Renal Cell Carcinoma in Children, Adolescents and Young Adults: A National Cancer Database Study

Ardavan Akhavan,* Morgan Richards, Margarett Shnorhavorian, Adam Goldin, Kenneth Gow and Paul A. Merguerian

From the Department of Urology, Division of Pediatric Urology, Johns Hopkins University School of Medicine, Baltimore, Maryland (AA), and Department of Urology, Division of Pediatric Urology (MR, MS, PAM) and Department of Surgery (AG), Division of General and Thoracic Surgery (KG), University of Washington, Seattle Children's Hospital, Seattle, Washington

Abbreviations and Acronyms

NCDB = National Cancer Database

NOS = not otherwise specified

RCC = renal cell carcinoma

WT = Wilms tumor

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* Correspondence: Charlotte R. Bloomberg Children's Center, Johns Hopkins University, 1800 Orleans St., Bloomberg 7308-B, Baltimore, Maryland 21287.

Purpose: We compared the presentation and outcomes of patients younger than 21 years with renal cell carcinoma and determined risk factors associated with mortality.

Materials and Methods: We searched the National Cancer Database for patients diagnosed with renal cell carcinoma between 1998 and 2011. We evaluated patients younger than 30 years with renal cell carcinoma, including clear cell, chromophobe, papillary and not otherwise specified subcategories. We used logistic regression to compare presenting cancer, demographics and treatment variables in patients 0 to 15 years, 15 to 21 years and 21 to 30 years old. Cox regression analysis was used to determine risk factors for mortality in patients younger than 21.

Results: Of 3,658 patients younger than 30 years included in the study 161 were younger than 15 and 337 were 15 to 21 years old. A higher proportion of younger patients had renal cell carcinoma not otherwise specified and papillary histology compared to those 21 to 30 years ($p < 0.001$). Younger patients presented with higher stage ($p < 0.0001$), higher grade ($p < 0.0001$) and larger tumors ($p < 0.0001$) than those 21 to 30 years. A higher percentage of younger patients underwent lymph node dissection ($p < 0.0001$) or chemotherapy as first-line treatment ($p < 0.0001$) compared to those 21 to 30 years. Cox regression analysis demonstrated that stage 4 presentation, government insurance status, nonchromophobic pathology results and not undergoing surgery as first-line treatment were independently associated with increased mortality in patients younger than 21 years.

Conclusions: Children and adolescents with renal cell carcinoma present with more advanced disease than those 21 to 30 years old. In patients younger than 21 years mortality was associated with the nonchromophobe histological subtype, stage 4 disease, government insurance and not undergoing surgery as first-line therapy.

Key Words: carcinoma, renal cell; kidney neoplasms; pediatrics

ESTIMATES for 2014 suggest that 3.8% of all new cancer diagnoses were kidney and renal pelvis malignancies.[1] In adults up to 85% of these masses are renal parenchymal carcinomas, almost all of which are renal cell carcinoma.[2] In contrast, Wilms tumors account for the majority of renal tumors in children, while renal cell carcinoma represents only

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2% to 5% of renal masses.[3–5] Renal cell carcinoma is rare in individuals younger than 21 years, accounting for only 0.5% to 2% of all cases,[2] resulting in an overall incidence of 0.01 per 100,000 population.[3] The natural history in children, adolescents and young adults is poorly described. Most contemporary studies focus on small, single institution series of 4 to 41 patients. Limited data suggest that the presentation and biology of these tumors are different in children compared to adults.[4,6–13] While up to 50% of renal cell carcinomas in adults are found incidentally, up to 88% of those in children are identified due to symptoms such as pain, hematuria, fever, weight loss and abdominal mass.[4,6–13]

We compared the presentation and outcomes between children, adolescents and young adults with RCC. We also determined risk factors associated with mortality in patients younger than 21 years with RCC. We hypothesized that younger patients (0 to 15 and 15 to 21 years) present with more advanced disease than older patients (21 to 30), and that mortality is associated with stage at presentation and histological subtype.

MATERIALS AND METHODS

We used data from the NCDB, a joint program of the American College of Surgeons Commission on Cancer and the American Cancer Society, consisting of more than 29 million records collected from more than 1,500 commission accredited cancer programs in the United States and Puerto Rico since 1989. The NCDB captures data from approximately 70% of newly diagnosed cancers in the United States yearly.[14] The database includes information on patient characteristics, cancer staging, tumor characteristics, type of first-line treatment administered and outcome. Individuals coded as being of Hispanic ethnicity were considered Hispanic regardless of other race codes. Data reported to the NCDB are retrospective, without patient or physician identifiers.

We queried the database for patients younger than 30 years and diagnosed with RCC between 1998 and 2011, defined by ICD-0-2 disease topography code C64.9 and histological codes 8260 (papillary adenocarcinoma), 8310 (clear cell adenocarcinoma), 8312 (RCC NOS) and 8317 (chromophobe RCC). All other patients, including those with histological codes 8960 (nephroblastoma), 8130 and 8120 (urothelial neoplasms) and those without documented histological codes, were excluded from the study. Given the particularly aggressive nature of medullary RCC, we excluded this subtype in our analysis. This study was hypothesis generating, and so no power calculations were performed.

Patients were stratified into 3 age groups, ie 0 to 15, 15 to 21 and 21 to 30 years. These age groups were chosen due to our assumptions that 1) pediatric RCC is biologically different than adult RCC, 2) children younger than 15 years have pediatric RCC and would be treated by a pediatric subspecialist, 3) patients 15 to 21 years would represent a mixture of pediatric and adult RCCs, and these patients would have been treated by a combination of adult and pediatric specialists, and 4) patients 21 to 30 years represent adult RCC but lack the confounding comorbidities associated with older patients.

Statistical analysis was performed using Stata®. Significance was defined as a p value of less than 0.05. To evaluate differences between the variables of patients in different age groups, categorical variables were compared with age using logistic regression analysis and continuous variables were compared with age using ANOVA. Cox regression analysis was performed in patients younger than 21 years to determine the effects of variables on mortality in children and adolescents when controlling for age, histological subtype, stage at presentation, insurance, race/ethnicity, region population and chemotherapy or surgery as first-line therapy.

RESULTS

Demographic, cancer and treatment data from 3,658 patients younger than 30 years with RCC were included in the analysis (tables 1 and 2). The incidence of RCC increased with age. Approximately 5% of patients were 0 to 15, 9% were 15 to 21 and 86% were 21 to 30 years old. Additional data are included in the supplementary table (http://jurology.com/).

While the group younger than 15 years contained a significantly higher proportion of females than males ($p = 0.046$), there was no significant difference in any of the other demographic variables between patients of different age groups. We found a higher proportion of younger patients had RCC NOS and papillary histology compared to older patients, who had a higher proportion of clear cell and chromophobe renal cell carcinomas ($p < 0.0001$). Younger patients also presented with higher stage ($p < 0.0001$), higher grade ($p < 0.0001$) and larger

Table 1. *Logistic regression analysis of demographic variables*

	Age Group (yrs)				
	0–15	15–21	21–30	Total/Av	p Value
No. pts	169	346	3,143	3,658	
% Race/ethnicity:					0.406
White	60.12	62.46	68.93	67.91	
Black	26.79	21.41	15.67	16.73	
Hispanic	8.93	9.97	11.47	11.21	
Asian	1.79	2.93	2.26	2.3	
Native American	1.19	1.47	0.55	0.67	
Other	1.19	1.76	1.13	1.19	
% Insurance:					0.794
Private	61.88	65.64	67.55	67.11	
Government	34.38	29.14	24.24	25.16	
Uninsured	3.75	5.21	8.2	7.72	
% Region:					0.679
Metropolitan	84.18	84.38	83.29	83.44	
Urban	14.56	11.88	14.95	14.64	
Rural	1.27	3.75	1.76	1.92	
% Gender:					0.109
Male	42.6	53.76	48.39	48.63	
Female	57.4	46.24	51.61	51.37	