Race/ethnicity is an Important Predictor of Life Expectancy in Localized Prostate Cancer Patients

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Abstract

PURPOSE:

To test the effect of race/ethnicity on Social Security Administration (SSA) life tables' life-expectancy (LE) predictions in localized prostate cancer (PCa) patients treated with either radical prostatectomy (RP) or external beam radiotherapy (EBRT). We hypothesized that LE will be affected by race/ethnicity.

PATIENTS AND METHODS:

We relied on the 2004-2006 Surveillance, Epidemiology, and End Results database to identify D'Amico intermediate- and high-risk PCa patients treated with either RP or EBRT. SSA life tables were used to compute 10-year LE predictions and were compared to OS. Stratification was performed according to treatment type (RP/EBRT) and race/ethnicity (Caucasian, African-American, Hispanic/Latino and Asian).

RESULTS:

Of 55,383 assessable patients, 40,490 were Caucasian (RP 49.3% vs. EBRT 50.7%), 7,194 African-American (RP 41.3% vs. EBRT 50.7%), 4,716 Hispanic/Latino (RP 51.0% vs. EBRT 49.0%) and 2,983 were Asian (RP 41.6% vs. EBRT 58.4%). In both RP and EBRT patients, OS exceeded life tables' LE predictions, except for African-Americans. However, in RP patients, the magnitude of the difference was greater than in EBRT. Moreover, in RP patients, OS of African-Americans virtually perfectly followed predicted LE. Conversely, in EBRT patients, the OS of African-American patients was worse than predicted LE.

CONCLUSIONS:

OS in RP and EBRT treated PCa patients is invariably better than respective life tables' derived LE predictions for Caucasians, Hispanic/Latinos and Asians, but not for African-Americans. The recorded survival disadvantage in African-American RP and EBRT patients, and if applicable also in other African-American populations, warrants detailed consideration and possibly corrective measures.

1. Background

Life expectancy (LE) needs to be taken into account in the localized prostate cancer (PCa) clinical decision-making process [1,2], especially when curative management such as radical prostatectomy (RP) or external beam radiotherapy (EBRT) is considered. In this regard, the National Comprehensive Cancer Network (NCCN) guidelines endorse the use of age-based Social Security Administration (SSA) life tables for LE prediction in North American PCa patients [3,4]. Although the SSA life tables were validated in general, the effect of race/ethnicity on LE has not been examined. [5]. Nevertheless, evidence suggests that race/ethnicity may be a determinant of LE [6,7] and this hypothesis has not been tested in the setting of localized PCa. To address this void, we tested for differences between observed overall survival (OS) and Social Security Administration (SSA) life tables' predicted LE according to four racial/ethnic groups: Caucasians, African-Americans, Hispanic/Latinos and Asians. Additionally, we stratified according to

treatment type, since LE characteristics at RP and EBRT are also known to vary [8,9]. We hypothesized that SSA life tables' derived LE predictions differ from OS rates between the four racial/ethnic groups.

2. Patients And Methods

We identified Caucasian, African-American, Hispanic/Latino and Asian patients with D'Amico intermediate- to high-risk localized PCa treated with either RP or EBRT between 2004 and 2006 and who have available follow-up of ten years within the Surveillance, Epidemiology, and End Results (SEER) database. D'Amico intermediate-risk was defined as clinical T-stage 2b (cT2b) and/or prostate specific antigen (PSA) of 10–20 ng/ml and/or Gleason Grade Group (GGG) 3. D'Amico high-risk was defined as clinical T-stage $\geq$ cT2c, PSA $>$ 20 ng/ml and/or GGG $\geq$ 4 [10]. We excluded patients with unknown metastatic status (n=2,965). These selection criteria resulted in a cohort of 55,383 assessable patients.

2.1 Statistical analyses

Monte Carlo simulation was used to create a simulated cohort resembling the exact age composition of the actual 2004-2006 SEER database population of 55,383 men with localized PCa, according to previous methodology [5]. Based on SSA life tables' predictions for a ten-year span up to the year 2016 (henceforth referred to as "predicted LE"), a Markov chain representing natural progression of age was constructed for each individual's age. Within the Markov chain, each simulated patient could either survive or die within each of ten simulated year intervals. For each examined scenario, the model provided a ten-year LE probability. The latter was included in Kaplan-Meier plots and compared with OS rates according to treatment type (RP and EBRT) and according to race/ethnicity (Caucasian, African-American, Hispanic/Latino and Asian). Furthermore, the differences OS and predicted LE for each year were calculated and plotted.

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 [11]. Descriptive statistics included frequencies and proportions for categorical variables. Medians and interquartile-ranges (IQR) were reported for continuously coded variables. Chi-square and Log-rank tested the statistical significance in proportions and survival differences. All tests were two-sided with a level of significance set at $p < 0.05$.

3. Results

3.1 Study population

Of 55,383 eligible patients with intermediate- or high-risk PCa, 40,490 were Caucasian, 7,194 African-American, 4,716 Hispanic/Latino and 2,983 were Asian (Table 1). RP patients were in general younger (62 years, interquartile range IQR 57-67) than EBRT patients (70 years, IQR 64-75). Median ages at diagnosis for RP/EBRT were 62 yrs/70 yrs, 60 yrs/66 yrs, 63 yrs/69 yrs and 64 yrs/72 yrs years for Caucasians, African-Americans, Hispanic/Latinos and Asians, in that order (Figure 1).

At diagnosis, median PSA values (in ng/ml) for RP patients were 5.9, 6.6, 6.7 and 7.0 respectively for Caucasians, African-Americans, Hispanic/Latinos and Asians. For EBRT patients, PSA values were 7.4, 8.8, 8.9 and 9.5, respectively for Caucasians, African-Americans, Hispanic/Latinos and Asians. Within all four racial/ethnic groups, both RP and EBRT patients predominantly harbored GGG 1-3 (81.3% overall) and cT1-2 stages (96.0% overall), regardless of treatment type (Table 1).

Table 1

Descriptive characteristics of Caucasian, African-American, Hispanic/Latino and Asian patients diagnosed with localized prostate cancer in the Surveillance, Epidemiology, and End Results database 2004-2006. Abbreviations: PSA Prostate specific antigen, GGG Gleason Grade Group, RP Radical prostatectomy, EBRT External beam radiotherapy

	Overall n= 55,383	Caucasian n= 40,490	African-American n= 7,194	Hispanic/Latino n= 4,716	Asian n= 2,983
Age (yr), median (IQR)	66 (60-72)	66 (60-72)	64 (58-69)	66 (60-71)	68 (63-74)
PSA (ng/ml), median (IQR)	6.9 (4.9-11.3)	6.6 (4.8-10.7)	7.9 (5.3-13.8)	7.8 (5.3-12.8)	8.3 (5.7-13.2)
Tumor stage, n (%)					
cT1	25563 (46.2)	18093 (44.7)	3836 (53.3)	2148 (45.5)	1486 (49.8)
cT2	27576 (49.8)	20739 (51.2)	3068 (42.6)	2399 (50.9)	1370 (45.9)
cT3	1968 (3.6)	1477 (3.6)	242 (3.4)	138 (2.9)	111 (3.7)
cT4	220 (0.4)	152 (0.4)	35 (0.5)	21 (0.4)	12 (0.4)
cTx	56 (0.1)	29 (0.1)	13 (0.2)	10 (0.2)	4 (0.1)
GGG, n (%)					
I	13986 (25.3)	10268 (25.4)	1732 (24.1)	1320 (28.0)	666 (22.3)
II	22667 (40.9)	16670 (41.2)	3013 (41.9)	1879 (39.8)	1105 (37.0)
III	8386 (15.1)	6096 (15.1)	1116 (15.5)	661 (14.0)	513 (17.2)
IV	5846 (10.6)	4189 (10.3)	804 (11.2)	476 (10.1)	377 (12.6)
V	3934 (7.1)	2863 (7.1)	434 (6.0)	335 (7.1)	302 (10.1)
Unknown	564 (1.0)	404 (1)	95 (1.3)	45 (1.0)	20 (0.7)

Lymph node status, n (%)					
cN0	53804 (97.1)	39347 (97.2)	6997 (97.3)	4561 (96.7)	2899 (97.2)
cN1	905 (1.6)	658 (1.6)	125 (1.7)	84 (1.8)	38 (1.3)
cNX	674 (1.2)	485 (1.2)	72 (1.0)	71 (1.5)	46 (1.5)
D'Amico Risk Group, n (%)					
Intermediate	35494 (64.1)	26252 (64.8)	4389 (61.0)	3048 (64.6)	1805 (60.5)
High	19889 (35.9)	14238 (35.2)	2805 (39.0)	1668 (35.4)	1178 (39.5)
Treatment type, n (%)					
RP	26568 (48)	19949 (49.3)	2973 (41.3)	2405 (51.0)	1241 (41.6)
EBRT	28815 (52)	20541 (50.7)	4221 (58.7)	2311 (49.0)	1742 (58.4)

3.2 Observed overall survival versus predicted life expectancy in radical prostatectomy patients

The comparison between OS and predicted LE at RP was stratified according to four racial/ethnic groups: Caucasians (Figure 2A), African-Americans (Figure 2B), Hispanic/Latinos (Figure 2C) and Asians (Figure 2D). For example, in Caucasians treated with RP, OS was 95.4% at five years and 86.7% at ten years. For the same timepoints, the respective predicted LE values were 91.0% and 80.0%. OS versus predicted LE values resulted in a difference of +4.4% at five years and +6.7% at ten years, favoring OS over predicted LE. The same analysis in African-Americans treated with RP yielded virtually the same OS and predicted LE values (OS at five years: 93.8%, ten years: 82.6% versus predicted LE at five years: 93.1%, ten years: 82.5%). These respectively resulted in virtually no differences at five years (+0.7%) and ten years (+0.1%). In Hispanic/Latinos treated with RP, the OS was 95.3% at five years and 87.8% at ten years. For the same timepoints, the respective predicted LE values were 91.4% and 78.5%. The OS versus predicted LE values resulted in a difference of +3.9% at five years and +9.3% at ten years, favoring OS over predicted LE. In Asian patients treated with RP, the OS was 95.9% at five years and 88.6% at ten years. For the same timepoints, the respective predicted LE values were 91.0% and 78.2%. The OS versus predicted LE values resulted in a difference in +4.9% at five years and +10.4% at ten years, favoring OS over predicted LE.

Figure 3A combines the recorded differences between OS versus predicted LE within the four examined racial/ethnic groups treated with RP. For African-Americans, the plotted line illustrating the difference between OS and predicted LE closely corresponds to the horizontal line and indicates a negligible difference between these two values. Conversely, the plotted differences between OS and predicted LE for Caucasians vs. Hispanic/Latinos vs. Asians indicate that OS invariably exceeded predicted LE. This phenomenon is evidenced by positive values denoting the difference between OS and predicted LE. Among these three racial/ethnic groups (Caucasian, Hispanic/Latinos, Asians) the greatest difference between OS and predicted LE (favoring OS) at ten years was recorded in Asians (+10.4%), followed by Hispanic/Latinos (+9.3%) and Caucasians (+6.7%), in that order.

3.3 Observed overall survival versus predicted life expectancy in external beam radiotherapy patients

The comparison between OS and predicted LE at EBRT was also stratified according to four racial/ethnic groups: Caucasians (Figure 4A), African-Americans (Figure 4B), Hispanic/Latinos (Figure 4C) and Asians (Figure 4D). In Caucasians treated with EBRT, the OS was 87.4% at five years and 66.2% at ten years. For the same timepoints, the respective predicted LE values were 83.2% and 65.1%. The OS versus predicted LE values resulted in a difference of +4.2% at five years and +1.1% at ten years, favoring OS over predicted LE. In African-Americans treated with EBRT, the OS was 86.2% at five years and 65.6% at ten years. For the same timepoints, the respective predicted LE values were 86.7% and 72.0%. The OS versus predicted LE values resulted in a difference of -0.5% at five years and -6.4% at ten years, favoring predicted LE over OS. In Hispanic/Latinos treated with EBRT, the OS was 89.5% at five years and 71.0% at ten years. For the same timepoints, the respective predicted LE values were 84.2% and 66.1%. The OS versus predicted LE values resulted in a difference of +5.3% at five years and +4.9% at ten years, favoring OS over predicted LE. In Asians treated with EBRT, the OS was 88.7% at five years and 71.0% at ten years. For the same timepoints, the respective predicted LE values were 82.7% and 61.7%. The OS versus predicted LE values resulted in a difference in +6.0% at five years and +9.3% at ten years, favoring OS over predicted LE.

Figure 3B combines the recorded differences between observed survival versus predicted LE within the four examined racial/ethnic groups treated with EBRT. For African-Americans, the plotted line illustrating the difference between OS and predicted LE exhibits a lower OS compared to their respective predicted LE from five years onwards. Conversely, the plotted differences between OS and predicted LE between Caucasians, Hispanic/Latinos and Asians invariably favored observed survival over predicted LE. This phenomenon is evidenced by positive values denoting the difference between OS and predicted LE. Among these three racial/ethnic groups (Caucasian, Hispanic/Latinos, Asians) the greatest difference between OS and predicted LE (favoring OS) at ten years was recorded in Asians (+9.3%), followed by Hispanic/Latinos (+4.9%) and Caucasians (+1.1%), in that order.

4. Discussion

We hypothesized that SSA life tables' derived LE predictions differ to OS rates between racial/ethnic groups [6,7]. Our analysis revealed several noteworthy findings.

First, in RP patients, we invariably recorded better OS than that predicted by SSA life tables. The exception to this rule consisted of African-American patients, whose OS virtually perfectly corresponded to their respective LE prediction. It is of interest, that Asian, Hispanic/Latino and Caucasian RP patients exhibited comparable patterns of OS, that exceeded their respective LE predictions to a similar extent. In contrast, African-American RP patients' OS exhibited virtually no departures from their predicted LE. This observation indicates, that overall survival of African-Americans is worse than that of other racial/ethnic groups. This is applicable, even in the context of younger age of African-Americans relative to the three other racial/ethnic groups.

Second, the above observations indicate, that RP patients, except for African-Americans, exhibit better OS than the general North American population, from which LE predictions are derived. An explanation for the discrepancy between OS of African-Americans versus other racial/ethnic groups can be proposed. It is possible, that the general health of African-Americans as a group is worse than that of the three other racial/ethnic groups and represents the determinant of subsequent survival. This observation is worrisome and may be indicative of the need to correct for potential general health disadvantages in African-Americans, including those treated for localized PCa. Worse general health of African-Americans has been previously reported [12–15]. However, to the best of our knowledge, no previous publication contrasted SSA life tables' derived predicted LE with OS. In consequence, no previous investigators were able to quantify the overall survival detriment relative to predicted LE in African-Americans. Furthermore, no other investigators contrasted the figures recorded in African-Americans with those recorded for other racial/ethnic groups.

Third, we also examined differences between OS and predicted LE in EBRT patients. Our findings were similar to those described for RP patients. Specifically, OS for Asian, Hispanic/Latino and Caucasian EBRT patients, in general, exceeded that of their predicted LE. However, relative to RP patients, the overall survival benefit was of smaller magnitude. In EBRT patients, the difference between OS and predicted LE in Hispanic/Latinos was roughly half of the benefit recorded in Asians and the long-term survival advantage of Caucasians only corresponded to a fraction of that recorded in Asians. These observations are different from those recorded in RP patients where Asians, Hispanic/Latinos and Caucasians exhibited better OS than respective predicted LE to very similar extents. These differences possibly suggest that general health, which determines OS in these three racial/ethnic groups, differs more appreciably in EBRT patients than in RP patients. Nonetheless, all three racial/ethnic groups (Asians, Hispanic/Latinos and Caucasians) treated with EBRT invariably demonstrate better OS than predicted LE. This phenomenon was not applicable to African-American EBRT patients. Not only did they exhibit worst OS of all examined EBRT racial/ethnic groups (as was also observed in RP patients), but also exhibited worse OS than that of their respective predicted LE as of five years of follow up.

In summary, the SSA life tables' derived LE predictions underestimate the OS of Asian, Hispanic/Latino and Caucasian RP and EBRT patients. The degree of LE underestimation is most pronounced in RP candidates, in whom the favorable selection bias resulted in best OS. Conversely, the magnitude of the survival benefit is less pronounced in EBRT patients. We also observed a striking difference in OS versus predicted LE in African-Americans, relative to the three other racial/ethnic groups, regardless of treatment type. In both RP and EBRT groups, African-Americans did not exhibit better OS than predicted LE, like it was displayed in the three other racial/ethnic groups. Instead, African-Americans either perfectly followed their respective LE predictions, or their observed survival was inferior to those predictions. The above observations are important in clinical decision making [1,3,8,9]. Specifically, Asian, Hispanic/Latinos and Caucasian patients should be given a benefit of doubt for better LE than that predicted by SSA life tables. Conversely, the opposite applies to African-American patients. Potential conditions underlying the substantially worse survival of African-American patients should be scrutinized with the intent of eradicating this unfavorable survival pattern of African-American localized PCa patients treated with RP or EBRT, and possibly of African-Americans in general [15,16]. To address general health issues, the World Health Organization (WHO) suggests examining physical, emotional and social aspects of general health. Additionally, self-sustainment and personal independence should also be examined in addition to environmental factors [17]. These recommendations are very far reaching and are not exclusively applicable to urological practice and should be addressed in primary and secondary prevention settings.

Despite its novelty, our study has limitations. The first limitation is the nature of the study population, which was diagnosed and treated between 2004 and 2006. The selection of these individuals was dictated by the need of complete ten year follow-up. In consequence, more contemporary data, that had less maturity, could not be included. However, it is possible, that contemporary African-American patients will no longer exhibit the observed survival disadvantage [18]. However, this hypothesis will either be proven or rejected in studies with complete ten year follow up. Second, although Caucasians are well represented in the SEER database, the representation of African-Americans, Hispanic/Latinos and Asians is suboptimal. 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. Nonetheless, despite those observations, also the smallest sample size in this cohort, namely Asian men treated with either RP (n=1,241) or EBRT (n=1,742), was still adequate. Third, we focused on intermediate and high-risk patients, since these two risk groups represent the optimal patient pool for active treatment [19,20]. Therefore, our analysis did not include patients treated with active surveillance. Fourth, SEER does not provide comorbidities, in consequence, we could not perform a more detailed analysis to examine the underlying comorbidity profiles according to each racial/ethnic group. However, a small proportion of PCa patients die of their disease, even among high risk patients [21]. Furthermore, it may be argued that African-American men may have exhibited the most unfavorable comorbidity profile, especially in the light of previous data displaying marginal differences in cancer-specific mortality between Caucasian and African-American patients [22].

5. Conclusion

OS in RP and EBRT treated PCa patients is invariably better than respective life tables' derived LE predictions for Caucasians, Hispanic/Latinos and Asians, but not for African-Americans. The recorded survival disadvantage in African-American RP and EBRT patients, and if applicable also in other African-American populations, warrants detailed consideration and possibly corrective measures.

Declarations

Funding:

Not applicable

Conflicts of interest:

Not applicable

Data/Code availability:

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. Used codes for analyses can be provided. The data that support the findings of this study are available from the Surveillance, Epidemiology and End results database, (SEER) but restrictions apply to the availability of these data, which were used under licence for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of SEER.

Contribution to the study:

Christoph Würnschimmel: Drafting of manuscript, data collection and analyses

Luigi Nocera: Statistical analyses

Mike Wenzel: Drafting of manuscript

Claudia Collà Ruvolo: data collection

Zhe Tian: Conceived and designed statistical analyses, data collection

Fred Saad: Interpretation of data and critical revision

Alberto Briganti: Interpretation of data and critical revision

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Vincenzo Mirone: Interpretation of data and critical revision

Felix K.H. Chun: Study concept and design, Interpretation of data and critical revision

Derya Tilki: Administrative support, supervision

Markus Graefen: Administrative support, supervision

Pierre I. Karakiewicz: Study concept and design, statistical analyses, drafting of manuscript

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Figures

Figure 1

Box plots displaying Age distribution between racial/ethnic groups (Caucasian,African-American, Hispanic/Latino and Asian) treated with either radical prostatectomy (RP) or external beam radiotherapy (EBRT).

Figure 2

Kaplan-Meier curves of OS within Caucasian (A), African-American (B), Hispanic/Latino (C) and Asian (D) localized prostate cancer patients in the Surveillance, Epidemiology, and End Results database (2004-2006) treated by radical prostatectomy compared to predicted life expectancy derived by the Social Security Administration (SSA) life tables.

Figure 3

Differences between Social Security Administration (SSA) life tables' predicted life expectancy (dotted line) and observed survival (solid lines) at different timepoints within a population of localized prostate cancer patients from Caucasian, Hispanic/Latino, African-American and Asian patients treated by radical prostatectomy (A) or external beam radiotherapy (B) within the Surveillance, Epidemiology, and End Results database (2004-2006).

Figure 4

Kaplan-Meier curves of OS within Caucasian (A), African-American (B), Hispanic/Latino (C) and Asian (D) localized prostate cancer patients in the Surveillance, Epidemiology, and End Results database (2004-2006) treated by external beam radiotherapy compared to predicted life expectancy derived by the Social Security Administration (SSA) life tables.