Effect of Collecting Duct Histology on Renal Cell Cancer Outcome

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Purpose: Collecting duct renal cell carcinoma is a rare entity. Recent surgical series of the condition showed conflicting results. We used an American population based data set to compare the survival experience of patients with collecting duct vs clear cell renal cell carcinoma.

Materials and Methods: Cases of collecting duct and clear cell renal cell carcinoma were identified in the Surveillance, Epidemiology and End Results program (2001 to 2005). Demographic and pathological characteristics at diagnosis were compared. Differences in disease specific survival were compared with univariate and multivariate Cox regression analysis.

Results: A total of 160 collecting duct renal cell carcinoma cases were present in the database from 2001 to 2005. In that time 33,252 clear cell renal cell carcinoma cases were diagnosed. Collecting duct renal cell carcinoma was more common in black than in white patients (23% vs 9%, $p < 0.001$). Collecting duct renal cell carcinoma was more commonly T3+ than T2/T1 (33% vs 18%, $p < 0.001$) and metastatic than regional/local (28% vs 17%, $p = 0.001$). Nephrectomy rates were similar (84% and 78%, $p = 0.06$). The 3-year disease specific survival rate was 58% and 79% for collecting duct and clear cell renal cell carcinoma, respectively. On multivariate analysis there was an increased mortality risk in patients with collecting duct vs clear cell renal cell carcinoma (HR 2.42, 95% CI 1.72–3.39, $p = 0.001$).

Conclusions: Compared to patients with clear cell renal cell carcinoma those with collecting duct renal cell carcinoma have higher stage and are more often black. Even after adjusting for demographic, surgical and pathological factors disease specific survival is significantly worse in patients with collecting duct rather than clear cell renal cell carcinoma. Further research into the biology of this rare tumor is required to explain these results.

Key Words: kidney; carcinoma, renal cell; kidney tubules, collecting; SEER program; mortality

Abbreviations and Acronyms

CCRCC = clear cell RCC

CDRCC = collecting duct RCC

DSS = disease specific survival

RCC = renal cell carcinoma

SEER = Surveillance, Epidemiology and End Results Program

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Collecting duct renal cell carcinoma is a rare entity, occurring in less than 2.0% of RCC cases. As a result, our knowledge of CDRCC comes primarily from small case series with a uniformly poor prognosis. Based on these limited data CDRCC is associated with a dismal prognosis compared to that of other RCC subtypes, including the most common type, CCRCC. Recently 2 multi-institutional surgical case series from Japan[1] and Europe[2] described collecting duct carcinoma. These series showed similarities in the high rate of nodal and metastatic disease at presentation but differed in the rates of pT3 disease, high grade disease and survival. These studies were limited by the nonpopulation based nature (referral bias) and ex-

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clusion of nonsurgical patients (treatment bias). We used an American population based data set to determine pathological findings and survival experience in patients with CDRCC vs CCRCC.

MATERIALS AND METHODS

Data Source

The SEER database was used to identify our patient cohort. SEER collects cancer incidence and survival data from 17 population based cancer registries, accounting for approximately 26% of the American population. Data on 2001 to 2005 from 17 SEER registries were used since CDRCC was not coded before 2000 and only 1 CDRCC case was recorded in 2000.

Study Population

Potential participants were initially identified using ICD-O-3 site codes for the kidney (C649). CDRCC cases were identified by ICD-O-3 histology code (8319). The comparison cohort consisted of cases with ICD-O-3 histology codes for clear cell adenocarcinoma not otherwise specified (8310) and clear cell adenocarcinoma, renal cell carcinoma (8312).

Data Collection and Coding

Demographic data included participant age, race, gender and tumor registry. Age was categorized into 10-year age groups. Race was categorized as white, black or other based on SEER coding. Treatment year and tumor registry were also ascertained. Pathological data included tumor size in cm, primary T stage (clinical stage was used when pathological stage was not available, ie nephrectomy not performed), SEER historical stage (localized, regional or distant), nodal status (negative, positive or not performed/unknown), metastatic status (present/absent) and tumor grade (well, moderately, poorly/undifferentiated or unknown). Surgical status was recoded (partial/complete nephrectomy) or no surgery (biopsy or autopsy confirmation of pathological condition). Fuhrman grade, chemotherapy, immunotherapy and comorbidity data are not available in SEER. Survival was calculated starting at the date of diagnosis to the date of death from kidney cancer. When death was not observed, patients were censored at the date of last followup.

Statistical Analysis

We report demographic and pathological data on the cohort. Kaplan-Meier survival curves were generated to compare the unadjusted survival experience in CRDCC and CCRCC cases. Multivariate Cox regression was done to evaluate the disease specific mortality risk. All covariates were included in the model. SEER historical stage was used in multivariate analysis rather than T stage since T stage is not recorded in SEER in patients with metastatic disease. This limitation was mitigated by including tumor size, which was available in 91% of patients. Subanalysis was done that included only 1) patients undergoing surgery, 2) T3a disease or less with nonmetastatic disease, 3) exclusion of nonhigh grade CCRCC and 4) patients with metastatic disease.

The proportional hazards assumption for the Cox regression was evaluated with Schoenfeld residuals. Stratified Cox regression was used for variables that violated the proportional hazards assumption. Individual variables and the combined model were then tested and met the proportional hazard assumption ($p = 0.32$, where $p < 0.05$ indicates evidence of nonproportionality). In the subset models of only patients with 1) surgical treatment, 2) T3a or less with no distant metastasis and 3) only high grade CCRCC vs all CDRCC the proportional hazards assumptions were also met ($p = 0.28$, 0.81 and 0.97, respectively). HRs are presented with the 95% CI. All statistical analysis was done with Stata®, version 8.

RESULTS

We identified 160 CDRCC cases in 2001 to 2005. In that period there were 33,252 CCRCC cases in the SEER database. Table 1 lists demographic and

Table 1. *CDRCC and CCRCC demographic and pathological characteristics*

	No. CDRCC (%)	No. CCRCC (%)	p Value
Age:			0.44
Less than 50	32 (20)	5,222 (16)	
51–59	36 (23)	7,634 (23)	
60–69	39 (24)	8,606 (26)	
70–79	31 (19)	7,853 (24)	
80+	22 (14)	3,937 (12)	
Race:			<0.001
White	112 (70)	28,495 (86)	
Black	36 (23)	2,849 (9)	
Other	12 (8)	1,759 (5)	
Gender:			0.03
M	112 (70)	20,502 (62)	
F	48 (30)	12,750 (38)	
Diagnosis yr:			0.44
2001	26 (16)	6,287 (19)	
2002	25 (16)	6,284 (19)	
2003	40 (25)	6,655 (21)	
2004	36 (23)	6,899 (21)	
2005	33 (21)	7,127 (21)	
Stage:			<0.001
T1a	42 (26)	11,008 (33)	
T1b	17 (11)	6,669 (20)	
T2	16 (10)	4,052 (12)	
T3/4	53 (33)	5,952 (18)	
No T stage	32 (20)	5,571 (17)	
SEER stage:			<0.001
Localized	68 (43)	20,803 (63)	
Regional	45 (28)	5,330 (16)	
Distant	44 (28)	5,705 (17)	
Unstaged	3 (2)	1,414 (4)	
Nodal status:			<0.001
N0	13 (8)	3,523 (10.6)	
N1	24 (15)	765 (2)	
Nx	123 (77)	28,964 (87)	
Metastasis	44 (28)	5,705 (17)	0.001
Grade:			<0.001
Well differentiated	10 (10)	3,610 (18)	
Moderately differentiated	20 (20)	10,612 (52)	
Poorly/undifferentiated	70 (70)	6,384 (31)	
Surgery	135 (84)	25,969 (78)	0.06