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Associations of Renal Cell Carcinoma Subtype with Patient Demographics, Comorbidities, and Neighborhood Socioeconomic Status in the California Population

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Abstract

Background: Renal cell carcinoma (RCC) subtypes differ in molecular characteristics and prognosis. We investigated the associations of RCC subtype with patient demographics, comorbidity, and neighborhood socioeconomic status (nSES).

Methods: Using linked California Cancer Registry and Office of Statewide Health Planning and Development data, we identified history of hypertension, diabetes, and kidney disease prior to RCC diagnosis in Asian/Pacific Islander, non-Latino Black, Latino, and non-Latino White adults diagnosed with their first pathologically-confirmed RCC from 2005 through 2015. We used multinomial multivariable logistic regression to model the association of demographics, comorbidity, and nSES with clear cell, papillary, and chromophobe RCC subtype.

Results: Of the 40,016 RCC cases included, 62.6% were clear cell, 10.9% papillary, and 5.9% chromophobe. The distribution of subtypes differed strikingly by race and ethnicity, ranging from 40.4% clear cell and 30.4% papillary in non-Latino Black adults to 70.7% clear cell and 4.5% papillary in Latino adults. In multivariable analysis, non-Latino Black individuals had a higher likelihood of presenting with papillary (odds ratio (OR) 3.99, 95% confidence interval 3.61-4.42) and chromophobe (OR 1.81, 1.54-2.13) vs clear cell subtype compared to non-Latino White individuals. Both hypertension (OR 1.19, 1.10-1.29) and kidney disease (OR 2.38, 2.04-2.77 end stage disease; OR 1.52, 1.33-1.72 non end-stage disease) were associated with papillary subtype. Diabetes was inversely associated with both papillary (OR 0.63, 0.58-0.69) and chromophobe (OR 0.61, 0.54-0.70) subtypes.

Conclusion: RCC subtype is independently associated with patient demographics, and comorbidity.

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Impact: Targeted RCC treatments or RCC prevention efforts may have differential impact across population subgroups.

Keywords

Renal cell carcinoma; Renal cell carcinoma subtypes; Population-based study

Introduction

Kidney cancer is one of the top 10 most commonly diagnosed cancers in both men and women in the United States[1]. The vast majority of kidney cancers are renal cell carcinomas (RCC),[2,3] a heterogeneous group comprised of distinct histological subtypes that exhibit different genetic, molecular, and clinical characteristics.[4–7] The histologic subtype of a renal tumor affects prognosis and has implications for disease management.[4,8] Furthermore, it has been suggested that RCC subtypes are etiologically distinct,[9] which has implications for prevention efforts.

The most common RCC subtype is clear cell RCC, accounting for approximately 70-75% of RCC in the United States, followed by papillary (15%) and chromophobe tumors (5%).[4] The distribution of RCC subtypes varies by race and ethnicity, sex, age, and comorbidity.[3,6,9,10 11,12] The prevalence of papillary RCC is reported to be approximately three-fold higher in Black individuals than White individuals.[3,6,9] Yet subtype distributions in Latino and Asian American/Pacific Islander groups have not been extensively explored in population-based data. Women have a lower prevalence of papillary[3,9] and higher prevalence of chromophobe RCC[3] than men. In single institution and case-control studies, end-stage renal disease (ESRD) has been associated with papillary and chromophobe subtypes,[3] and obesity has been associated with clear cell and chromophobe RCC[9]. Using population-based cancer registry data from the entire state of California, we described the associations of RCC subtype with patient demographics, comorbidity, and neighborhood socioeconomic status (nSES). This study is unique in that we were able to assess all these factors using one racially and socioeconomically diverse population-based sample.

Materials and Methods

The California Cancer Registry (CCR) is a state-mandated registry collecting high quality data on all cancer cases diagnosed in California residents since 1988. These population-based data are incorporated in the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program and the Center for Disease Control and Prevention's (CDC) National Program of Cancer Registries (NPCR).

The CCR routinely collects information on patient demographics and tumor characteristics (such as site, histology, and stage), and geocodes patient address at time of diagnosis. Geocoded addresses are linked to Census data and appended to a composite index of neighborhood socio-economic status consisting of block group level measures of income, education, housing, and employment[13 14]. Patients are assigned to quintiles of neighborhood SES based on the statewide distribution, with 1 corresponding to the lowest quintile of nSES. Additionally, patient comorbidity data is available from linkage to the California

Office of Statewide Health Planning and Development (OSHPD) patient discharge, emergency department, and ambulatory surgery data[15].

Using CCR data we identified Asian American/Pacific Islander, non-Latino Black, Latino, and non-Latino White adult (age >=18 years) men and women diagnosed with their first pathologically confirmed RCC from 2005 through 2015, excluding cases diagnosed on death certificate or autopsy only. We also excluded patients with no OSHPD data available prior to their date of cancer diagnosis (n=3,343), resulting in N=40,016 RCC cases for analysis.

We identified RCC histologies using International Classification of Disease (ICD) for Oncology version 3.1 morphology codes, and defined RCC subtypes as follows: clear cell (8310); papillary (8050, 8260, 8342); chromophobe (8270, 8317); other (8318, 8319, 8290, 8510); and unclassified/not otherwise specified (8312).

We defined hypertension (HTN), diabetes (DM), chronic kidney disease (CKD), and end-stage renal disease (ESRD) if any of these ICD-9 and ICD-10 diagnosis codes (Supplementary table S1) were present in OSHPD data at any time prior to RCC diagnosis. HTN and CKD are closely related and have a bidirectional relationship: hypertension can both lead to and result from chronic kidney disease. We therefore created a joint kidney disease/hypertension variable that prioritized the presence of kidney disease over the presence of hypertension using the following categories: ESRD (with or without hypertension), CKD (not end-stage, with or without hypertension), hypertension without kidney disease, neither kidney disease nor hypertension.

We conducted multinomial multivariable logistic regression to examine the associations of demographic, comorbidity, and nSES characteristics with clear cell, papillary, and chromophobe RCC subtype. Odds ratios (OR) and 95% confidence intervals (CI) were estimated, using clear cell subtype as the referent group. Variables included in the model were determined *a priori* and included age, sex, a joint race and ethnicity variable, a joint kidney disease/hypertension variable, diabetes, nSES, and year of diagnosis. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC). Two-sided p values of $p<.05$ were considered significant.

This study is covered under the Greater Bay Area Cancer Registry protocol approved by the Institutional Review Board of the Cancer Prevention Institute of California.

Data Availability

The data analyzed in this study were obtained from the California Cancer Registry. More information on how to request California Cancer Registry is available at https://www.ccrcal.org/retrieve-data/data-for-researchers/how-to-request-ccr-data/.

Results

As shown in Table 1, the study population included 40,016 individuals with RCC. Clear cell tumors represented the most common subtype (62.6%), followed by unclassified or not otherwise specified (18.3%), papillary (10.9%), chromophobe (5.9%), and other (2.3%). The majority of the study population was non-Latino White (57.4%) and male (64.2%). The

median age at diagnosis was 63 (IQR 54-72). Over half of the cases (59.9%) were diagnosed at stage I. The prevalence of DM among RCC cases was 24.7%, and the prevalence of HTN 58.3%. Almost 13% of individuals with RCC had a diagnosis code of CKD prior to their diagnosis of RCC, of which one third of patients had evidence of ESRD.

Table 2 shows the distributions of race and ethnicity, sex, age, comorbidity, and nSES by RCC subtype. There were striking differences in the proportion of clear cell and papillary subtypes by race and ethnicity, ranging from 40.4% clear cell and 30.4% papillary in non-Latino Black adults to 70.7% clear cell and 4.5% papillary in Latino adults. In multivariable regression, non-Latino Black patients had much higher odds than non-Latino White patients of diagnosis with papillary (OR 3.99, 3.61-4.42) and chromophobe RCC (OR 1.81, 1.54-2.13) compared to clear cell RCC (Table 2). Conversely, Latino and Asian American/Pacific Islander patients had lower odds than non-Latino White patients of diagnosis with papillary (OR 0.38, 0.34-0.42 and OR 0.55, 0.48-0.64, respectively) or chromophobe tumors (OR 0.72, 0.64-0.80, and OR 0.78, 0.66-0.92, respectively) compared to clear cell. Females had lower odds than males of papillary (OR 0.51, 0.48-0.56) and higher odds of chromophobe (OR 1.41, 1.30-1.54) versus clear cell tumors. Compared to patients in their seventh decade of life, younger patients had lower odds of papillary RCC (OR 0.72, 0.64-0.80 age <50 years; OR 0.86, 0.79-0.94 age 50-59 years) versus clear cell RCC. At the extremes of age, patients had higher odds of being diagnosed with chromophobe versus clear cell subtype when compared to patients in their 60's (OR 1.53, 1.35-1.74 age <50 years; OR 1.21, 1.02-1.43 age >=80 years). Residing in neighborhoods of lower socio-economic status was inversely associated with both papillary and chromophobe subtype compared to clear cell (lowest versus highest nSES quintile OR 0.85, 0.76-0.96 papillary; and OR 0.68, 0.59-0.79 chromophobe).

Patients with end-stage renal disease (OR 2.38, 2.04-2.77) and those with chronic kidney disease (OR 1.52, 1.33-1.72) had higher odds of papillary RCC, as did those with hypertension (OR 1.19, 1.10-1.29). Conversely, diabetic patients had lower odds of a diagnosis of either papillary (OR 0.63, 0.58-0.69) or chromophobe subtypes (OR 0.61, 0.54-0.70) compared to clear cell RCC. The associations of diabetes with subtype were similar in models stratified by sex (Supplementary table S2). Patients with hypertension or kidney disease were less likely to be diagnosed with chromophobe subtype compared to clear cell, but this inverse association only reached statistical significance for CKD (OR 0.78, 0.64-0.95).

The effect of these comorbidities was independent. There was no significant interaction between diabetes and kidney disease/hypertension ($p_{interaction}$ =0.31); the associations of kidney disease/hypertension with subtype were similar in a model stratified by diabetes, as were the associations of diabetes with subtype in a model stratified by the kidney disease/hypertension variable. Table 3 shows the associations of comorbidity and subtype using a joint comorbidity variable. A diagnosis of diabetes attenuated the association of hypertension and kidney disease with papillary subtype and accentuated the inverse association between hypertension and kidney disease with chromophobe subtype.

Discussion

RCC subtype distribution varies across patient populations. We found strong and consistent associations between RCC subtype and race and ethnicity. Notably, when compared to non-Latino White RCC patients, non-Latino Black patients had four-fold higher odds of being diagnosed with papillary RCC and almost two-fold higher odds of diagnosis with chromophobe RCC. These are similar to odds reported in both single-institution[3] and population-based[6] studies. We also found that Latino and Asian American/Pacific Islander RCC patients were more likely to be diagnosed with clear cell RCC than papillary or chromophobe, with approximately two-fold lower odds of papillary versus clear cell RCC. These findings are also supported by previous studies. Using nationwide SEER data[6], Olshan et al reported similar estimates favoring clear cell subtype in Asian American/Pacific Islander patients, and in a population-based study using data from the Arizona Cancer Registry, Batai et al reported Latinos had almost two-fold greater odds of diagnosis with clear cell than other RCC histologies[12].

As has been demonstrated in other kidney diseases, genetic variation may play a role in observed racial/ethnic differences in RCC subtypes. For example, renal medullary carcinoma primarily affects people of African descent. This subtype of RCC occurs almost exclusively in the context of sickle cell trait,[16] which results from a mutation in the hemoglobin beta gene and is more prevalent in people of African ancestry and those from subtropical regions. Similarly, variants of the apoprotein L1 (*APOL1*) gene, which are present only in people of recent African ancestry, have been associated with various nephropathies and ESRD.[17] While a role for *ApoL1* in RCC has been proposed,[18] to date there is no evidence linking the two. Although race and ethnicity are social constructs that do not equate to genetic ancestry, it is probable that individuals identified in the cancer registry data as having Black race are more likely to have African ancestry. We were unable to examine cases of renal medullary carcinoma due to small sample size.

It has been suggested that the strong racial associations with RCC subtype may reflect the different prevalence of comorbidities such as ESRD in different racial/ethnic groups. However, we found a significant association of comorbidity with subtype in a model that included race and ethnicity. Both kidney disease and hypertension were associated with papillary, but not chromophobe RCC. This association appeared to correlate with severity of kidney disease, with the strongest association observed for end-stage renal disease, which had over two-fold increased odds of papillary versus clear cell histology. We also noted a very strong and consistent association of diabetes with clear cell subtype, independent of HTN and CKD; for patients with diabetes, the odds were 50% greater of having clear cell subtype than either papillary or chromophobe. Our findings align with those from a single institution study by Lowrance et al. who found an association between diabetes and clear cell histology of borderline statistical significance[19] but contrast with findings from the Nurse's Health Study, where type 2 diabetes was associated with a stronger risk of developing non-clear cell RCC in women.[20]

Higher BMI has previously been associated with increased risk of developing clear cell [9,19,21–23] and less consistently, chromophobe [9,21,23] subtype. We did not have data on BMI

available in our study and it is likely that the association we detected with diabetes may be at least in part mediated by obesity. It is likely that diabetes and obesity act via the same mechanism to increase the risk of clear cell RCC. Both conditions are associated with a state of insulin resistance and increased circulating levels of insulin-like growth factor 1 (IGF-1), which stimulates cellular proliferation and inhibits apoptosis. Furthermore, hyperglycemia stimulates tumor cell proliferation and hyperleptinemia stimulates angiogenesis[24]. In addition, chronic inflammation and chronic renal hypoxia have also been proposed mechanisms linking obesity and diabetes to clear cell RCC[21,22].

Differences by sex exist both in overall RCC incidence rates and subtype distribution. Consistent with previous studies, we found that females were less likely than males to be diagnosed with papillary RCC[3,9] and more likely to be diagnosed with chromophobe RCC[3]. Gender differences in lifestyle factors such as smoking could play a role in these differences. In a single-institution study, Patel et al reported the prevalence of smoking was significantly lower in patients with chromophobe compared to clear cell RCC.[25] Similarly, a study using data collected through the CDC's National Program for Cancer Registries Enhancing Cancer Registry Data for Comparative Effectiveness Research (CER) Project found an inverse association of smoking with chromophobe RCC compared to clear cell[26]. Women have a lower prevalence of smoking than men[27] and the difference in smoking prevalence between men and women was more pronounced historically, during the time period that would have affected the diagnosis years included in our study[28]. While the role of genetics, genomics, and sex hormones has been studied in relation to differences in RCC risk and progression by sex, their influence on RCC subtype has not been determined.[29] Our finding that lower nSES, independent of race and ethnicity and comorbidity, was associated with clear cell subtype likely also reflects the role of lifestyle factors (such as diet and smoking) and shared environmental and contextual exposures on RCC pathogenesis.

Our study has several limitations. Although the California Cancer Registry consistently meets the highest quality standards, it is possible that tumor histology was misclassified for a small number of cases. We conducted a review of 498 cases for whom we had electronic pathology reports available and found that overall agreement between the subtype recorded in the registry and that found in the pathology report was 88.8% (Supplementary table S3). Using pathology reports as the gold standard, the specificity was uniformly high ranging from 97.6 to 99.8, and sensitivity ranged from 86.2 to 99.6. These results are comparable to those reported by Shuch et al.[30]

The proportion of RCC that are histologically unclassified has steadily decreased over time following the release of the 2004 WHO Classification of Tumors. Gansler et al report variation in this trend by facility type, with a larger decrease in NCI-designated programs and academic centers[31]. In our study the proportion of unclassified RCC dropped from 22.4% in 2005 to 14.7% in 2015. Yet the proportions of clear cell, papillary, and chromophobe subtypes within cases of specified histologic type remained fairly constant, suggesting that this trend in histology coding practice would not largely influence our results.

Because the comorbidity data relied on hospital encounters (inpatient, emergency department, and ambulatory surgery center) we were unable to accurately determine the onset and duration of comorbidities, limiting our ability to incorporate timing of comorbidity in our analysis. Additionally, there may have been misclassification of comorbidity status. Hospital encounter-based data are more likely to reflect more severe disease. Some conditions, such as diabetes and hypertension, which are usually managed on an outpatient basis, may therefore have been under-captured in these data. To maximize our sensitivity for detecting these conditions our definitions required the presence of one diagnostic code with a date preceding the cancer diagnosis. Although the prevalence of hypertension and diabetes in our study falls within the ranges reported in similar RCC studies,[3,9,10,19,32–34] we recognize that our approach may have resulted in some degree of misclassification. We therefore performed sensitivity analyses using comorbidity definitions that required the presence of a diagnostic code on a minimum of two separate discharges, and definitions that required the date of the diagnostic code to precede the cancer diagnosis date by at least two years. Results of these sensitivity analyses were similar to those using the more liberal definition (Supplementary table S4).

The prevalence of CKD in our study was higher than that reported in other RCC studies[10,32]. The relationship between RCC and CKD is bidirectional and it is likely that we may have misclassified some patients with CKD secondary to RCC as having pre-existing CKD; this non-differential misclassification may have biased our results toward the null. Sensitivity analyses restricting to CKD codes present at least two years prior to RCC diagnosis yielded prevalence estimates that were more comparable to those reported in the other studies and showed similar associations with subtype as analyses with our original CKD classification.

Finally, as previously mentioned, we were unable to control for smoking or obesity as these risk factors are not routinely collected registry data items. Nor were we able to distinguish between papillary type 1 and 2 tumors because the ICD-O-3 codes used to record tumor histology in the registry did not distinguish these.

Despite these limitations, our study clearly shows that the RCC subtypes are distributed differently across population groups. Importantly, this is the first study of renal cell subtypes in a racially and socioeconomically diverse population-based sample to include comorbid conditions. While the primary objective of our study was to describe the associations of RCC subtype with patient characteristics and comorbidity, our results could have implications for both primary prevention efforts and treatment outcomes. Interventions targeting specific RCC risk factors will likely have greater effects on certain RCC subtypes, and will therefore have differential effects on certain populations. For example, interventions targeting obesity may be expected to have greater effects on clear cell RCC whereas those targeting hypertension and kidney disease would likely have greater effects on papillary RCC. At the population level, this could affect racial/ethnic disparities in RCC rates. Similarly, targeted treatments whose efficacy is subtype-specific could result in differential improvements in survival outcomes at the population level.

Conclusion

RCC subtype is associated with patient demographic characteristics, comorbidity status, and nSES. These associations suggest that prevention efforts aimed at reducing the prevalence of RCC risk factors or targeted treatments developed focusing on one subtype may have differential impact across population subgroups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations list:

CI	confidence interval
CKD	chronic kidney disease
DM	diabetes mellitus
ESRD	end-stage renal disease
HTN	hypertension
ICD	International Classification of Disease
NL	non-Latino
NOS	not otherwise specified
nSES	neighborhood socioeconomic status
OR	odds ratio
RCC	renal cell carcinoma
SEER	Surveillance Epidemiology and End Results
SES	socioeconomic status

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Table 1.

Microscopically-confirmed renal cell carcinoma diagnosed in adult California residents, 2005-2015

	N	Percent
Total	40,016	100.0%
Histologic subtype		
Clear cell	25,051	62.6%
Papillary	4,363	10.9%
Chromophobe	2,372	5.9%
Other	924	2.3%
RCC NOS	7,306	18.3%
Race and ethnicity		
Asian American/Pacific Islander	3,149	7.9%
Latino	10,924	27.3%
NL Black	2,982	7.5%
NL White	22,961	57.4%
Sex		
Female	14,321	35.8%
Male	25,695	64.2%
Age at diagnosis, years		
Median (interquartile range)	63	(54-72)
<50	6,456	16.1%
50-59	9,413	23.5%
60-69	11,971	29.9%
70-79	8,604	21.5%
80+	3,572	8.9%
Neighborhood SES quintile at time of diagnosis		
1 (lowest SES)	6,746	16.9%
2 (lower-middle SES)	8,026	20.1%
3 (middle SES)	8,497	21.2%
4 (upper-middle SES)	8,651	21.6%
5 (highest SES)	8,096	20.2%
AJCC stage		
Stage I	23,972	59.9%
Stage II	3,730	9.3%
Stage III	5,560	13.9%
Stage IV	5,557	13.9%
Unknown	1,197	3.0%
HTN		
No HTN	16,687	41.7%
HTN	23,329	58.3%

	N	Percent
DM		
No DM	30,150	75.3%
DM	9,866	24.7%
CKD		
No CKD	34,880	87.2%
CKD, not end stage	3,397	8.5%
ESRD	1,739	4.3%
Combined comorbidities		
No CKD no DM no HTN	15,579	38.9%
ESRD no DM	721	1.8%
ESRD + DM	1,018	2.5%
CKD no DM	1,512	3.8%
CKD + DM	1,885	4.7%
HTN only	12,338	30.8%
HTN + DM	6,027	15.1%
DM only	936	2.3%
Year of diagnosis		
2005	2,671	6.7%
2006	2,876	7.2%
2007	3,065	7.7%
2008	3,521	8.8%
2009	3,606	9.0%
2010	3,677	9.2%
2011	3,841	9.6%
2012	3,923	9.8%
2013	4,086	10.2%
2014	4,181	10.4%
2015	4,569	11.4%

Limited to first kidney primary and patients with Office of Statewide Health Planning and Development data.

Percentages may not add to 100% due to rounding.

Abbreviations: RCC NOS = renal cell carcinoma, not otherwise specified; NL = non-Latino; SES = socioeconomic status; HTN = hypertension; DM = diabetes mellitus; CKD = chronic kidney disease; ESRD = end-stage renal disease.

Table 2.

Associations of patient and tumor characteristics with renal cell carcinoma subtype in adult California residents, 2005-2015.

		Clear cell (N=25,051)	Papillary (N=4,363)	Chromophobe (N=2,372)	Papillary vs Clear cell	Chromophobe vs Clear cell
		N (%)	N (%)	N (%)	OR (95% CI)	OR (95% CI)
Race and ethnicity	Asian American/Pacific Islander	2,125 (8.5%)	225 (5.2%)	175 (7.4%)	**0.55 (0.48-0.64)**	**0.78 (0.66-0.92)**
	Latino	7,728 (30.8%)	496 (11.4%)	546 (23.0%)	**0.38 (0.34-0.42)**	**0.72 (0.64-0.80)**
	NL Black	1,205 (4.8%)	907 (20.8%)	203 (8.6%)	**3.99 (3.61-4.42)**	**1.81 (1.54-2.13)**
	NL White	13,993 (55.9%)	2,735 (62.7%)	1,448 (61.0%)	Reference	Reference
Sex	Female	9,331 (37.2%)	997 (22.9%)	1,068 (45.0%)	**0.51 (0.48-0.56)**	**1.41 (1.30-1.54)**
	Male	15,720 (62.8%)	3,366 (77.1%)	1,304 (55.0%)	Reference	Reference
Age at diagnosis, years	<50	4,230 (16.9%)	518 (11.9%)	562 (23.7%)	**0.72 (0.64-0.80)**	**1.53 (1.35-1.74)**
	50-59	6,046 (24.1%)	977 (22.4%)	517 (21.8%)	**0.86 (0.79-0.94)**	1.01 (0.90-1.15)
	60-69	7,533 (30.1%)	1,444 (33.1%)	627 (26.4%)	Reference	Reference
	70-79	5,252 (21.0%)	1,026 (23.5%)	463 (19.5%)	1.04 (0.95-1.13)	1.08 (0.95-1.23)
	80+	1,990 (7.9%)	398 (9.1%)	203 (8.6%)	1.04 (0.92-1.18)	**1.21 (1.02-1.43)**
Kidney disease and hypertension	ESRD	950 (3.8%)	338 (7.7%)	65 (2.7%)	**2.38 (2.04-2.77)**	0.81 (0.62-1.06)
	CKD, not end-stage	2,040 (8.1%)	481 (11.0%)	135 (5.7%)	**1.52 (1.33-1.72)**	**0.78 (0.64-0.95)**
	HTN without kidney disease	11,614 (46.4%)	2,033 (46.6%)	1,010 (42.6%)	**1.19 (1.10-1.29)**	0.93 (0.84-1.02)
	No kidney disease and no HTN	10,447 (41.7%)	1,511 (34.6%)	1,162 (49.0%)	Reference	Reference
Diabetes	Diabetes	6,573 (26.2%)	908 (20.8%)	373 (15.7%)	**0.63 (0.58-0.69)**	**0.61 (0.54-0.70)**
	No diabetes	18,478 (73.8%)	3,455 (79.2%)	1,999 (84.3%)	Reference	Reference
Neighborhood SES	1 (lowest SES)	4,199 (16.8%)	622 (14.3%)	332 (14.0%)	**0.85 (0.76-0.96)**	**0.68 (0.59-0.79)**
	2 (lower-middle SES)	5,050 (20.2%)	814 (18.7%)	433 (18.3%)	**0.87 (0.78-0.97)**	**0.71 (0.62-0.81)**
	3 (middle SES)	5,370 (21.4%)	873 (20.0%)	442 (18.6%)	**0.83 (0.75-0.92)**	**0.67 (0.58-0.76)**
	4 (upper-middle SES)	5,453 (21.8%)	1,023 (23.4%)	536 (22.6%)	0.94 (0.85-1.03)	**0.79 (0.70-0.89)**
	5 (highest SES)	4,979 (19.9%)	1,031 (23.6%)	629 (26.5%)	Reference	Reference
Year of diagnosis	2005-2010	11,923 (47.6%)	2,013 (46.1%)	1,073 (45.2%)	Reference	Reference
	2011-2015	13,128 (52.4%)	2,350 (53.9%)	1,299 (54.8%)	**1.11 (1.04-1.18)**	**1.16 (1.06-1.26)**

Limited to first kidney primary and patients with Office of Statewide Health Planning and Development data. Estimates computed from logistic regression model including terms for race and ethnicity, sex, age at diagnosis, comorbidity, neighborhood SES and year of diagnosis. Abbreviations: OR = odds ratio; CI = confidence interval; NL = Non-Latino; ESRD = end-stage renal disease; CKD = chronic kidney disease; HTN = hypertension; SES = socioeconomic status.

Table 3.

Association of comorbidity with renal cell carcinoma subtype in adult California residents, 2005-2015

		Clear cell N (%)	Papillary N (%)	Chromophobe N (%)	Papillary vs Clear cell OR (95% CI)	Chromophobe vs Clear cell OR (95% CI)
Joint Comorbidities	ESRD no DM	355 (1.4)	175 (4.0)	32 (1.3)	**2.30 (1.88-2.81)**	**0.67 (0.46-0.99)**
	ESRD + DM	595 (2.4)	163 (3.7)	39 (1.6)	**1.54 (1.27-1.87)**	**0.59 (0.42-0.83)**
	CKD no DM	813 (3.2)	281 (6.4)	79 (3.3)	**1.67 (1.43-1.95)**	0.83 (0.65-1.06)
	CKD + DM	1,227 (4.9)	200 (4.6)	60 (2.5)	0.86 (0.72-1.01)	**0.44 (0.33-0.58)**
	HTN only	7,507 (30.0)	1,540 (35.3)	780 (32.2)	**1.18 (1.09-1.28)**	0.92 (0.83-1.02)
	HTN + DM	4,107 (16.4)	493 (11.3)	250 (10.3)	**0.78 (0.69-0.87)**	**0.57 (0.49-0.67)**
	DM only	644 (2.6)	52 (1.2)	36 (1.5)	**0.61 (0.46-0.82)**	**0.56 (0.39-0.78)**
	No CKD no DM no HTN	9,803 (39.1)	1,459 (33.4)	1,145 (47.3)	Reference	Reference

Estimates computed from logistic regression model including terms for race and ethnicity, sex, age at diagnosis, comorbidity, neighborhood SES and year of diagnosis. Abbreviations: OR = odds ratio; CI = confidence interval; ESRD = end-stage renal disease; DM = diabetes mellitus; CKD = chronic kidney disease; HTN = hypertension