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Original article

Cystic renal cell carcinoma carries an excellent prognosis regardless of tumor size

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Abstract

Introduction: Cystic renal cell carcinoma (cystic RCC) is thought to carry an improved prognosis relative to clear cell RCC (CCRCC); however, this is based on small case series. We used a population-based tumor registry to compare clinicopathologic features and cancer-specific mortality (CSM) of cystic RCC with those of CCRCC.

Materials and methods: The Surveillance, Epidemiology, and End Results database was queried for all patients diagnosed and treated for cystic RCC and CCRCC between 2001 and 2010. Clinical and pathologic factors were compared using *t* tests and chi-square tests as appropriate. Kaplan-Meier survival analysis compared CSM differences between cystic RCC and CCRCC.

Results: A total of 678 patients with cystic RCC and 46,677 with CCRCC were identified. The mean follow-up duration was 52 and 40 months, respectively. When compared with CCRCC patients, those with cystic RCC were younger (mean age 58 vs. 61 y, $P < 0.001$), more commonly black (22% vs. 9%, $P < 0.001$), and female (45% vs. 41%, $P = 0.02$). Cystic RCCs were more commonly T1a tumors (66% vs. 55%, $P < 0.001$), well differentiated (33% vs. 16%, $P < 0.001$), and smaller (mean size = 3.8 vs. 4.5 cm, $P < 0.001$). Cystic RCC was associated with a reduction in CSM when compared with CCRCC ($P = 0.002$). In a subset analysis, this reduction in CSM was seen only for those with T1b/T2 tumors ($P = 0.01$) but not for those with T1a RCCs lesions ($P = 0.31$).

Conclusions: We report the largest series of cystic RCC and corroborate the findings of improved CSM when compared with CCRCC for larger tumors; however, no difference was noted in smaller tumors, suggesting that tumor biology becomes more relevant to prognosis with increasing size. These data may suggest a role for active surveillance in appropriately selected patients with small, cystic renal masses.

Keywords: Renal cell carcinoma; Cystic RCC; Clear cell RCC; Survival

1. Introduction

It is estimated that up 15% of renal cell carcinomas (RCCs) may have a cystic component [1] that can be benign or malignant in nature (e.g., simple cyst vs. cystic degeneration with necrosis). Postulated mechanisms for cyst formation include intrinsic multilocular growth, intrinsic unilocular growth, cystic necrosis, or growth from the wall of a preexisting simple cyst [1].

A distinct subset of RCC, described as "cystic RCC," accounts for <5% of all renal cell carcinomas [2]. The World Health Organization defines this as a "tumor composed of numerous cysts, the septa of which contain small groups of clear cells indistinguishable from grade I clear cell carcinoma" [3]. On gross examination, these tumors are typically well circumscribed, composed entirely of cysts, and separated from adjacent parenchyma by a fibrous wall [2–5]. Microscopically, the cysts are generally lined by epithelial cells, single-celled or multilayered, with some forming papillary structures [3,5]. In the existing literature, the cystic component required for a cystic RCC diagnosis has varied from 75% to 90% among studies by different authors [4,6–11].

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Overall, RCC remains a surgical disease with variant histology that is predictive of survival [12]. Cystic RCC is considered to have a favorable prognosis when compared with that of clear cell RCC (CCRCC); however, this perception is based on small retrospective series [4,6–11,13,14], which may not represent the true natural history. To further clarify the prognosis of cystic RCC, we accessed the population-based Surveillance, Epidemiology, and End Results (SEER) database to delineate the clinicopathologic features of cystic RCC as well as compare cancer-specific mortality (CSM) between patients with cystic and CCRCC.

2. Materials and methods

2.1. Data source

Cases were identified from the SEER database, which comprises 17 cancer registries and accounts for approximately 26% of the U.S. population. We queried cancer incidence and survival data and restricted the analysis to the years 2001 to 2010, as reporting of cystic RCC was minimal before 2001.

2.2. Study population

Cases were identified using International Classification of Diseases for Oncology (third edition, ICD-O-3) site codes for the kidney (C649). Cystic RCC cases were identified by the ICD-O-3 histology code (8316). The comparison CCRCC cohort was identified using ICD-O-3 histology codes 8310 (Clear Cell Adenocarcinoma NOS) and 8312 (Clear Cell Adenocarcinoma, and Renal Cell Carcinoma). We limited the analysis to those with organ-confined RCC (pT1a/b, pT2, N0/x, and M0/x) to limit misclassification bias of larger tumors (e.g., CCRCC with cystic degeneration). We also limited the analysis to those undergoing surgical excision with radical or partial nephrectomy to ensure pathologic confirmation of histology rather than rely on radiographic and biopsy diagnoses.

2.3. Data collection and coding

Demographic data included patient age, sex, and race. Age was categorized in 10-year increments ranging from younger than 50 to greater than 80 years old. Race was categorized as white, black, or other. Surgery (partial or complete nephrectomy) and year of treatment were also recorded. Pathologic data include tumor size, pathologic T category classification, and tumor grade (well differentiated, moderate, poorly/undifferentiated, or missing). Fuhrman grade, chemotherapy, immunotherapy, and comorbidity data are not available in the SEER database. CSM stratified by pT1a vs. pT1b/T2 tumors was calculated from date of diagnosis to date of death due to kidney cancer. Patients were censored at the date of last follow-up if alive or a non–kidney cancer–related death had occurred. Pathologic staging was based on the TNM classification from the American Joint Committee on Cancer (Chicago, IL), seventh edition.

2.4. Statistical analysis

Demographic and pathologic data comparing cystic RCC with CCRCC are presented using t tests for continuous variables and chi-square tests for categorical variables as appropriate. Unadjusted survival experience between cystic RCC and CCRCC was compared with Kaplan-Meier curves using log-rank tests. As there was a low overall event rate, multivariate analysis was not performed. All statistical analyses were conducted using Stata, version 13 (Stata, Inc., College Station, TX).

3. Results

Demographic and pathologic data are shown in Table 1. A total of 678 patients were identified as having cystic RCC and 46,677 patients had CCRCC. The mean follow-up duration was 52 and 40 months, respectively. There were 1,760 deaths (3.8%) due to CCRCC and 12 deaths (1.8%) due to cystic RCC. Patients with cystic RCC were younger and were more commonly black and female. Patients with cystic RCC were also more likely to present with lower stage disease, well-differentiated tumors, and to receive nephron-sparing surgery. There were no differences in tumor laterality between the 2 groups.

Kaplan-Meier survival curves for cystic RCC vs. CCRCC are shown in Fig. 1. Using the log-rank test, survival was significantly better for patients with cystic RCC when compared with CCRCC patients ($P = 0.002$). In Fig. 2, Kaplan-Meier survival curves stratified by stage category (T1a vs. T1b/T2) are shown. We found a non-significant reduction in CSM in patients with T1a tumors ($P = 0.31$); however, in patients with T1b/T2 tumors, cystic RCC histology predicted a significant reduction in CSM ($P = 0.01$).

4. Discussion

In this study, we report the largest series of patients with cystic RCC to date and describe the clinical features and survival experience compared with CCRCC. We confirm the findings from small case series of improved survival in cystic RCC, although this appears to be driven by the survival benefit in larger (pT1b or T2) tumors specifically.

Cystic RCC is an uncommon variant of RCC accounting for $<5\%$ of all RCCs [2]. The knowledge of its presenting characteristics and outcomes is derived from small case series, all with fewer than 100 patients and most with fewer