Impact of Clinical and Histopathological Parameters on Disease Specific Survival in Patients with Collecting Duct Renal Cell Carcinoma: Development of a Disease Specific Risk Model

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Abbreviations and Acronyms

CDRCC = collecting duct RCC
c-index = concordance index
DSM = disease specific mortality
DSS = disease specific survival
LND = lymph node dissection
LVI = lymphovascular invasion
RCC = renal cell carcinoma

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Purpose: Collecting duct renal cell carcinoma is a rare, aggressive histological subtype of renal cell carcinoma. Since few groups have evaluated the oncological prognosis in these patients based on clinical and pathological parameters, we assessed parameters prognostic for disease specific mortality.

Materials and Methods: From a cohort of 14,047 patients with renal cell carcinoma we retrieved the records of 95 with collecting duct renal cell carcinoma at a total of 16 European and American centers of the CORONA (Collaborative Research on Renal Neoplasms Association) and SATURN (Surveillance and Treatment Update Renal Neoplasms) projects, and another 2 centers. Multivariable Cox regression analysis was applied to determine the influence of parameters on disease specific mortality. Median followup was 48.1 months (IQR 24–103).

Results: The disease specific survival rate at 1, 2, 5 and 10 years was 60.4%, 47.3%, 40.3% and 32.8%, respectively. American Society of Anesthesiologists (ASA) score 3–4, tumor size greater than 7 cm, stage M1, Fuhrman grade 3-4 and lymphovascular invasion independently predicted disease specific mortality. Based on these parameters, patients were divided into 26 (27%) at low, 13 (14%) at intermediate and 56 (59%) at high risk with a 5-year disease specific survival rate of 96%, 62% and 8%, respectively (bootstrap corrected c-index 0.894, 95% CI 0.820–0.967, p <0.001).

Conclusions: While patients with collecting duct renal cell carcinoma are commonly diagnosed at advanced stage and have poor prognosis after surgery, a subset has excellent survival. Histopathological features can help risk stratify patients based on the described, highly accurate risk model to predict disease specific mortality, facilitating patient counseling and risk based clinical decision making for adjuvant therapy and clinical trial inclusion.

Key Words: kidney; carcinoma, renal cell; mortality; pathology; prognosis

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Collecting duct RCC is a rare histological subtype of RCC that develops in about 0.5% to 1.5% of RCC cases and is characterized by a poor clinical course due to early tumor dissemination.[1–6] Predicting the postoperative prognosis in patients with CDRCC remains difficult since clinical data on this disease are insufficient and mainly based on small series and case reports. Local tumor extension and metastasis remain the most widely used factors for clinical decision making in these patients.[1–6]

Recently, Karakiewicz et al compared outcomes in 41 patients with CDRCC and clear cell RCC in matched pair analysis.[2] Matching criteria were age, gender, symptoms at presentation, grade and TNM stage. In contrast with other studies,[3,4] histological subtype did not risk stratify patients but pathological features did.[2] Interestingly, patients in that study had better survival than those in previous series (3-year DSS 68% vs 45% to 58%).[1–3]

Overall, only 3 groups have investigated data on at least 50 patients with CDRCC, including Wright et al (135),[1] Abern et al (195)[5] and Tokuda et al (81).[3] Wright[1] and Abern[5] et al used the Surveillance, Epidemiology and End Results (SEER) database.

In the current multicenter study, which to our knowledge is the largest series to date except population based studies, we evaluated the prognostic value of clinical and histopathological features that are not yet described or well evaluated. Our secondary aim was to develop a tool that could facilitate clinical decision making in patients with CDRCC.

MATERIALS AND METHODS

Patient Selection, Data Collection and Pathological Evaluation

After receiving local ethics committee approval, we analyzed clinical and pathological data on 95 patients (0.68%) with CDRCC from a cohort of 14,047 with RCC at a total of 16 centers of the CORONA and SATURN projects, and the Universities of Hamburg and Regensburg. Patients underwent radical or partial nephrectomy between 1992 and 2010. Local pathologists with uropathological expertise confirmed the CDRCC diagnosis in all cases.

Preoperatively, clinical stage was assessed by abdominal computerized tomography, chest imaging with computerized tomography or chest x-ray and a serum comprehensive metabolic panel. Bone scan and brain imaging were done as indicated by symptoms. None of the 95 patients with CDRCC received neoadjuvant or adjuvant treatment. Information on patient characteristics, ie age, gender, local or systemic symptoms, location, surgery type and metastasis, was obtained from institutional databases. American Society of Anesthesiologists (ASA) score at surgery was recorded.

All surgical specimens were processed according to standard pathological procedures and evaluated by experienced genitourinary pathologists at each institution. Histopathological confirmation of CDRCC included macroscopic and microscopic aspects of tumors and, in case of doubt, further immunohistochemical analysis. All tumors had a tubulopapillary or tubular growth pattern according to the definition of Srigley and Eble.[7] In a fraction of CDRCCs desmoplastic stroma were present with intense inflammatory infiltrates, comprising predominantly plasma cells or lymphocytes (fig. 1).

Pathological stage (pTN) was reassigned according to the 2009 American Joint Committee on Cancer TNM staging system.[8] Fuhrman classification was used to assess nuclear grade.[9] LVI was defined as tumor cells in endothelium lined spaces without underlying muscular walls. Tumor size, sarcomatoid dedifferentiation (coded as positive in cases of at least 10% sarcomatoid proportions) and coagulative tumor necrosis (considered when at least 20% microscopic necrosis was detected) were also recorded.

Followup

Patients were followed according to protocols established at each institution according to guideline recommendations.[10,11] Cause of death was determined by treating physicians, chart review corroborated by death certificates or death certificates alone. Death was coded as cancer related or not cancer related. To decrease bias in the cause of death attribution, only patients with RCC or CDRCC listed on the death certificate and who had previous disease progression were considered to have died of cancer. Perioperative deaths (within 30 days of surgery) were censored. The database was frozen in November 2011. Followup was assessed from the date of surgery to the last followup. DSS served as the study end point.

Statistical Analysis

The Shapiro-Wilk normality test was used to investigate the distribution of continuous variables. Continuous variables are presented as the median and IQR.

DSS was estimated using the Kaplan-Meier method as the time from primary surgery to cancer related death.

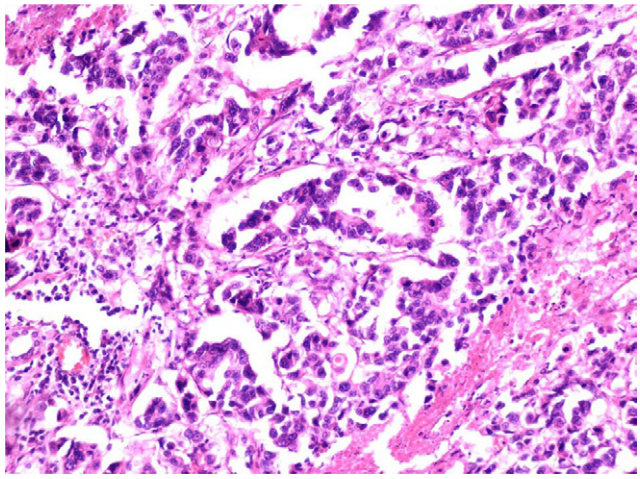

Figure 1. CDRCC (Bellini) featuring haphazardly arranged neoplastic tubular structures with high grade nuclei (Fuhrman nuclear grade 3 or 4) embedded in inflamed stroma. H&E, reduced from ×10.