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Urologic Oncology: Seminars and Original Investigations ▮ (2017) ▮▮▮–▮▮▮

UROLOGIC ONCOLOGY

Original Article

Collecting duct carcinoma of the kidney: Disease characteristics and treatment outcomes from the National Cancer Database

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Received 13 December 2016; received in revised form 17 March 2017; accepted 10 April 2017

Abstract

Objective: To use a large population-level database to assess survival outcomes for collecting duct renal cell carcinoma (CDRCC).

Materials and methods: The National Cancer Database was queried for all cases of CDRCC and clear cell renal cell carcinoma (CCRCC) from 2004 to 2013. After removing patients with other cancer diagnoses, the analytic cohort was composed of 201,686 CCRCC and 577 CDRCC cases. Kaplan-Meier and cox proportional hazards analysis were employed to model survival.

Results: Compared to CCRCC, patients with CDRCC presented with higher grade and stage, node positive, and metastatic disease (70.7% vs. 30.0% with metastasis; $P < 0.001$). Overall median survival for CDRCC was 13.2 months (95% CI: 11.0–15.5) compared to the 122.5 months (95% CI: 121.0–123.9) for CCRCC. On multivariate analysis of the CDRCC cohort, increasing T stage, high-grade disease, and metastasis were predictors of mortality. Of 184 patients with metastatic CDRCC, 113 underwent cytoreductive nephrectomy (CNx) whereas the rest were treated with chemo/radiation or observed. Survival outcomes were improved in patients who received both CNx with chemo/radiation compared to CNx alone (hazard ratio = 0.51, 95% CI: 0.32–0.79) or chemo/radiation alone (hazard ratio = 0.57, 95% CI: 0.37–0.89) on multivariate analysis.

Conclusion: CDRCC is an aggressive subtype of renal cell carcinoma. Median survival is 13 months after diagnosis, drastically lower than for CCRCC. More than 70% of patients have metastatic disease at diagnosis. Chemo/radiation in addition to CNx is associated with a survival benefit over single mode therapy.

Keywords: Renal cancer; Collecting duct carcinoma; Chemotherapy; Survival

1. Introduction

Collecting duct renal cell carcinoma (CDRCC) is a rare, but aggressive, genitourinary malignancy, estimated to comprise 0.4% to 2.0% of all renal cell carcinomas [1,2]. It is associated with an overall poorer prognosis as it is more likely than clear cell renal cell carcinoma (CCRCC) to present as locally advanced, metastatic, and poorly differentiated [3]. First described in 1949 [4] the available literature for CDRCC is dominated by case reports or small institution studies [1,2,5]. The largest series to date include European [6,7] and Japanese [8] cohorts as well as US-based surveillance, epidemiology and end results (SEER) studies [9,10].

Current treatment options for CDRCC are based on the established standards for more traditional forms of renal cell carcinoma (RCC) but they may not be directly applicable based on the fact that, stage for stage, it is more aggressive. Comparatively more patients present with metastatic disease, which may limit the potential survival benefit from interventions such as cytoreductive nephrectomy (CNx) that have survival benefit for CCRCC [11,12]. Furthermore, CDRCC is histologically distinct from other forms of RCC in that it is

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http://dx.doi.org/10.1016/j.urolonc.2017.04.010
1078-1439/

derived from the epithelial layer of the collecting duct, and appears histologically more similar to urothelial cells than renal cells [13,14]. This similarity forms the basis for the rationale of trialing chemotherapeutic agents used for advanced urothelial carcinoma (UC) in metastatic CDRCC [15,16]. The response rates, however, have proven suboptimal and as such CDRCC is thought to be relatively chemo- and radio-insensitive, much like its clear cell counterpart [17].

The rarity of this cancer makes it virtually impossible to study in a large-scale prospective manner, but there is still a need to deepen our understanding given the paucity of evidence currently available. In this study, we sought to characterize the epidemiology, treatment patterns and outcomes of CDRCC using the multi-institutional National Cancer Database (NCDB).

2. Materials and methods

2.1. Dataset

The NCDB captures more than 70% of all new cancer diagnoses annually, and includes data from 2004 to 2013 [18]. The American College of Surgeons Commission on Cancer approvals program manages this multi-institution collaboration, and includes over 1,500 programs that contribute patient demographics, facility information, tumor characteristics, and treatment utilization.

2.2. Cohort

All patients with kidney cancer were identified between 2004 and 2013 using the WHO 2004 International Classification of Disease-O-3 (ICD-O-3) topography code C64.9. Of these 351,112 patients, we identified 263,230 patients with CCRCC using the ICD-O-3 morphologic codes 8310 and 8312 and 762 patients with CDRCC using code 8319 [13]. We removed patients with any other cancer diagnoses for a final analytic cohort of 201,686 patients with CCRCC and 577 patients with CDRCC.

2.3. Outcome

Our primary outcome was overall survival after diagnosis of CDRCC. Our secondary objective was to characterize treatment patterns and outcomes. Patient mortality status was updated at the time of last follow-up.

2.4. Independent variables

Demographic and clinical characteristics included patient age, race, year of diagnosis, insurance status, and Deyo-Charlson comorbidity index [19]. Treatment facility type was defined as community, comprehensive community, academic/research, integrated network, or other based on the Commission on Cancer Accreditation program. American Joint Committee on Cancer clinical and pathological stage were available to describe cancer characteristics. Primary T category was defined as pathologic T category and clinical stage was used when pathologic stage was missing (no surgery performed). Lymph node status was defined as pathologically confirmed lymph node involvement, not performed/missing or negative (clinical stage was not used). Tumor grade was coded per ICD-O-3 grading and differentiation system. Treatment information included either receipt of chemotherapy (CT) or radiotherapy (RT), or both. The sequence and timing in which these systemic therapies were utilized was used to determine whether they were used as neoadjuvant ($\leq$180 d before surgery), adjuvant ($\leq$90 d after surgery), or salvage ($>$90 d after surgery) therapies.

2.5. Analysis

Kaplan-Meier survival analysis and stratified log-rank tests were used to compare survival outcomes by histology, tumor stage, and treatment. Independent variables, which were found to be significant on univariate cox proportional hazards analysis or clinically relevant, were included in the multivariate analysis. Multivariate cox proportional hazards analysis included age, sex, race, T category, Charlson/Deyo score, and treatment as independent predictors of overall mortality. For all statistical measures, $P < 0.05$ was considered statistically significant. All analyses were performed using SPSS v23.0.

3. Results

Overall, 577 CDRCC patients and 201,686 CCRCC patients were included in our analysis. There were significant differences in the distribution of demographic characteristics and tumor-specific information (Table 1). Patients with CDRCC were more commonly male (65.3% vs. 59.9%, $P = 0.007$) and black (20.5% vs. 9.1%, $P = 0.001$). Collecting duct carcinoma was more likely to present as high grade, high stage ($>$T2), lymph node positive, and metastatic disease. In fact, 70.7% of patients with CDRCC with complete staging had metastatic disease compared to 30.0% of the patients with CCRCC.

Median survival for the CDRCC group was 13.2 months (95% CI: 11.0–15.5), compared to 122.5 months (121.0–123.9) for the CCRCC group (Supplementary Table 1). Median follow-up for the entire cohort was 67.6 (95% CI: 59.3–75.9) months. Survival was significantly worse for CDRCC compared to CCRCC when stratified by T category, nodal status, or metastatic disease.

On multivariate analysis of factors associated with overall survival within the cohort of $n = 577$ patients with CDRCC (Table 2), T3/T4 disease (hazard ratio [HR] = 2.2, 95% CI: 1.5–3.2), high-grade disease (HR = 5.0, 95% CI: 2.6–9.7), and metastatic disease (HR = 2.1, 95% CI: 1.5–2.8) predicted worse overall survival. The choice of