Pediatric Urology

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

Accepted for publication October 10, 2014.

* 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

0022-5347/15/1934-1336/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2014.10.108
Vol. 193, 1336-1341, April 2015
Printed in U.S.A.

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	

Table 2. *Logistic regression analysis of cancer variables*

	Age Group (yrs)				
	0–15	15–21	21–30	Total/Av	p Value
% Histology:					<0.0001
Clear cell	13.04	18.99	35	32.49	
RCC NOS	64.6	55.79	48.04	49.52	
Chromophobe	3.11	7.42	8.73	8.35	
Papillary	19.25	17.8	8.24	9.64	
% Analytic stage:					<0.0001
1	37.14	51.9	73.98	70.35	
2	17.14	20.57	11.18	12.31	
3	21.43	10.76	6.12	7.2	
4	24.29	16.77	8.72	10.13	
% Grade:					<0.0001
Well differentiated	14.43	15.23	19.4	18.87	
Moderately differentiated	30.93	46.09	55.42	53.77	
Poorly differentiated	43.3	34.98	21.5	23.42	
Undifferentiated	11.34	3.7	3.68	3.94	
Mean tumor length (cm)	6.86	6.93	5.07	5.33	<0.0001
% Laterality:					0.926
Unil	99.4	99.71	99.42	99.45	
Bilat	0.6	0.29	0.58	0.55	
% Margin status:					0.017
Neg	91.61	95.56	95.89	95.67	
Pos	8.39	4.44	4.11	4.33	
% Nodal status:					0.005
All neg	53.85	54.88	71.53	66.67	
1+ Node(s) pos	46.15	45.12	28.47	33.33	

tumors (p <0.0001) than older patients. Additionally younger patients had a higher proportion of positive lymph nodes (p = 0.005) and positive margins (p = 0.017). Less than 1% of all patients had bilateral disease.

There was no significant difference in the proportion of patients who underwent surgery as first-line therapy between the age groups (p = 0.144). A significantly higher percentage of younger patients underwent lymph node dissection (46.1%, 77.68% and 87.52% by ascending age group, p <0.0001) or chemotherapy as first-line treatment (16.98%, 8.68% and 4.31%, respectively, p <0.0001) than older patients. There was no significant difference in the proportion of patients who underwent radiation therapy as first-line treatment (p = 0.392).

Cox regression analysis was performed in patients younger than 21 years to evaluate differences in survival after controlling for age (0 to 15 vs 15 to 21 years), histological subtype, stage, insurance status, race, surgery or chemotherapy as first-line treatment and region population (table 3). We found that stage 4 at presentation, government insurance, Asian race/ethnicity and not undergoing surgery as first-line therapy were independently associated with increased mortality when controlling for all other variables. We also discovered that chromophobe pathology results and Native American and "other" race/ethnicity categories were associated with improved survival. In a separate analysis we compared survival between patients younger than 21 with those 21 to 30 years and found no significant difference in survival when controlling for the same variables (HR 1.246, CI 0.86–1.80, p = 0.242).

Table 3. *Cox regression analysis of mortality in patients younger than 21 years*

	HR (95% CI)		p Value
Age (yrs):			
0–15	Reference		
15–21	1.63	(0.71–3.76)	0.247
Histology:			
Clear cell	Reference		
RCC NOS	2.73	(0.44–16.75)	0.277
Chromophobe	3.33E-15	(3.87E-16–2.86E-14)	<0.0001
Papillary	1.51	(0.21–10.70)	0.681
Stage:			
1	Reference		
2	1.2	(0.44–3.52)	0.683
3	2.34	(0.66–8.34)	0.19
4	9.65	(3.49–26.70)	<0.0001
Insurance:			
Private	Reference		
Government	2.64	(1.34–5.20)	0.005
Uninsured	2.77	(0.62–12.50)	0.184
Race:			
White	Reference		
Black	1.09	(0.54–2.22)	0.812
Hispanic	0.65	(0.04–10.56)	0.764
Asian	3.97	(1.29–12.23)	0.016
Native American	1.17E-17	(1.22E-18–1.13E-16)	<0.0001
Other	4.47E-18	(2.77E-19–7.22E-17)	<0.0001
Surgery:			
Yes	Reference		
No	6.04	(2.11–17.32)	0.001
Region:			
Metropolitan	Reference		
Urban	2.17	(0.75–6.27)	0.153
Rural	0.77	(0.15–3.94)	0.758
Chemotherapy:			
Yes	Reference		
No	0.72	(0.30–1.70)	0.454

DISCUSSION

Due to the rarity of RCC in children, prior studies have been limited by small cohorts.[4] To our knowledge, with 515 patients younger than 21 years, our study represents the largest evaluation of pediatric RCC. We compared our pediatric and adolescent cohorts with patients 21 to 30 years old to minimize unrelated differences in comorbidities and outcomes.

Children and adolescents presented with more advanced disease compared to young adults. Younger age was also associated with an increased proportion of cases of RCC NOS and papillary subtypes. Children were more likely to undergo lymph node dissection or chemotherapy as first-line treatment. Stage 4 at presentation, government insurance, Asian race/ethnicity and not undergoing surgery as first-line treatment were all independently associated with increased mortality after controlling for all other variables. Patients with chromophobe histology results and those of Native

American and "other" race/ethnicities had improved survival. However, the latter findings should be interpreted with caution, as there were few patients younger than 21 years who were classified as having chromophobe RCC or were considered Native American or "other" race/ethnicity, and none died of the disease.

Prior studies have confirmed a favorable prognosis in adults with the chromophobe subtype of RCC.[15] Given the small number of patients in our group with these characteristics, our findings may be due to an artifact of our data set. Further studies are needed before any conclusions are drawn regarding the significance of Native American or "other" race/ethnicity on mortality in patients with RCC younger than 21 years.

The limitations of the NCDB prohibit us from evaluating presenting symptoms. However, we speculate that the decreased rate of incidentally found cancers in younger patients means that tumors are diagnosed when patients are presenting with symptoms and thus more advanced disease.[4,6–13] Our data support this hypothesis as we found that younger patients presented with higher stage, higher grade and larger tumors, as well as a greater frequency of positive margins and lymph nodes compared to older patients. Interestingly we found no difference in survival between patients younger than 21 and those 21 to 30 years when controlling for histological subtype, stage, insurance status, race/ethnicity, region population and surgery or chemotherapy as first-line treatment.

Prior studies have confirmed the increased frequency of papillary RCC in children and adolescents. Up to a third of children with RCC have comorbidities associated with genetic RCC syndromes.[4,6] Papillary RCC, which is often associated with familial RCC syndromes, is found in 20% to 50% of children with RCC.[5,16] While we do not have data on the prevalence of familial syndromes in our cohort, we found papillary RCC in 19.25%, 17.8% and 8.24% of patients 0 to 15, 15 to 21 and 21 to 30 years old, respectively. However, clear cell carcinoma and chromophobe RCC can also be associated with familial Von Hippel-Lindau and Birt-Hogg-Dubé syndromes, respectively, so the explanation of familial syndromes does not completely account for the increased prevalence of papillary RCC in children.

Additionally studies have confirmed that up to 25% of pediatric RCC tumors do not fit neatly into the pathological subtypes defined for adult RCC.[5,17,18] Instead these tumors are designated as heterogeneous RCC NOS. This subcategory in young children may represent a different set of tumors than in adolescents. Genetic translocations can be found in more than a third of pediatric RCCs and are believed to account for some of the unique pathological findings in children that are not present in adults, leading to the increased frequency of RCC NOS diagnosis.[5,19] While RCC NOS subtype is not specific to translocation morphology, these patients are encapsulated by this subset classification, which was identified in 64.6%, 55.79% and 48.04% of our patients 0 to 15, 15 to 21 and 21 to 30 years old, respectively.

Unfortunately data on histology do not completely capture genetic differences in the tumors between children and adults in our series. However, we are limited by our data set. Future studies are necessary to evaluate the difference between adult and pediatric renal tumors, to determine whether genetic variations account for differences in survival. It is also unclear why our proportion of RCC NOS is higher than that reported in the literature. However, we suspect that differences in subjective pathological scoring may account for the different rates in the varying series. Additionally this number may reflect inconsistent histological data input in the NCDB, which may be a limitation of our study. In patients younger than 21 years neither papillary RCC nor RCC NOS was independently associated with mortality.

We also found Asian race/ethnicity to be independently associated with mortality. This finding is in contrast to prior studies that have shown increased mortality to be associated with black race/ethnicity,[20–22] and that Asian status is actually associated with *improved* survival.[23] The reasons for this discrepancy are unclear. However, they may be associated with differences in the variables included in our Cox regression analysis.

Additionally our study only included patients younger than 21 years, whereas other series have considered cohorts of mostly older patients. It is also noteworthy that we considered Hispanic as a distinct race/ethnicity group regardless of identified race. Additionally all Asian subtypes were classified together. Again this result may also be an artifact of the data, since Asian subtypes comprise less than 3% of the cohort. Additionally we excluded patients with medullary RCC, a particularly aggressive form of RCC typically found in the black population with sickle cell disease.

We also found that patients with government insurance had worse survival compared to patients with private or no insurance. These findings warrant further investigation to evaluate differences in access to health care.

In addition, we discovered that while there was no difference between rates of surgery between children, adolescents and young adults, younger patients underwent lymph node dissection at a higher rate. While lymph node dissection is not

proved to be beneficial in adults with RCC, the procedure is standard care for treatment of children with Wilms tumors. Given that the majority of pediatric renal masses are Wilms tumors, the higher rate of lymph node dissection in younger patients is likely a reflection of the surgeons empirically treating children with RCC as if they had Wilms tumor until proved otherwise. Alternatively there may have been greater preoperative suspicion of lymph node metastasis due to imaging findings. Interestingly patients younger than 21 years had a surprisingly high rate of lymph node positivity, ie 46.15% of patients younger than 15 years had lymph node positivity, compared to 45.12% of those 15 to 21 and 28.47% of those 21 to 30 years. However, it is noteworthy that nodal status data were missing in 84.1% of patients overall. While the higher rate of positive nodes in children is likely due to the increased rate of lymph node dissection, the high survival rates suggest that lymph node sampling may be beneficial in children.

A greater proportion of younger patients underwent chemotherapy as first-line treatment compared to older patients. Given the limitations of the NCDB, we do not know the specific treatment regimens and cannot comment on the therapeutic efficacy of chemotherapy. However, the increased use of chemotherapy was stage dependent. After controlling for stage and other variables patients undergoing chemotherapy as first-line treatment did not have increased mortality over those treated with other modalities. Nevertheless, caution should be used when interpreting these data, since these patients uniformly had advanced disease and poor outcomes regardless of treatment.

We also discovered that patients not undergoing surgery as first-line therapy had increased mortality. This finding is likely due to selection bias, since these children were likely poor surgical candidates due to unresectability or comorbidity. Again caution is advised when interpreting these data, as we do not know the clinical indications that precluded surgery.

Our study has limitations. While the NCDB captures data from 70% of cancers in the United States, the data are only collected from institutions accredited by the Commission on Cancer, so there is questionable generalizability as safety net hospitals are underrepresented. Additionally we are limited by the retrospective data already entered in the database, and cannot account for errors in coding or omissions. Also cause of death is not recorded, so while we assume that mortality is cancer related, this may not be the case. Furthermore, we cannot account for presenting symptoms, clinical status or comorbidities that may result in differences in treatment approaches or mortality. Also our age cutoffs were based on assumptions of treating providers. The large age ranges in these subsets may disguise potential differences that are only evident in subset analyses of smaller age groups. Future studies are warranted to investigate this issue further.

Another area that warrants further study is the year of diagnosis. While it is beyond the scope of this article, our group is currently investigating changes in presentation, first-line therapy and outcomes based on year of diagnosis.

CONCLUSIONS

After evaluating a large national database we determined that children and adolescents with RCC present with more advanced disease than young adults 21 to 30 years old. After controlling for treatment, demographic and cancer variables in patients younger than 21 years mortality was associated with the chromophobe histological subtype, stage 4 disease at presentation, government insurance and not undergoing surgery as first-line therapy. Further studies are needed before definitive conclusions can be drawn.

REFERENCES

1. Siegel R, Ma J, Zou Z et al: Cancer statistics, 2014. CA Cancer J Clin 2014; **64:** 9.
2. Lipworth L, Tarone RE and McLaughlin JK: The epidemiology of renal cell carcinoma. J Urol 2006; **176:** 2353.
3. Silberstein J, Grabowski J, Saltzstein SL et al: Renal cell carcinoma in the pediatric population: results from the California Cancer Registry. Pediatr Blood Cancer 2009; **52:** 237.
4. Sausville JE, Hernandez DJ, Argani P et al: Pediatric renal cell carcinoma. J Pediatr Urol 2009; **5:** 308.
5. Ahmed HU, Arya M, Levitt G et al: Part I: Primary malignant non-Wilms' renal tumours in children. Lancet Oncol 2007; **8:** 730.
6. Selle B, Furtwangler R, Graf N et al: Population-based study of renal cell carcinoma in children in Germany, 1980-2005: more frequently localized tumors and underlying disorders compared with adult counterparts. Cancer 2006; **107:** 2906.
7. Indolfi P, Terenziani M, Casale F et al: Renal cell carcinoma in children: a clinicopathologic study. J Clin Oncol 2003; **21:** 530.
8. Cook A, Lorenzo AJ, Salle JL et al: Pediatric renal cell carcinoma: single institution 25-year case series and initial experience with partial nephrectomy. J Urol 2006; **175:** 1456.
9. Estrada CR, Suthar AM, Eaton SH et al: Renal cell carcinoma: Children's Hospital Boston experience. Urology 2005; **66:** 1296.
10. Labanaris AP, Schott GE and Zugor V: Renal cell carcinoma in children under 10 years old: a presentation of four cases. Pediatr Surg Int 2007; **23:** 327.

11. Bosquet M, Domínguez C, Balaguer J et al: Pediatric renal adenocarcinoma: a review of our series. Urology 2008; **72:** 790.

12. Tsai HL, Chin TW, Chang JW et al: Renal cell carcinoma in children and young adults. J Chin Med Assoc 2006; **69:** 240.

13. Geller JI and Dome JS: Local lymph node involvement does not predict poor outcome in pediatric renal cell carcinoma. Cancer 2004; **101:** 1575.

14. Bilimoria KY, Stewart AK, Winchester DP et al: The National Cancer Data Base: a powerful initiative to improve cancer care in the United States. Ann Surg Oncol 2008; **15:** 683.

15. Steffens S, Roos FC, Janssen M et al: Clinical behavior of chromophobe renal cell carcinoma is less aggressive than that of clear cell renal cell carcinoma, independent of Fuhrman grade or tumor size. Virchows Arch 2014; **465:** 439.

16. Renshaw AA, Granter SR, Fletcher JA et al: Renal cell carcinomas in children and young adults: increased incidence of papillary architecture and unique subtypes. Am J Surg Pathol 1999; **23:** 795.

17. Renshaw AA: Pediatric renal cell carcinomas: where do they fit in the new histologic classification of renal cell carcinoma? Adv Anat Pathol 2000; **7:** 135.

18. Bruder E, Passera O, Harms D et al: Morphologic and molecular characterization of renal cell carcinoma in children and young adults. Am J Surg Pathol 2004; **28:** 1117.

19. Argani P and Ladanyi M: Translocation carcinomas of the kidney. Clin Lab Med 2005; **25:** 363.

20. Chow WH, Shuch B, Linehan WM et al: Racial disparity in renal cell carcinoma patient survival according to demographic and clinical characteristics. Cancer 2013; **119:** 388.

21. Chow WH and Devesa SS: Contemporary epidemiology of renal cell cancer. Cancer J 2008; **14:** 288.

22. Vaishampayan UN, Do H, Hussain M et al: Racial disparity in incidence patterns and outcome of kidney cancer. Urology 2003; **62:** 1012.

23. Stafford HS, Saltzstein SL, Shimasaki S et al: Racial/ethnic and gender disparities in renal cell carcinoma incidence and survival. J Urol 2008; **179:** 1704.

EDITORIAL COMMENT

The National Wilms Tumor Study, which was one of the first multidisciplinary, multi-institutional collaborations to standardize and improve patient care, resulted in substantially better clinical outcomes for children with WT.[1] The attention directed at and the success achieved with treatment of WT should not detract from efforts to understand and manage other childhood kidney cancers. There are limited data on non-WT pediatric renal neoplasms, with most publications being case reports or small, single institution case series.[2,3] The authors nicely describe the current landscape of pediatric renal tumors. Inherent in the use of administrative data are limitations, including lack of granularity and inability to assess causality. However, given the rarity of these tumors, a national database provides more comprehensive descriptive data. The limitations of these data, nicely addressed by the authors, should not overshadow the message that a crucial first step in winning any battle is knowing the enemy.

Kathleen Kieran
Department of Urology
University of Iowa Hospitals and Clinics
Iowa City, Iowa

REFERENCES

1. Green DM: The evolution of treatment for Wilms tumor. J Pediatr Surg 2013; **48:** 14.

2. Indolfi P, Spreafico F, Collini P et al: Metastatic renal cell carcinoma in children and adolescents: a 30-year unsuccessful story. J Pediatr Hematol Oncol 2012; **34:** e277.

3. Helmy T, Sarhan O, Sarhan M et al: Renal cell carcinoma in children: single-center experience. J Pediatr Surg 2009; **44:** 1750.