HR: 0.96, CI: 0.79–1.16, $p = 0.7$).

In multivariable Cox regression models addressing OM in M1c substage, EBRT was also unrelated to OM (HR: 1.03, $p = 0.7$). In multivariable Cox regression models addressing CSM in M1c substage, EBRT associated with higher CSM (HR: 1.09, $p = 0.4$). Due to insufficient number of observations, stratified analyses within the M1a substages could not be completed.

3.4 | CRR analyses with propensity score matching

In the final part of the study, we relied on CRR to adjust for the potentially confounding effect of OCM on CSM. Additionally, we also relied on 1:4 propensity score matching to adjust for residual patient and tumor characteristics that may remain even after multivariable adjustment. Before matching, 680 EBRT and 3646 no EBRT patients were available. After 4:1 propensity score matching for age, PSA, M-stage, stage, and Grade Group, 674 EBRT and 2696 no EBRT

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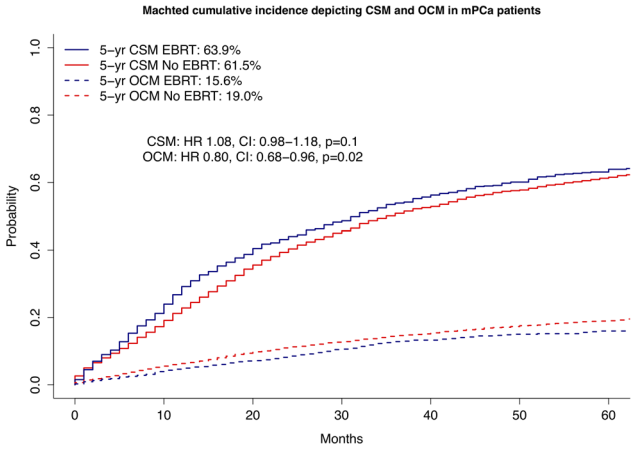

FIGURE 4 Cumulative incidence plots illustrating cancer-specific mortality (CSM) and other cause mortality (OCM) after 1:4 propensity score matching for age at diagnosis, PSA, M-stage (M1a vs. M1b vs. M1c vs. M1x) T-stage (T1-2 vs. T3-4), cN-stage (cN0 vs. cN1 vs. cNx), and Grade Group (I vs. II vs. III, IV vs. V vs. unknown) comparing external beam radiation therapy (EBRT; $n = 674$) versus no EBRT ($n = 2696$) in elderly men who were newly diagnosed with metastatic prostate cancer. CI, confidence interval; HR, hazard ratio; PSA, prostate-specific antigen [Color figure can be viewed at wileyonlinelibrary.com]

patients remained and were included in further analyses. After matching, no residual differences for matched variables remained.

After propensity score matching (Figure 4), in cumulative incidence plots that adjusted for OCM, 5-year CSM was 63.9% after EBRT versus 61.5% after no EBRT patients ($p = 0.1$). After OCM and additional multivariable adjustment (Table 3), EBRT was unrelated to CSM (HR: 1.07, $p = 0.1$).

4 | DISCUSSION

We postulated that the added benefit of EBRT in elderly men who were newly diagnosed with mPCa cannot be claimed without a significant amount of uncertainty. The latter originates from a small proportion of elderly patients that were enrolled in the STAMPEDE trial (12.5% >73 years aged), where added benefit of EBRT was identified.[3] In consequence, we tested the association between EBRT and OM and CSM in elderly men who were newly diagnosed with mPCa. Our results generated several noteworthy observations.

First, we made important observations about patient and tumor characteristics in elderly men who were newly diagnosed with mPCa. We observed that EBRT patients had lower PSA at diagnoses, relative to no EBRT patients (81.5 vs. 98.0 ng/ml). Except for PSA at diagnosis, we did not identify other clinically meaningful patient or cancer characteristics' differences. In consequence, it may be postulated that EBRT is used infrequently: Only 17% of elderly metastatic patients received EBRT. Our data indicate that lower PSA at new mPCa diagnosis represents a potential determinant of EBRT among elderly men who were newly diagnosed with mPCa. Conversely, other variables appear to overlap between EBRT and no EBRT patients. Similarly, no significant regional variability existed. In consequence, EBRT is used equally infrequently across SEER regions.

Second, we also made important observations regarding the current study population, relative to the STAMPEDE trial. This trial validated the notion of EBRT in low volume newly diagnosed mPCa patients and illustrated its benefit on OS. The PSA values of the current study were highly comparable to the STAMPEDE trial: Median PSA STAMPEDE trial 98 ng/ml versus median PSA of the current study 96.8 ng/ml.[3] This observation partially validates the comparability of patient tumor burdens within the current study, relative to that of the STAMPEDE trial. This observation is particularly important since the strict definition of low volume mPCa used in the STAMPEDE trial could not be directly applied to the SEER database. Additionally, our cohort consisted of 6556 elderly men (>75 years) who were newly diagnosed with mPCa. Conversely, only 12.5% of the STAMPEDE trial patients were aged 74 years or higher ($n = 258$). Therefore, the current study represents a substantially more robust source of data for elderly men who were newly diagnosed with mPCa. Moreover, our study focused on North American elderly men who were newly diagnosed with mPCa. Such individuals were not included in the STAMPEDE trial. In consequence, our study provides are robust cohort of elderly men who were newly diagnosed with mPCa. In addition, it also provides a robust sample of North American elderly men who were newly diagnosed with mPCa. All of the above points validate the importance of our contribution to the knowledge of EBRT in the context of elderly newly diagnosed mPCa patients.

Third, we recorded no decrease in OM or CSM in EBRT exposed patients, relative to their EBRT unexposed counterparts in elderly men who were newly diagnosed with mPCa. Regardless of analysis type (Kaplan–Meier, Cox regression models, Cumulative Incidence, CRR), EBRT patients did not exhibit more favorable survival outcomes (OM and CSM) than their no EBRT counterparts. Finally, lack of more favorable survival outcomes after EBRT was equally recorded in Cox regression models and in CRR models that accounted for potential bias related to OCM. Taken together, these observations indicate that EBRT neither clearly nor convincingly associated with a survival advantage in elderly North American men who were newly diagnosed with mPCa. These finding are in contrast to studies focusing on elderly patients with localized prostate cancer, who exhibited a survival benefit with EBRT, relative to their counterparts in whom EBRT was not delivered.[15–17] It is also of note that EBRT-related side effects may be especially important to consider in elderly men who were newly diagnosed with mPCa due to higher toxicity rates that have been well documented in elderly prostate cancer patients, relative to their younger counterparts.[18–20] In consequence, potential EBRT-related side effects would be in contrast to the aim of maximally increase quality of life in mPCa patients.[21–23]

Our work has limitations and should be interpreted in the context of its retrospective and population-based design. First, the variables that we relied on in our analyses do not approximate the detail

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TABLE 3 Univariable and multivariable competing-risks regression models for elderly men who were diagnosed with metastatic prostate cancer after 1:4 matching for age at diagnosis, PSA, M-stage (M1a vs. M1b vs. M1c vs. M1x) T-stage (T1-2 vs. T3-4), cN-stage (cN0 vs. cN1 vs. cNx) and Grade Group (I vs. II vs. III, IV vs. V vs. unknown) predicting cancer-specific mortality (CSM) and other cause mortality (OCM)

	CSM				OCM			
	Univariable		Multivariable		Univariable		Multivariable	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Treatment								
No EBRT	1.00 (Ref.)	—	1.00 (Ref.)	—	1.00 (Ref.)	—	1.00 (Ref.)	—
EBRT	1.08 (0.98–1.18)	0.11	1.07 (0.98–1.18)	0.1	0.80 (0.68–0.96)	0.01	0.81 (0.69–0.97)	0.02
Chemotherapy								
No/Unknown	1.00 (Ref.)	—	1.00 (Ref.)	—	1.00 (Ref.)	—	1.00 (Ref.)	—
Yes	1.15 (0.97–1.37)	0.1	1.14 (0.96–1.36)	0.1	0.54 (0.34–0.86)	<0.01	0.55 (0.34–0.88)	0.01
Race/ethnicity								
Caucasian	1.00 (Ref.)	—	1.00 (Ref.)	—	1.00 (Ref.)	—	1.00 (Ref.)	—
African-American	0.99 (0.89–1.11)	0.9	1.00 (0.89–1.11)	0.9	1.04 (0.86–1.26)	0.7	1.03 (0.85–1.24)	0.8
Hispanic	0.96 (0.84–1.08)	0.45	0.96 (0.85–1.09)	0.5	0.74 (0.58–0.95)	0.02	0.74 (0.58–0.95)	0.02
Asian	0.74 (0.64–0.86)	<0.001	0.74 (0.64–0.87)	<0.001	0.80 (0.60–1.070)	0.1	0.79 (0.59–1.06)	0.1

Abbreviations: CI, confidence interval; EBRT, external beam radiation therapy; HR, hazard ratio.

of recorded variables in prospective randomized studies. In consequence, the amount of detail that could be used for adjustment of potentially confounding variables is not comparable to prospective studies or high-quality, albeit smaller scale, institutional datasets. Second, no information regarding comorbidities is available in the SEER-database. We compensated for this limitation by relying on CRR models that adjust for OCM. Here, we adjusted for the most important comorbidities that may resulted in OCM. Additionally, none of potentially important other cancer-control outcomes, such as biochemical recurrence, progression-free survival or metastatic progression were available. We could not adjust for type or length of androgen deprivation therapy (ADT). However, it can be assumed that almost all newly diagnosed mPCa patients received ADT to reduce the risk of CSM. Moreover, we could not account for selection biases related to primary treatment assignment (EBRT vs. no EBRT). Finally, no meaningful analyses could be conducted for M1a substage due to sample size limitations.

5 | CONCLUSION

In elderly men who were newly diagnosed with mPCa, EBRT does not affect OS or CSS. In consequence, our findings question the added value of local EBRT in elderly newly diagnosed mPCa patients.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

All data generated for this analysis were from the SEER 18 database. The code for the analyses will be made available after request.

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