INTERNATIONAL JOURNAL OF UROLOGY
International Journal of Urology (2021) doi: 10.1111/iju.14701

Check for updates

Original Article: Clinical Investigation

External beam radiotherapy and radical prostatectomy are associated with better survival in Asian prostate cancer patients

Christoph Würnschimmel,[1,2] Mike Wenzel,[2,3] Francesco Chierigo,[4] Rocco Simone Flammia,[5] Zhe Tian,[2] Fred Saad,[2] Alberto Briganti,[6] Shahrokh F Shariat,[7,8,9,10,11,12] Nazareno Suardi,[4] Carlo Terrone,[4] Michele Gallucci,[5] Felix KH Chun,[3] Derya Tilki,[1,13] Markus Graefen[1] and Pierre I Karakiewicz[2]

[1]Martini-Klinik Prostate Cancer Center, University Hospital Hamburg-Eppendorf, Hamburg, Germany, [2]Cancer Prognostics and Health Outcomes Unit, Division of Urology, University of Montréal Health Center, Montréal, Quebec, Canada, [3]Department of Urology, University Hospital Frankfurt, Frankfurt am Main, Germany, [4]Department of Urology, Policlinico San Martino Hospital, University of Genova, Genoa, [5]Department of Maternal-Child and Urological Sciences, Policlinico Umberto I Hospital, Sapienza Rome University, Rome, [6]Department of Urology and Division of Experimental Oncology, Urological Research Institute, IRCCS San Raffaele Scientific Institute, Milan, Italy, [7]Department of Urology, Comprehensive Cancer Center, Medical University of Vienna, Vienna, Austria, [8]Department of Urology, Weill Cornell Medical College, New York City, New York, [9]Department of Urology, University of Texas Southwestern, Dallas, Texas, USA, [10]Department of Urology, Second Faculty of Medicine, Charles University, Prague, Czech Republic, [11]Institute for Urology and Reproductive Health, I.M. Sechenov First Moscow State Medical University, Moscow, Russia, [12]Division of Urology, Department of Special Surgery, Jordan University Hospital, The University of Jordan, Amman, Jordan, and [13]Department of Urology, University Hospital Hamburg-Eppendorf, Hamburg, Germany

Abbreviations & Acronyms
ADT = androgen deprivation therapy
CI = confidence interval
CRR = competing risks regression
CSM = cancer-specific mortality
EBRT = external beam radiotherapy
GGG = Gleason Grade Group
HR = hazard ratio
OCM = other-cause mortality
PCa = prostate cancer
PSA = prostate-specific antigen
PSM = propensity score matched
RP = radical prostatectomy
SEER = Surveillance, Epidemiology and End Results

Correspondence: Christoph Würnschimmel M.D., Martini-Klinik Prostate Cancer Center, University Hospital Hamburg-Eppendorf, Martinistraße 52, 20246 Hamburg, Germany. Email: c.wuernschimmel@uke.de

Received 5 July 2021; accepted 30 August 2021.

Objectives: To test the effect of race/ethnicity on cancer-specific mortality after radical prostatectomy or external beam radiotherapy in localized prostate cancer patients.

Methods: In the Surveillance, Epidemiology and End Results database 2004–2016, we identified intermediate-risk and high-risk white (n = 151 632), Asian (n = 11 189), Hispanic/Latino (n = 20 077) and African American (n = 32 550) localized prostate cancer patients, treated with external beam radiotherapy or radical prostatectomy. Race/ethnicity-stratified cancer-specific mortality analyses relied on competing risks regression, after propensity score matching for patient and cancer characteristics.

Results: Compared with white patients, Asian intermediate- and high-risk external beam radiotherapy patients showed lower cancer-specific mortality (hazard ratio 0.58 and 0.70, respectively, both $P \leq 0.02$). Additionally, Asian high-risk radical prostatectomy patients also showed lower cancer-specific mortality than white patients (hazard ratio 0.72, $P = 0.04$), but not Asian intermediate-risk radical prostatectomy patients ($P = 0.08$). Conversely, compared with white patients, African American intermediate-risk radical prostatectomy patients showed higher cancer-specific mortality (hazard ratio 1.36, $P = 0.01$), but not African American high-risk radical prostatectomy or intermediate- and high-risk external beam radiotherapy patients (all $P \geq 0.2$). Finally, compared with white people, no cancer-specific mortality differences were recorded for Hispanic/Latino patients after external beam radiotherapy or radical prostatectomy, in both risk levels ($P \geq 0.2$).

Conclusions: Relative to white patients, an important cancer-specific mortality advantage applies to intermediate-risk and high-risk Asian prostate cancer patients treated with external beam radiotherapy, and to high-risk Asian patients treated with radical prostatectomy. These observations should be considered in pretreatment risk stratification and decision-making.

Key words: cancer-specific mortality, external beam radiotherapy, localized prostate cancer, other-cause mortality, radical prostatectomy, Surveillance, Epidemiology and End Results.

Introduction

African American race/ethnicity represents an adverse risk factor for less favorable pathological stage and grade at diagnosis, as well as for higher CSM after treatment for localized

PCa.[1,2] However, little, if any attention has been directed to other race/ethnicity groups, including Asian and/or Hispanic/Latino people.[3–5] To the best of our knowledge, no dedicated CSM analyses directly compared outcomes between Asian, Hispanic/Latino and African American patients with the reference group of white patients, after EBRT or RP for localized PCa, within a large-scale, contemporary, epidemiological patient population. Existing large-scale analyses provided fragmented data, without relying on propensity score matched and OCM-adjusted CRR analyses, which are crucial in the context of localized PCa comparisons, as important population differences exist between race/ethnicity groups, and as OCM represents an important and well-documented confounder.[6–9] We addressed this knowledge gap and tested for race/ethnicity CSM differences in RP and EBRT treated patients, and applied further stratification according to intermediate versus high-risk levels. We hypothesized that a similar disadvantage, as previously reported in African American patients, might also apply to the two other race/ethnicity groups (Asian and Hispanic/Latino), relative to white people.

Methods

Within the SEER database we identified white, Asian, Hispanic/Latino and African American patients diagnosed with intermediate- or high-risk localized PCa, treated with either RP or EBRT, between 2004 and 2016. Survival analyses addressed race/ethnicity CSM differences. In all analyses, white race/ethnicity represented the reference category. Three separate race/ethnicity comparisons were carried out. These focused on (i) Asian patients versus white patients; (ii) Hispanic/Latino patients versus white patients; and (iii) African American patients versus white patients. Within each of these comparisons, two separate analyses, respectively, addressed: (i) EBRT, and (ii) RP patients. Among EBRT patients, as well as RP patients, additional stratification was made for intermediate-risk versus high-risk groups. In consequence, a total of 12 separate models addressing CSM were fitted. Within each of these 12 CSM comparisons according to race/ethnicity, separate PSM was carried out for age at diagnosis (in 1-year intervals), PSA at diagnosis (in 1-ng/mL intervals), exact GGGs (1–5), exact cT/cN stages (for EBRT-treated patients) and exact pT/pN stages (for RP-treated patients). Based on sample size differences, PSM relied on three white controls for Asian patients, two white controls for Hispanic/Latino patients and one white control for African American patients. After PSM for each of the 12 CSM comparisons, cumulative incidence plots were complemented with multivariable CRR analyses that adjusted for OCM, in addition to further multivariable adjustment for year of diagnosis and socioeconomic status.[10,11] R software environment for statistical computing and graphics (version 3.4.0 for MAC OS X; http://www.r-project.org/) was used for all statistical analyses.[12] All tests were two-sided with a level of significance set at $P < 0.05$.

Results

Of 215 448 assessable PCa patients, 90 546 were treated with EBRT (60 599 white patients, 16 202 African American patients, 8645 Hispanic/Latino patients and 5100 Asian patients) and 124 902 were treated with RP (91 033 white patients, 16 348 African American patients, 11 432 Hispanic/Latino patients and 6089 Asian patients). In general, EBRT patients were older, and showed higher stage and grade than their RP counterparts. These differences also applied to each of the four examined race/ethnicity groups.

Asians showed the most aggressive tumor characteristics of all four race/ethnicity groups. Specifically, median PSA was highest in Asian patients (9.6 ng/mL in EBRT and 6.9 ng/mL in RP), followed by African American patients (9.3 mg/mL in EBRT and 6.6 ng/mL in RP), Hispanic/Latino patients (9.2 ng/mL in EBRT and 6.7 ng/mL in RP) and white patients (7.9 ng/mL in EBRT and 5.9 ng/mL in RP), in that order. Also, the highest GGG IV–V rates were recorded in Asians, in both EBRT (32.3%) and RP (21.5%) patients. Conversely, white, Hispanic/Latino and African American EBRT patients showed GGG IV–V of 26.6, 25.3 and 23.8%. In RP patients, these rates were 15.0, 15.8 and 15.1% for white, Hispanic/Latino and African American patients, respectively. No clinically meaningful stage differences were recorded according to race/ethnicity (Table 1). Finally, in both EBRT and RP patients, the median age at diagnosis was highest in Asian patients (72 years in EBRT *vs* 64 years in RP), followed by white patients (71 years in EBRT *vs* 62 years in RP), Hispanic/Latino patients (70 years in EBRT *vs* 62 years in RP) and African American patients (66 years in EBRT *vs* 59 years in RP), in that order. In RP patients, Asian patients showed the lowest 10-year OCM rates (7.4%), versus 8.0, 8.4 and 11.2% in Hispanic/Latino, white and African American patients, respectively. Finally, in EBRT patients, Asian patients showed the second lowest 10-year OCM rates (24.1%), after Hispanic/Latino patients (23.1%), versus 10-year OCM rates of 29.0% and 28.3% in white and African American patients, respectively. Based on the aforementioned differences in patient and PCa characteristics, PSM was applied in all 12 comparisons and resulted in no statistically significant residual differences in patient age or tumor characteristics (all $P \geq 0.6$).

Propensity score matched CSM analyses according to race/ethnicity

Asian versus white patients

In high-risk EBRT-treated Asian versus white patients (Fig. 1), respective 10-year CSM rates were 10.4% versus 13.4%, which resulted in a multivariable CRR HR of 0.70 ($P < 0.001$), showing a decreased risk for Asian patients (Table 2). In intermediate-risk EBRT-treated Asian versus white patients, 10-year CSM rates were 3.0% versus 4.9%, which resulted in a multivariable CRR HR of 0.58 ($P < 0.001$), showing a decreased risk for Asian patients. In high-risk RP-treated Asian versus white patients, 10-year CSM rates were 4.8% versus 6.7%, which resulted in a multivariable CRR HR of 0.72 ($P = 0.04$), showing a decreased risk for Asian patients. Conversely, no statistically significant CSM differences were recorded between Asian and white patients in intermediate-risk RP-treated patients ($P = 0.08$, Table 2).

Table 1 Patient and tumor characteristics of 90 546 EBRT-treated patients and 124 902 RP-treated PCa patients within the SEER 2004–2016 database

Variable	EBRT-treated						RP-treated					
	Overall (*n* = 90 546)	White patients (*n* = 60 599)	African American patients (*n* = 16 202)	Hispanic/Latino patients (*n* = 8645)	Asian patients (*n* = 5100)	*P*-value (EBRT)	Overall (*n* = 124 902)	White patients (*n* = 91 033)	African American patients (*n* = 16 348)	Hispanic/Latino patients (*n* = 11 432)	Asian patients (*n* = 6089)	*P*-value (RP)
Age, years, median (IQR)	70 (64–75)	71 (65–75)	66 (60–71)	70 (64–75)	72 (66–76)	<0.001	62 (57–67)	62 (57–67)	59 (54–64)	62 (57–67)	64 (59–68)	<0.001
PSA, ng/mL, median (IQR)	8.3 (5.6–13.9)	7.9 (5.4–12.9)	9.3 (5.9–16.8)	9.2 (5.9–15.6)	9.6 (6.4–15.7)	<0.001	6.0 (4.6–9.2)	5.9 (4.5–8.7)	6.6 (4.8–10.5)	6.7 (4.9–10.6)	6.9 (5.1–10.7)	
GGG (*n*, %)												
I	13 141 (14.5)	8504 (14.0)	2292 (14.1)	1595 (18.4)	750 (14.7)	<0.001	20 372 (16.3)	14 932 (16.4)	2519 (15.4)	2102 (18.4)	819 (13.5)	<0.001
II	31 075 (34.3)	20 868 (34.4)	5986 (36.9)	2703 (31.3)	1518 (29.8)		57 394 (46.0)	42 333 (46.5)	7747 (47.4)	4808 (42.1)	2506 (41.2)	
III	16 565 (18.3)	11 115 (18.3)	3012 (18.6)	1501 (17.4)	937 (18.4)		19 367 (15.5)	14 069 (15.5)	2539 (15.5)	1661 (14.5)	1098 (18.0)	
IV	13 936 (15.4)	9296 (15.3)	2361 (14.6)	1296 (15.0)	983 (19.3)		12 129 (9.7)	8463 (9.3)	1702 (10.4)	1149 (10.1)	815 (13.4)	
V	9877 (10.9)	6832 (11.3)	1494 (9.2)	887 (10.3)	664 (13.0)		7133 (5.7)	5216 (5.7)	769 (4.7)	654 (5.7)	494 (8.1)	
Unknown	5952 (6.6)	3984 (6.6)	1057 (6.5)	663 (7.7)	248 (4.9)		8507 (6.8)	6020 (6.6)	1072 (6.6)	1058 (9.3)	357 (5.9)	
Clinical stage (*n*, %)												
cT1-2	85 558 (94.5)	57 103 (94.2)	15 512 (95.7)	8156 (94.3)	4787 (93.9)	<0.001	118 814 (95.1)	86 763 (95.3)	15 492 (94.8)	10 839 (94.8)	5720 (93.9)	<0.001
cT3-4	4701 (5.2)	3330 (5.5)	640 (4.0)	440 (5.1)	291 (5.7)		3331 (2.7)	2465 (2.7)	412 (2.5)	296 (2.6)	158 (2.6)	
Unknown	287 (0.3)	166 (0.3)	50 (0.3)	49 (0.6)	22 (0.4)		2757 (2.2)	1805 (2.0)	444 (2.7)	297 (2.6)	211 (3.5)	
Nodal stage (*n*, %)												
cNX/cN0	89 444 (98.8)	59 850 (98.8)	16 022 (98.9)	8546 (98.9)	5026 (98.5)		121 029 (96.9)	88 277 (97.0)	15 822 (96.8)	11 002 (96.2)	5928 (97.4)	<0.001
cN1	1102 (1.2)	749 (1.2)	180 (1.1)	99 (1.1)	74 (1.5)	0.2	3873 (3.1)	2756 (3.0)	526 (3.2)	430 (3.8)	161 (2.6)	

Stratification was carried out according to race/ethnicity: white versus African American versus Hispanisc/Latino versus Asian patients.

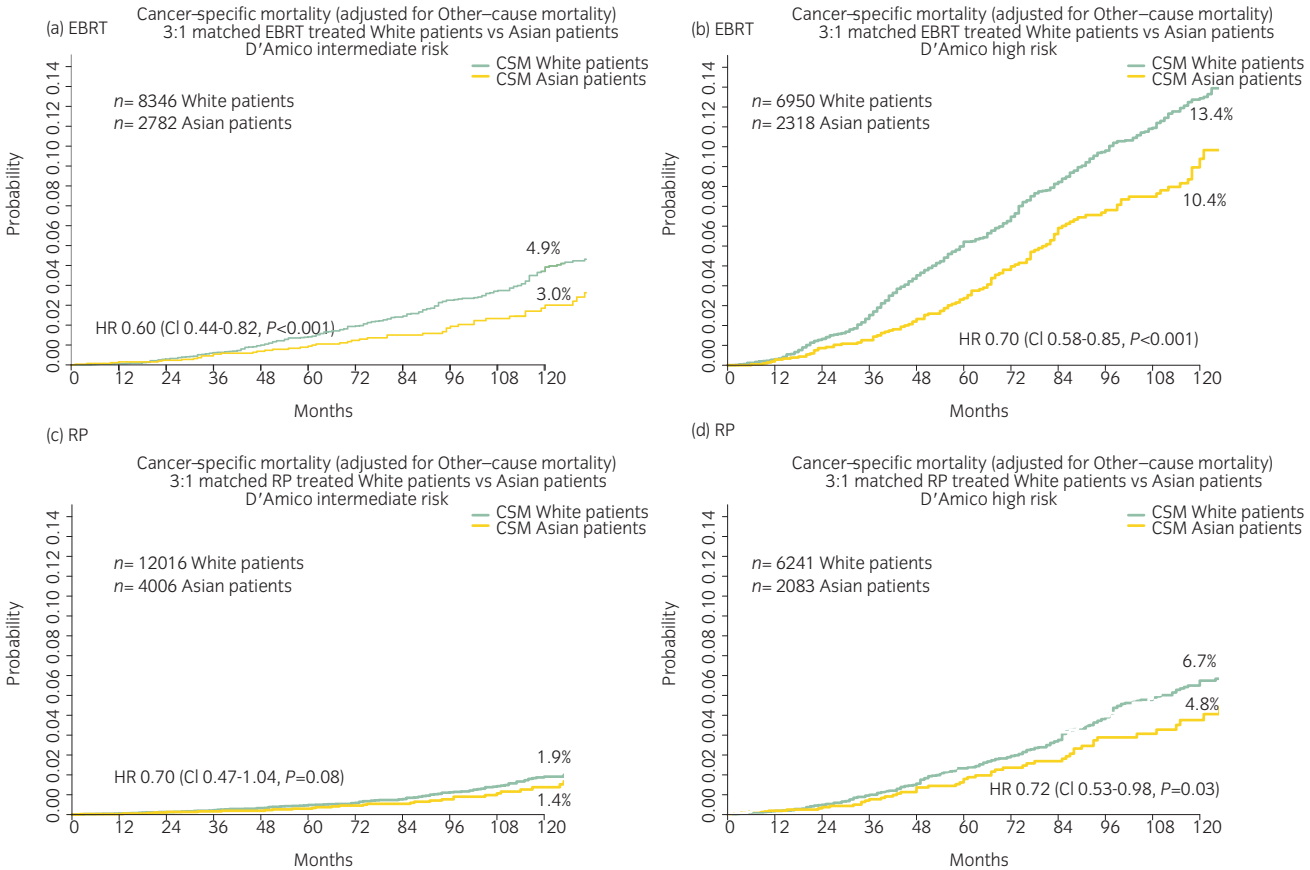

Fig. 1 Cumulative incidence plots after 3:1 propensity score matching of EBRT- and RP-treated white patients versus Asian patients stratified by D'Amico risk groups (intermediate/high risk).

Table 2 Results of multivariable CRR analyses regarding CSM, according to race/ethnicity within PSM populations of Asian, African American and Hispanic/Latino patients versus white patients in EBRT or RP groups of intermediate- and high-risk levels

Race/ethnicity	Treatment type (risk group)	Sample size (before PSM)	PSM ratio	Sample size (after PSM)	CSM at 10 years	HR	95% CI	*P*-value
Asian *vs* white patients	EBRT (high-risk)	2318 *vs* 23 820	1:3	2318 *vs* 6950	10.4% *vs* 13.4%	0.70	0.57–0.85	<0.001
	EBRT (intermediate-risk)	2782 *vs* 36 779	1:3	2782 *vs* 8346	3.0% *vs* 4.9%	0.58	0.43–0.80	<0.001
	RP (high-risk)	2083 *vs* 25 916	1:3	2083 *vs* 6241	4.8% *vs* 6.7%	0.72	0.53–0.98	0.04
	RP (intermediate-risk)	4006 *vs* 65 117	1:3	4006 *vs* 12 016	1.4% *vs* 1.9%	0.70	0.47–1.04	0.08
African American *vs* white patients	EBRT (high-risk)	6547 *vs* 23 820	1:1	6494 *vs* 6494	12.6% *vs* 12.8%	1.05	0.93–1.17	0.4
	EBRT (intermediate-risk)	9655 *vs* 36 779	1:1	9602 *vs* 9602	4.5% *vs* 4.4%	1.09	0.93–1.27	0.3
	RP (high-risk)	5082 *vs* 25 916	1:1	5080 *vs* 5080	5.6% *vs* 4.8%	1.13	0.94–1.35	0.2
	RP (intermediate-risk)	11 266 *vs* 65 117	1:1	11 255 *vs* 11 255	1.6% *vs* 1.3%	1.36	1.09–1.70	0.01
Hispanic/Latino *vs* white patients	EBRT (high-risk)	3489 *vs* 23 820	1:2	3488 *vs* 6967	12.9% *vs* 11.9%	0.96	0.84–1.13	0.7
	EBRT (intermediate-risk)	5156 *vs* 36 779	1:2	5155 *vs* 10 304	4.5% *vs* 4.7%	0.98	0.79–1.18	0.8
	RP (high-risk)	3602 *vs* 25 916	1:2	3600 *vs* 7198	6.7% *vs* 5.2%	1.08	0.88–1.33	0.5
	RP (intermediate-risk)	7830 *vs* 65 117	1:2	7830 *vs* 15 656	1.2% *vs* 1.5%	0.82	0.62–1.11	0.2

African American versus white patients

In intermediate-risk RP-treated African American versus white patients (Fig. 2), respective 10-year CSM rates were 1.3% versus 1.6%, which resulted in a multivariable CRR HR of 1.36 (P = 0.01), showing a decreased risk for white patients. Conversely, no statistically significant CSM differences were recorded for all three remaining comparisons between African American and white patients: high-risk RP, intermediate-risk EBRT and high-risk EBRT (Table 2).

Hispanic/Latino versus white patients

In all comparisons between Hispanic/Latino versus white patients (Fig. 3), no statistically significant CSM differences

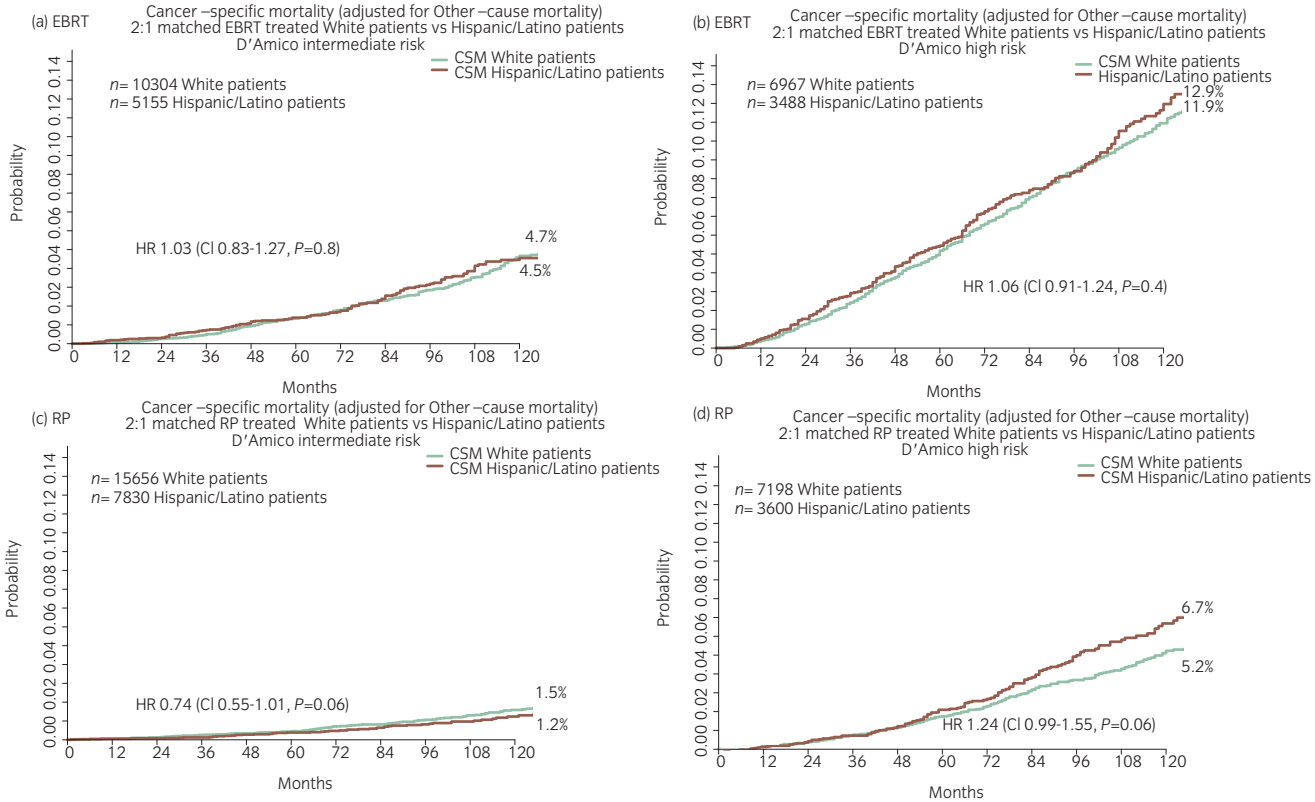

Fig. 2 Cumulative incidence plots after 1:1 propensity score matching of EBRT- and RP-treated white patients versus African American patients stratified by D'Amico risk groups (intermediate/high risk).

were recorded ($P \geq 0.2$), regardless of treatment type (EBRT and RP) or risk level (intermediate- or high-risk, Table 2).

Discussion

We hypothesized that CSM of EBRT and RP-treated Asian, Hispanic/Latino and African American patients is higher than that of white patients, even after matching for patient and cancer characteristics. Our hypothesis was derived from previous large-scale data that focused on comparisons between African American and white patients. However, comparisons between Asian and white patients, as well as between Hispanics/Latino and white patients, using the same amount of detail and equally robust sample sizes, were never carried out.[1,2,5,9,13] We addressed this void and tested the study hypothesis within a large contemporary SEER database sample.[14] Our analyses showed several noteworthy findings.

First, the present data validated previously established differences between EBRT and RP patients regarding age, stage and grade.[15,16] In consequence, the SEER database is consistent with other large- and small-scaled databases, in that regard.

Second, important differences in patient and tumor characteristics were recorded according to race/ethnicity group distribution. Although, abundant comparisons were made in that regard between African American and white patients, little is known about race/ethnicity differences between Asian and white patients, as well as between Hispanic/Latino and white patients.[1,3,9] In the current study, Asian patients always showed the most unfavorable characteristics. For example, Asian patients were the oldest at diagnosis (in EBRT, 72 years in Asian patients *vs* 66–71 years in the other three races/ethnicities, as well as in RP, 64 years in Asian patients *vs* 59–62 years in the other three races/ethnicities). Furthermore, Asian patients showed the highest PSA values (in EBRT, 9.6 ng/mL in Asian patients *vs* 7.9–9.3 ng/mL in the other three races/ethnicities, as well as in RP, 6.9 ng/mL in Asian patients *vs* 5.9–6.7 ng/mL in the other three races /ethnicities). Finally, Asian patients also showed the most aggressive GGG distribution (in EBRT, 32.3% GGG IV–V rates in Asian patients *vs* 23.8–26.6% in the three other races/ethnicities, as well as in RP, 21.5% GGG IV–V rates in Asian patients *vs* 15.0–15.8% in the three other races/ethnicities). These findings are consistent with another SEER-based analysis by Deuker *et al.* (n = 380 705) that compared Asian patients with white patients of all PCa stages, regardless of treatment type, or its absence.[7] Conversely, no clinically meaningful PSA, stage and grade differences were recorded between Hispanic/Latino and white patients in the current study, which is in agreement with a previous SEER analysis by Chinea *et al.* (n = 393 348), who compared Hispanic/Latino patients with white patients of all stages, but also did not carry out stratified analyses according to treatment type.[5] Taken together, the above findings emphasize race-/ethnicity-specific profiles that apply to Asian, Hispanic/Latino and African-American patients. Based on these differences,

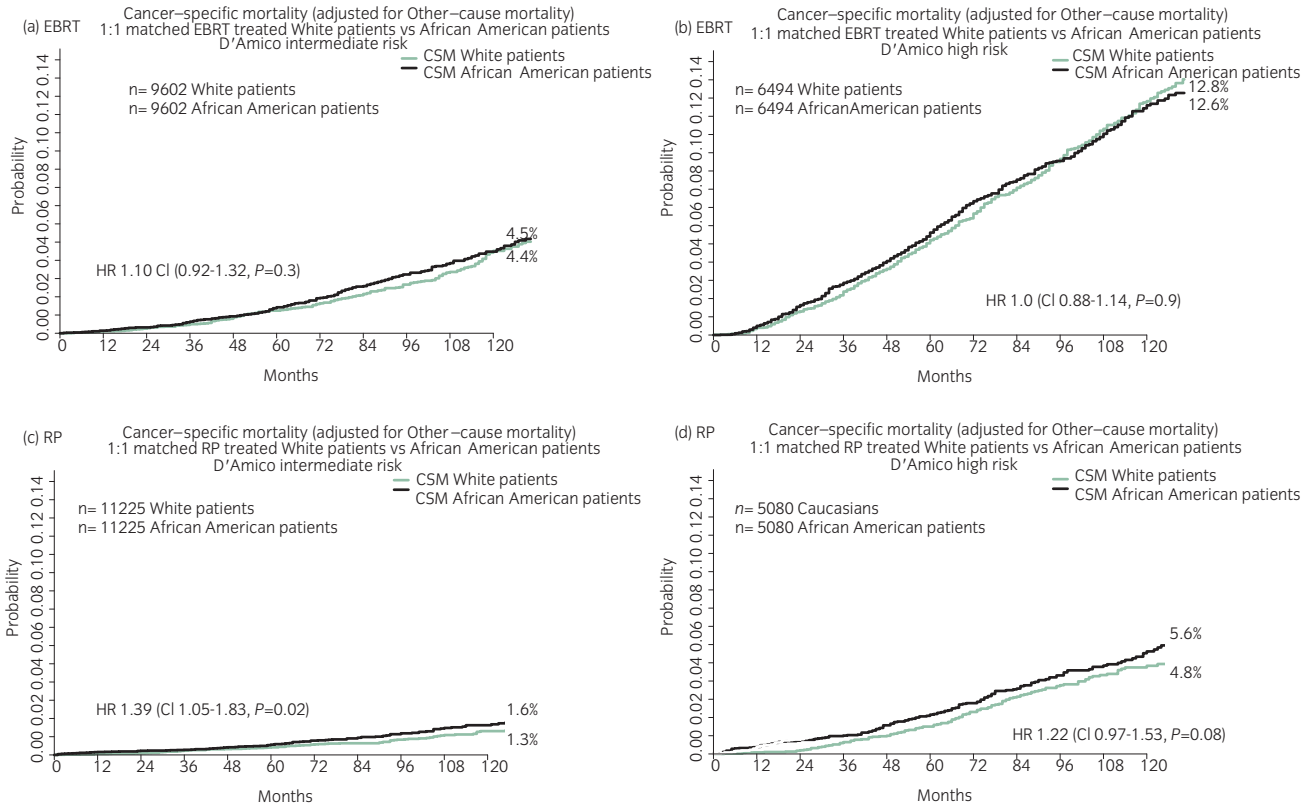

Fig. 3 Cumulative incidence plots after 2:1 propensity score matching of EBRT- and RP-treated white patients versus Hispanic/Latino patients stratified by D'Amico risk groups (intermediate/high risk).

meaningful comparisons based on non-randomized study designs should ideally rely on the strictest statistical adjustment, which can be achieved with PSM, as was applied in our analyses.

Third, we also recorded important OCM rate differences within all four race/ethnicity subgroups. Specifically, at 10 years, OCM rates were generally higher in EBRT patients. Furthermore, RP-treated Asian patients showed the lowest OCM rates (7.4%) and EBRT-treated Asian patients showed the second-lowest OCM rates (24.1 *vs* 23.1% in Hispanic/Latino patients). Conversely, white and African American patients generally showed the highest OCM rates (8.4–11.2% in RP and 28.3–29.0% in EBRT). In consequence, Asian patients were more likely than other race/ethnicity groups to succumb to PCa, based on most favorable OCM profiles. This observation validates the absolute need for consideration of OCM in survival analyses. In consequence, we relied on CRR that adjusts CSM rates, after accounting for OCM.[9] Conversely, all previous reports did not rely on CRR.[7,8]

Fourth, we observed important CSM differences according to race/ethnicity. In the comparison between Asian and white patients, we recorded lower CSM in Asian patients, after EBRT for intermediate- (HR 0.58, $P < 0.001$) and high-risk PCa (HR 0.70, $P < 0.001$), as well as after RP for high-risk PCa (HR 0.72, $P = 0.04$). Conversely, in African American patients, we recorded the opposite effect: higher CSM in intermediate-risk African American patients treated with RP (HR 1.36, $P = 0.01$). Finally, no CSM differences were recorded in comparisons between Hispanic/Latino and white patients ($P \geq 0.2$).

To the best of our knowledge, we are the first to report lower CSM rates in Asian patients after EBRT, in both intermediate-risk and high-risk groups, and in the high-risk group after RP. The present findings are in partial agreement with a previous SEER based analysis by Wang *et al.*, comparing 21 991 white patients and 2253 Asian patients treated with EBRT or RP (2004–2013). Specifically, Wang *et al.* reported significantly higher CSM in white patients compared with Asian patients (HR 1.9).[8] However, Wang *et al.* did not stratify CSM outcomes separately for EBRT- and RP-treated patients. Similarly, the present observations are also in partial agreement with Deuker *et al.*, who compared Asian to white PCa patients of all stages and treatment modalities, including those without treatment. Within their analyses, a CSM HR of 0.6, suggesting a decreased risk for Asian patients, was recorded. However, Deuker *et al.* also did not account for the confounding effect of OCM, as was carried out in the present analysis. In consequence, the present findings relied on a stricter methodology than the two previous studies, and furthermore, provide treatment- and risk group-specific comparisons. All of the aforementioned considerations result in more robust evidence emphasizing the potential CSM advantage in Asian patients, relative to white patients. These observations can be interpreted in several ways. First, it might be postulated that Asian patients benefit from better cancer control with EBRT and/or from

ADT than white patients. Indeed, especially the influence of ADT might have played a very important role, as more favorable cancer-specific outcomes have also been reported earlier in a group of Japanese PCa patients treated with primary ADT (from the Japan Cancer of the Prostate Registry Database, J-CaP) versus white PCa patients treated with primary ADT (from the USA Cancer of the Prostate Strategic Urologic Research Endeavor database; CaPSURE).[17] Similar findings were also reported in a more historical and smaller cohort of Japanese American and white PCa patients.[18] Therefore, the CSM advantage of Asian patients, and especially of those treated with EBRT, might be attributed to the stronger effects of concomitant ADT in Asian patients compared with white patients.

Second, it might also be postulated, that the same PSA, stage and grade characteristics could result in more favorable CSM-free survival in Asian patients than in white patients. Interestingly, a lack of CSM differences between intermediate-risk Asian versus white patients after RP questions PSA, stage and grade phenotype differences being responsible for lower CSM in Asian patients. However, the retrospective nature of our database does not allow to validly distinguish between inherent patient characteristics versus treatment characteristics affecting the reported race-/ethnicity-related CSM differences between Asian and white patients.

Third, the present findings also resulted in novel observations regarding CSM rate differences between Hispanic/Latino versus white patients. Unlike in comparisons between Asian versus white patients, no CSM differences were recorded in either EBRT- or RP-treated patients, regardless of risk level. These observations are in partial agreement with findings by Chinea *et al*., who analyzed the SEER 2000–2013 database (352 886 white *vs* 40 462 Hispanic/Latino patients).[5] Within their analyses, Hispanic/Latino patients showed a HR of 1.02 ($P = 0.5$) versus white patients. However, a direct comparison to the present findings is not possible, as Chinea *et al*. relied on PCa patients of all risk groups, including all treatment types, as well as those without treatment, and furthermore, did not report stratified analyses according to risk group.

Taken together, the present findings showed that Asian patients were older, and exhibited higher PSA and less favorable GGG distribution than white patients. Furthermore, Asian patients showed lower OCM. Finally, the study showed lower CSM in intermediate- and high-risk Asian patients after EBRT relative to white patients, as well as in high-risk Asian relative to white patients, after RP.

The clinical implications of these observations apply to treatment decision-making. Specifically, older Asian patients, and those with higher PSA values and higher GGG should be given greater consideration for EBRT, as more favorable CSM rates might be expected than in white patients, who represent the benchmark for most currently available cancer control outcomes in localized PCa. Similarly, older high-risk Asian patients, despite potential presence of higher PSA and less favorable GGG should also be given greater consideration for RP, for the same reasons. These considerations do not apply to intermediate-risk or high-risk Hispanic/Latino PCa patients. In consequence, the same EBRT and RP considerations should be made in those individuals, as for white patients.

The present study had limitations, and should be interpreted in the context of its retrospective and population-based design. First, although white patients are well represented in the SEER database, the representation of African American, Hispanic/Latino and Asian patients is suboptimal, with Asian patients representing the group with the lowest sample size. Therefore, oversampling of these patients should be encouraged in the future, to allow better generalizability of observed findings within samples of African American, Hispanic/Latino and Asian men. Nevertheless, despite most important sample size limitations that applied most strikingly to Asian patients, highly statistically significant CSM differences were recorded in three out of four Asian versus white patient comparisons. This observation emphasizes the importance of the effect size that underlies the observed results, within the smallest race/ethnicity cohort (Asians). Second, despite the best efforts aimed at PSM, retrospective analyses, and matching for known and available variables might still suffer from remaining differences related to unmeasured or unavailable confounding variables. For example, as SEER does not provide data on comorbidity, we could not further evaluate the underlying comorbidity profiles according to each racial/ethnic group. However, OCM accounts for the most important biases. Furthermore, SEER does not provide explicit treatment data. In particular, for EBRT-treated patients, we were unable to adjust for applied radiation dose or ADT type and duration. Finally, the SEER database only includes North American patients. Therefore, the present findings are only applicable to Asian patients from the USA and are not generalizable to Asian patients from other parts of the world. In addition, the term, Asian, encompasses a variety of potentially different races/ethnicities, such as Chinese, Vietnamese, Korean or Japanese, to mention a few. Therefore, when interpreting our analyses, this inherent heterogeneity needs to be considered.

In conclusion, relative to white patients, an important CSM advantage applies to intermediate-risk and high-risk Asian PCa patients treated with EBRT, and to high-risk Asian patients treated with RP. These observations should be considered in pretreatment risk stratification and decision-making.

Acknowledgment

Open Access funding enabled and organized by Projekt DEAL.

Conflict of interest

None declared.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable (approval was waived by the local ethics committee, as SEER data is publicly available and de-identified. In lieu of a formal ethics committee, the principles of the Helsinki Declaration were followed).

Informed consent

Not applicable.

Registry and Registration No. of the study/trial

Not applicable.

Animal studies

Not applicable.

References

1 Mahal BA, Berman RA, Taplin M-E *et al*. Prostate cancer-specific mortality across Gleason Scores in Black vs Nonblack Men. *JAMA* 2018; **320**: 2479.

2 Steele CB, Li J, Huang B *et al*. Prostate cancer survival in the United States by race and stage (2001–2009): findings from the CONCORD-2 study. *Cancer* 2017; **123**: 5160–77.

3 Gray PJ, Lin CC, Cooperberg MR *et al*. Temporal trends and the impact of race, insurance, and socioeconomic status in the management of localized prostate cancer. *Eur. Urol.* 2017; **71**: 729–37.

4 Man A, Pickles T, Chi KN. Asian race and impact on outcomes after radical radiotherapy for localized prostate cancer. *J. Urol.* 2003; **170**: 901–4.

5 Chinea FM, Patel VN, Kwon D *et al*. Ethnic heterogeneity and prostate cancer mortality in Hispanic/Latino men: a population-based study. *Oncotarget* 2017; **8**: 69709–21.

6 Chao GF, Krishna N, Aizer AA *et al*. Asian Americans and prostate cancer: a nationwide population-based analysis. *Urol. Oncol. Semin. Orig. Investig.* 2016; **34**: 233.e7–233.e15.

7 Deuker M, Stolzenbach LF, Pecoraro A *et al*. PSA, stage, grade and prostate cancer specific mortality in Asian American patients relative to Caucasians according to the United States Census Bureau race definitions. *World J. Urol.* 2021; **39**: 787–96.

8 Wang C, Kamrava M, King C *et al*. Racial disparity in prostate cancer-specific mortality for high-risk prostate cancer: a population-based study. *Cureus* 2017; **9**: e961.

9 Dess RT, Hartman HE, Mahal BA *et al*. Association of black race with prostate cancer-specific and other-cause mortality. *JAMA Oncol.* 2019; **5**: 975.

10 Fine JP, Gray RJ. A proportional Hazards model for the subdistribution of a competing risk. *J. Am. Stat. Assoc.* 1999; **94**: 496–509.

11 Dignam JJ, Zhang Q, Kocherginsky M. The use and interpretation of competing risks regression models. *Clin. Cancer Res.* 2012; **18**: 2301–8.

12 R Core Team. *R: A language and environment for statistical computing. R Foundation for Statistical Computing*. Vienna, Austria. 2013. [Cited 30 Mar 2021.] Available from URL: http://www.r-project.org/

13 Lichtensztajn DY, Gomez SL, Sieh W *et al*. Prostate cancer risk profiles of Asian-American Men: disentangling the effects of immigration status and race/ethnicity. *J. Urol.* 2014; **191**: 952–6.

14 Howlader N, Noone A, Krapcho M *et al*. SEER Cancer Statistics Review, 1975–2016, National Cancer Institute. Bethesda, MD. 2018. Based on November 2018 SEER data submission, posted to the SEER web site, April 2019. [30 Mar 2021.] Available from URL: https://seer.cancer.gov

15 Nemirovsky A, Huang H, Al Kibria GM *et al*. Surgery associated with increased survival compared to radiation in clinically localized Gleason 9–10 prostate cancer: a SEER analysis. *World J. Urol.* 2021; **39**: 415–23.

16 Pompe RS, Davis-Bondarenko H, Zaffuto E *et al*. Population-based validation of the 2014 ISUP Gleason Grade Groups in patients treated with radical prostatectomy, brachytherapy, external beam radiation, or no local treatment. *Prostate* 2017; **77**: 686–93.

17 Cooperberg MR, Hinotsu S, Namiki M *et al*. Trans-Pacific variation in outcomes for men treated with primary androgen-deprivation therapy (ADT) for prostate cancer. *BJU Int.* 2016; **117**: 102–9.

18 Fukagai T, Namiki TS, Carlile RG *et al*. Comparison of the clinical outcome after hormonal therapy for prostate cancer between Japanese and Caucasian men. *BJU Int.* 2006; **97**: 1190–3.