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Effect of African-American race on cancer specific mortality differs according to clear cell vs. non-clear cell histologic subtype in metastatic renal cell carcinoma

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ABSTRACT

Aim: To test the effect of African-American race on cancer specific mortality (CSM) in clear cell metastatic renal cell carcinoma (ccmRCC) and non-ccmRCC.

Patients and methods: Within Surveillance, Epidemiology and End Results registry (2001–2014), we identified patients with ccmRCC and non-ccmRCC. We relied on propensity score (PS) matching to reduce the effect of inherent differences between African-American vs. Caucasian patients. After PS matching that included access to cytoreductive nephrectomy (CNT), cumulative incidence, competing-risks regression (CRR) models and landmark analyses tested the effect of race on CSM.

Results: Before PS matching, African-American patients accounted for 7.0 and 24.5% of respectively ccmRCC (N = 6742) and non-ccmRCC patients (N = 766). After PS matching, African-American patients accounted for 22.3 and 33.5% of respectively ccmRCC (N = 2050) and non-ccmRCC (N = 391) matched cohorts. In multivariable CRR models focusing on ccmRCC, higher CSM was recorded in African-Americans (HR:1.27, $p < 0.001$). Conversely, in non-ccmRCC, lower CSM was recorded in African-Americans (HR:0.54, $p < 0.001$). Landmark analyses rejected the hypothesis of immortal time bias.

Conclusion: African-Americans experienced higher CSM in ccmRCC. Conversely, African-Americans experienced lower CSM, when diagnosed with non-ccmRCC. These differences are independent of access to CNT and warrant further study since they may have an impact on efficacy or access to systemic therapies.

1. Introduction

To date only two studies specifically examined the effect of race, defined as African-American vs. Caucasian, in the setting of metastatic renal cell carcinoma (mRCC) [1,2].

Specifically, Rose et al. relied on National Cancer Database (NCDB) (1998–2011) and studied patients with either advanced or mRCC. Authors showed a survival disadvantage for African-Americans relative to Caucasians, despite the survival improvement since the introduction of targeted therapies [1]. Similarly, Tripathi et al., in a historical (1992–2002) and small institutional cohort (N = 122 patients), also recorded a survival disadvantage in African-American relative to Caucasian patients [2]. However, analyses focusing on non-clear cell mRCC (non-ccmRCC) were not performed. Thus, a comparison of survival outcomes between African-American vs. Caucasian patients could not be performed according to histologic subtype [1,2].

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Table 1
Clinical and pathological characteristics of patients with clear cell metastatic renal cell stratified according to race (African-American vs. Caucasian) before and after propensity score matching.

Variables names No of patients (%)	Clear-Cell Metastatic Renal Cell Carcinoma							
	Before propensity-score matching				After propensity-score matching			
	Overall (N = 6742)	African-American (N = 473, 7.0%)	Caucasian (N = 6269, 93.0%)	*P-value*	Overall (N = 2050)	African-American (N = 457, 22.3%)	Caucasian (N = 1593, 77.7%)	*P-value*
Age group				< 0.001				1.0
≤65	4072 (60.4)	321 (67.9)	3751 (59.8)		1391 (67.9)	311 (68.1)	1080 (67.8)	
> 65	2670 (39.6)	152 (32.1)	2518 (40.2)		659 (32.1)	146 (31.9)	513 (32.2)	
Year of diagnosis				0.5				0.6
2001–2005	1696 (25.2)	123 (26.0)	1573 (25.1)		488 (23.8)	116 (25.4)	372 (23.4)	
2006–2009	2003 (29.7)	149 (31.5)	1854 (29.6)		650 (31.7)	144 (31.5)	506 (31.8)	
2010–2014	3043 (45.1)	201 (42.5)	2842 (45.3)		912 (44.5)	197 (43.1)	715 (44.9)	
Gender				0.3				0.3
Male	4625 (68.6)	314 (66.4)	4311 (68.8)		1431 (69.8)	309 (67.6)	1122 (70.4)	
Female	2117 (31.4)	159 (33.6)	1958 (31.2)		619 (30.2)	148 (32.4)	471 (29.6)	
Marital status				< 0.001				0.2
Married	4240 (62.9)	214 (45.2)	4026 (64.2)		1045 (51)	214 (46.8)	831 (52.2)	
Never Married	928 (13.8)	125 (26.4)	803 (12.8)		483 (23.6)	119 (26.0)	364 (22.8)	
Previously Married	1355 (20.1)	112 (23.7)	1243 (19.8)		465 (22.7)	109 (23.9)	356 (22.3)	
Unknown	219 (3.2)	22 (4.7)	197 (3.1)		57 (2.8)	15 (3.3)	42 (2.6)	
T-stage				0.04				0.9
T_{1-2}	1993 (29.6)	153 (32.3)	1839 (29.4)		640 (31.2)	146 (31.9)	494 (31.0)	
T_{3-4}	3213 (47.7)	199 (42.1)	3014 (48.1)		889 (43.4)	194 (42.5)	695 (43.6)	
T_{x-0}	1536 (22.8)	121 (25.6)	1416 (22.6)		521 (25.4)	117 (25.6)	404 (25.4)	
Grade				< 0.001				0.8
G_{1-2}	1387 (20.6)	102 (21.6)	1285 (20.5)		406 (19.8)	95 (20.8)	311 (19.5)	
G_{3-4}	3034 (45.0)	176 (37.2)	2858 (45.6)		797 (38.9)	173 (37.9)	624 (39.2)	
Gx	2321 (34.4)	195 (41.2)	2126 (33.9)		847 (41.3)	189 (41.4)	658 (41.3)	
Cytoreductive nephrectomy				< 0.001				0.5
No	2614 (38.8)	233 (49.3)	2381 (38.0)		976 (47.6)	224 (49.0)	752 (47.2)	
Yes	4128 (61.2)	240 (50.7)	3888 (62.0)		1074 (52.4)	233 (51.0)	841 (52.8)	

To the best of our knowledge, the effect of race on cancer-specific mortality (CSM) has never been examined in specific analyses that were formally stratified according to histologic subtype, defined as clear cell metastatic RCC (ccmRCC) vs. non-ccmRCC. To address this void, we examined the effect of race (African-American vs. Caucasian) on CSM after stratification according to histologic subtype (ccmRCC, non-ccmRCC).

2. Material and methods

2.1. Data source and study population

Within the SEER database (2001–2014), we focused on African-American and Caucasian patients with mRCC (International Classification of Disease for Oncology C64.9) that included ccmRCC or non-ccmRCC (papillary and chromophobe) histologic subtypes, aged ≥ 18 years old with histologically confirmed mRCC. Death certificate only, autopsy cases and patients with missing information about laterality or bilateral tumors were removed from analyses.

2.2. Variables definition

Race was coded as either African-American or Caucasian according to the SEER database.

Covariates included surgical treatment [cytoreductive nephrectomy (CNT), no-CNT], gender, age at diagnosis (≤65, > 65), marital status (married, never married, previously married and unknown), year of diagnosis (historical: 2001–2005, intermediate: 2006–2009, contemporary: 2010–2014), T-stage ($T_{1/2}$, $T_{3/4}$, $T_{x/0}$) and tumor grade (G_1/G_2, G_3/G_4, G_x). CSM was defined as a death related to kidney cancer according to SEER mortality code. All other deaths were considered as other-cause mortality (OCM).

2.3. Statistical analyses

Descriptive statistics relied on tests of means and proportions and respectively, used the t-test and the chi-square. Three sets of analyses were performed in separate cohorts of patients with either ccmRCC or non-ccmRCC.

First, within each cohort, we relied on propensity score matching according to the nearest neighbor between Caucasian and African-American patients to reduce the effect of selection bias. The propensity matched cohorts of ccmRCC and non-ccmRCC were balanced according to all covariates including year of diagnosis, gender, age at diagnosis, marital status, tumor grade, T-stage and CNT status [3].

Second, we tested the effect of African-American vs. Caucasian race on OCM and CSM in cumulative incidence plots and competing risks regression (CRR) models. Cumulative incidence plots depicted 24-month OCM and CSM rates, after respectively accounting for CSM and OCM [4,5]. Multivariable CRR models accounted for the effect of CSM on OCM, or for the effect of OCM on CSM, to provide the most unbiased estimates of both outcomes after adjusting for year of diagnosis, gender, age at diagnosis, marital status, tumor grade, T-stage and CNT status [6]. Third, landmark analyses were performed at 6 months after time of diagnosis, to address the potential effect of immortal time bias, which may favorably affect either African-American or Caucasian patients [7].

All statistical tests were two-sided. The level of significance was set at $p < 0.05$. Analyses were performed using the R software environment for statistical computing and graphics (version 3.4.1; http://www.r-project.org/).

3. Results

3.1. Characteristics of ccmRCC patients

Among 6742 ccmRCC patients, 7.0% were African-American