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Review

Biomarkers for evaluating racial disparities in clinical outcome in patients with renal cell carcinoma

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ABSTRACT

The bulk of the literature on kidney cancer in African Americans comes from population-based studies of incidence and survival over varying periods of time using databases from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (NCI). The purpose of this review is to summarize the literature on racial disparities in clinical outcome in patients with renal cell carcinoma (RCC) with the objective of identifying any biomarkers that might point to a biological explanation for these differences. Special attention is given to biomarkers of systemic inflammation and their potential utility for kinetic risk assessment. In addition, arguments are presented as to why the study of ethnic and racial disparities is a promising strategy for accelerating the pace of biomarker development for all patients with RCC.

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1. Introduction

The Centers for Disease Control and Prevention report that an estimated 41.7 million people living in the U.S. in 2013 identified themselves as being black or African American representing 13.2% of the U.S. population (Centers for Disease Control and Prevention, http://www.cdc.gov/minorityhealth/populations/REMP/black.html#Demographics). The bulk of the literature on kidney cancer in African Americans comes from population-based studies of incidence and survival over varying periods of time using databases from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (NCI). The purpose of this review is to summarize the literature on racial disparities in clinical outcome in patients with renal cell carcinoma (RCC) with the objective of identifying any biomarkers that might point to a biological explanation for these differences. In addition, arguments are presented as to why the study of ethnic and racial disparities is a promising strategy for RCC biomarker development.

2. Risk factors for developing RCC

Risk factors for developing RCC include such lifestyle influences as tobacco use, alcohol use, and obesity as well as hypertension (Lipworth et al., 2011a). Racial and ethnic differences in lifestyle may thereby contribute to racial disparities in the propensity for developing in RCC though the limited amount of published data on African Americans prevent one from drawing any firm conclusions in this regard. However, these factors likely account for less than half of all cases of RCC among non-Hispanic whites. Physical activity is a lifestyle influence that was assessed as a risk factor for RCC in a population based case-control study of 1217 cases (361 black, 856 white) and 1235 controls (523 black, 712 white) that were frequency-matched for age, race, and gender (Xiao et al., 2014). The authors concluded that physical activity may be inversely associated with RCC risk for whites, but not for blacks.

3. Descriptive epidemiology

Demographic differences in incidence and survival have been reported for patients with RCC though this has not been uniformly the case. There is evidence to suggest that access to nephrectomy with curative intent is limited for blacks relative to whites and that this may be the primary reason for any differences in clinical outcome. However, differences in nephrectomy rates were not associated with racial disparities in overall survival (OS) when assessed in a study of SEER data that included 12,516 patients of all stages diagnosed and treated for RCC between 2000 and 2004 (Zini et al., 2008). Conversely, a different conclusion was drawn from a study that linked data from the SEER and Medicare databases to select patients who were 65 years old or older and diagnosed with RCC from 1986 to 1999 (Berndt et al., 2007). The percentage of blacks (n = 964) who underwent nephrectomy in this study was significantly lower than the percentage of whites (n = 10,482) at 61.2% versus 70.4%, respectively ($p < 0.0001$). Even with adjustment for age, gender, median income, cancer stage, tumor size, and comorbidity index, blacks were less likely to undergo nephrectomy than whites (risk ratio = 0.93; 95% CI, 0.90–0.96). Furthermore, a racial disparity in OS remained after adjustment for demographic and cancer prognostic factors (hazard ratio [HR] = 1.16; 95% CI, 1.07–1.25), though additional adjustment for comorbidity index and nephrectomy status substantially reduced the disparity (HR = 1.00; 95% CI, 0.93–1.09). One may infer from these data that the lower survival rate among blacks relative to whites can largely be explained by the increased number of comorbid health conditions and the lower rate of surgical treatment for blacks.

Incidence and OS for RCC were also examined in a study of patients listed in the California Cancer Registry as having a diagnosis of RCC from 1988 to 2004 (Stafford et al., 2008). Blacks in this study (n = 2762) were found to have a significantly higher incidence ($p < 0.0001$) and lower OS ($p < 0.0001$) than whites (n = 27,304) and other ethnicities despites having more localized cancer ($p < 0.005$). In addition, blacks were diagnosed at a younger age ($p < 0.0001$) whereas Asian/Pacific Islanders (n = 1984) had a lower incidence ($p < 0.0001$) and a higher OS rate (<0.05). Unfortunately, nephrectomy rates were not reported in this study and cannot thereby shed light on this seemingly paradoxical finding.

Trends in incidence and OS of blacks and whites were also assessed in a large study from the national SEER database of adults over the age of 19 who were diagnosed with RCC between 1975 and 1998 (Vaishampayan et al., 2003). In addition, blacks and whites were independently subdivided by age to compare younger patients (ages 20–59) to patients who were ≥60 years of age. A total of 40,785 cases of adult non-urothelial cancers of the kidney were included in the analysis with 86.9% classified as RCC and 13.1% classified as other histologic subtypes. The incidence of RCC was found to be increasing for blacks and whites, though the relative incidence was higher for African Americans (n = 3552) than whites (n = 37,233). This rise in incidence was largely attributed to increases in localized disease (50.74% of all patients) presumably secondary to incidental findings associated with the introduction and widespread availability of computerized tomography scanners. A total of 24,993 adult RCC cases were included in the survival analysis for the years of 1975–1993 (2024 blacks and 22,969 whites). The magnitude of the demographic difference in survival was greatest among younger patients with localized disease with a median OS of 190 months (15.8 years) versus 259 months (21.6 years) for blacks versus whites, respectively ($p < 0.0001$). Again, no data on treatment were included in the analysis. However, a more recent study from the national SEER database of blacks (n = 4359) and whites (n = 34,991) who were diagnosed with invasive RCC from 1992 to 2007 and followed through 2008 reported a survival advantage for whites regardless of age, gender, tumor stage or size, histological subtype, or surgical treatment (Chow et al., 2013). The only exception to this pattern was found among patients who did not undergo nephrectomy (10.5% of whites and 14.5% of blacks) where the relative 5-year OS rates were similarly poor at 10.0% (95% CI 8.8, 11.2) and 11.0% (95% CI 8.3, 14.1), respectively.

Taken as a whole, the data on nephrectomy status consistently indicate that rates are lower for blacks versus whites regardless of stage. This difference in nephrectomy rates may