Kidney Failure in Children with Wilms Tumor: A Study Based on Urine Analysis and Ultrasound

Ali Ghasemi1, Kazem Ghaffari2, Alireza Gohari3, Aziz Eghbali4, Parsa Yousefichaijan5, Vahid Falahati3

1Department of Biochemistry and Hematology, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran, 2Department of Basic and Laboratory Sciences, Khomein University of Medical Sciences, Khomein, Iran, 3Clinical Research Development Center of Amir Kabir Hospital, Arak University of Medical Sciences, Arak, Iran, 4Department of Pediatric Nephrology, Arak University of Medical Sciences, Arak, Iran, 5Clinical Research Development Center of Aliasghar Hospital, Iran University of Medical Sciences, Tehran, Iran

Abstract

Background: Renal insufficiency is one of the inevitable complications in patients with Wilms tumor (WT). The purpose of this study was to assess the renal function in children with WT at baseline and every 3 months to 2 years.

Materials and Methods: In a descriptive-analytical study from 2018 to 2020, 48 children with WT were included in the study. Urine creatinine (Uc/Cr), serum calcium (Sr/Cr), blood pressure (BP), estimated glomerular filtration rate (eGFR), and urinary protein (Up/Ur) were evaluated at baseline and every 3 months during the study. Spot Uc/Cr and spot Up/Ur/Uc ratio were calculated. Kidney ultrasonography was used in all patients. Independent Sample t-test and Chi-square tests were utilized to compare age and sex, respectively.

Results: The mean age of patients at follow-up was 7.3 years. There was no significant difference in mean Uc/Cr, Sr/Cr, eGFR, 24-h Ur/Ur, Uc/Cr ratio, and spot Ur/Ur ratio at baseline and end of study (Pbaseline > 0.05, Pend of study > 0.05). Analysis of kidney size showed a statistical association with tumor stage (P < 0.05). Comparison of the kidney size in patients showed that there is a statistically significant difference (P < 0.0001) at baseline and end of the study.

Conclusion: This study showed that as WT progressed, the size of the kidneys increases without any renal insufficiency. Therefore, it seems that urinalysis of patients with WT along with sonography is necessary to determine renal insufficiency and the use of ultrasound alone to determine kidney insufficiency is not recommended.

Keywords: Child, renal insufficiency, Wilms tumor

INTRODUCTION

Wilms tumor (WT) is the most common renal malignancy and is one of the most common abdominal tumors in children, also known as nephroblastoma or renal embryoma. The prevalence of WT in children under 15 years of age is 1 in 100,000 and accounts for about 5% of all childhood malignancies,[1] which can emerge as a simple nodule, unilateral multifocal lesion, and bilateral tumors.[2] Bilateral tumors are found in 5%–14% of WT patients.[3]

Several studies had shown that aging independently increases the risk of nonmetastatic WT recurrence. The age of fewer than 2 years is recognized as a pleasant factor in prognosis and the age of more than 4 years is known as the factor of poor prognosis in children.[2,4]

The clinical symptoms of WT in infants are as same as signs in older children and were usually diagnosed by a randomly identified abdominal mass; however, some patients with kidney

Quick Response Code: 
Website: www.advbiores.net
DOI: 10.4103/abr.abr_367_21

How to cite this article: Ghasemi A, Ghaffari K, Gohari A, Eghbali A, Yousefichaijan P, Falahati V. Kidney failure in children with Wilms tumor: A study based on urine analysis and ultrasound. Adv Biomed Res 2022;11:89.
tumors at this age may also present hematuria, hypertension, and metastatic symptoms such as hydrocephalus or a mass on neonatal ultrasound. The survival of the patients with WT had increased drastically from 30% in previous years to 90% survival of 5–7 years in the current years. As the number of children rescued increases, the problem of delayed toxicity from treatment is significant. The application of radiation therapy is one of the significant factors causing long-term complications.

In treated patients, as long as nephrectomy is an important part of the treatment of the disease. Chronic kidney disease is a unique potential complication and the quality of life after treatment depends on kidney function. Although end-stage renal disease is uncommon in nonsyndromic unilateral tumors; but studies have shown a decrease in glomerular filtration rate (GFR) in the long term in these patients. Maintaining normal renal function in patients with bilateral WT is essential for hemodialysis and prevention of renal dysfunction, but this procedure is very complicated in tumors larger than 4 cm in diameter and multifocal nephroblastoma. Furthermore, a dramatic decrease in the number of nephrons is associated with the development of hypertension and progressive renal failure, known as the Brenner-Barker hypothesis. Therefore, a better understanding of the late effects of WT disease is essential to increase patient survival and quality of life. Evaluation of late complications of tumors in children, such as risk factors and prevalence, are important topics for risk management and selecting appropriate treatment strategies. The purpose of this study was to assess the renal function in children with WT at baseline and every three months to 2 years.

**Materials and Methods**

**Patients**

In a descriptive-analytical study from 2018 to 2020, 48 children with WT were selected at the Amir-Kabir Hospital, Arak, Iran, and have a minimum follow-up of 2 years. All ethical principles were observed according to the ethical protocol approved by the Research Ethics Committee of Arak University of Medical Sciences (IR.ARAKMU.REC.1397.310) and the criteria for excluding the study included conscious dissatisfaction, unwillingness to continue to participate in the study. After obtaining informed consent children aged 2–8 years were selected and included in the study. The study was done according to the Declaration of Helsinki. One of the most important treatment and prognostic criteria for patients with WT are the grade. WT grading criteria are not based on biological and molecular markers but the anatomic extent of the tumor. Patients grading was determined as described elsewhere. Based on the stage, patients were classified into 4 categories (WT-I, WT-II, WT-III, and WT-IV).

**Anthropometric data**

Demographic and clinical information of patients were initially recorded. Weight was measured using the standard methods as recommended by Lohman. The error due to heavy clothing and shoes in calculating the weight of patients was calculated. Height was calculated to the nearest 0.1 cm using commercial stadiometers available in the market (Leicester Height Measure, Invicta Plastics Ltd., UK). To measure height, conditions such as removing the shoes, the body is fully stretched, upright without bending, arms stretched along shoulder width, face directly in front of the researcher so that the Frankfort plane was considered. Body mass index (BMI) was measured using Quetelet’s equation (weight in kg/height in m²). BMI was calculated based on Z-score using the WHO method. Waist circumference (WC) was measured to the level of umbilicus using a measuring tape, by measured midway between the lower surface of the ribs and the iliac crest in a horizontal line. Hip circumference (HC) was measured at the widest part of the hip. Three measurements to the nearest 0.1 cm were recorded for each WC and HC. Then, the average of the measurements was calculated. All measurements were calculated with the same tape and without clothes. The weight-to-height ratio (WHtR) was obtained by dividing the mean WC by the mean height. The waist-to-hip ratio (WHR) was obtained by dividing the mean WC by the mean HC.

Blood pressure (BP) was measured 3 times at 1-min intervals after the patients had rested for 10 min in a sitting position. A suitable cuff was used based on the size of the patient’s arm to prevent false results. The mean values of the first two readings for systolic BP (SBP) and diastolic BP (DBP) were calculated separately. If the difference in the first two readings was more than 10, the average of the two close readings was calculated. SBP and DBP were measured by a researcher on the right arm using a standard sphygmomanometer according to the World Health Organization (WHO) recommendations. Hypertension is defined as average SBP and/or DBP that is greater than the 95th percentile for gender, age, and height.

**Evaluation of renal function**

Various laboratory tests were performed to assess kidney activity. Spot urine and 24-h urine sample were collected from patients. Both first morning and random samples are acceptable, although first morning samples are preferable if possible. Urine creatinine concentration (U_{C_r}), urine calcium concentration (U_{C_a}), and urine protein (U_{U_ro}) were determined and recorded at the baseline and every three months during the study for renal function evaluating by Kinetic Jaffe reaction, the colorimetric method with methylthymol blue, and turbidimetric method, respectively, using an Auto Analyzer Roche/Hitachi Modular DPP. Five milliliter of blood samples were collected to evaluate serum creatinine (S_{C_r}). The standard range of S_{C_r} was classified according to age and sex.

Then spot U_{C_a}/U_{C_r} ratio and spot U_{U_ro}/U_{C_r} ratio were calculated by dividing the U_{C_a} to the U_{C_r} and the U_{U_ro} to the U_{C_r}, respectively. A normal reference interval for the U_{C_a}/U_{C_r} (mg/mg) ratio is <0.14. Hypercalciuria was considered as U_{C_a}/U_{C_r} >0.25 mg/mg. However, the upper limit of U_{C_a}/U_{C_r}
is controversial for accurately determining hypercalciuria.\[16\] Spot U\textsubscript{pro}/U\textsubscript{cre} ratio >0.7 mg/mg is defined as proteinuria.\[17\]

Hemoglobin concentration (Hb) was measured in potassium EDTA using standard methods. Estimated GFR (eGFR) was calculated using the conventional Schwartz equation (k × height of the child in cm/serum creatinine concentration in mg/dl, k=0.55 for children aged 2–12 years).\[18\]

Kidney ultrasonography was used in all patients to determine kidney size. Patients were evaluated in the position of supine decubitus. Two well-trained radiologists performed an ultrasound examination of the kidneys using a standard B-mode gray-scale ultrasound machine (EUB-8500, Hitachi Medical Corp., Tokyo, Japan), with a 7.5–13.0 MHz frequency probe. At maximal length points, kidney size was measured. Standard laboratory methods were used to measure the desired blood and urine parameters. Before and during the study, all equipment used for the measurement was calibrated. Each measurement was performed three times by experienced and trained members of the research team.

**Statistical analysis**

Data were expressed as mean ± standard deviation (SD). The analysis was performed applying GraphPad Prism 6.0 (GraphPad Software, San Diego, CA). Independent Sample t-test and Chi-square tests were utilized to compare age and sex, respectively. Pearson correlation test was used to identify the correlations for continuous variables. A cumulative hazard of renal dysfunction (%) was reported for patients with WT. To evaluate renal dysfunction, U\textsubscript{pro} excretion was calculated. The significance level of the P value was considered less than 0.05.

**RESULTS**

A total of 48 patients with a mean age at diagnosis of 5 ± 3.2 years (range 2.6–9.4 years) were enrolled and selected to participate in the study. The mean age of patients at follow-up was 7.3 years (range 3.7–11.1 years), mean follow-up time was 1.9 years (range 0.5–2.0 years). Of the 48 WT included, 28 (58.3%) were female, 20 (41.7%) were male. The right kidney was affected by the tumor in 52% of cases and the left kidney in 48% of cases. Ten patients (20.8%) had grade I (WT-I) of the disease, 21 (43.7%) had grade II of the disease (WT-II), 9 (18.8%) had grade III of the disease (WT-III), and 8 (16.7%) had grade IV of the disease (WT-IV). None of the patients had a urinary tract infection at the time of evaluation.

Demographic and anthropometric characteristics are shown in Table 1. An estimated cumulative hazard of renal dysfunction in patients was noticeably increased beyond 2 years of follow-up [Figure 1]. Analysis of BP in the present study showed that overall, 4 of the patients (8%) were found to have abnormal SBP and 2 (4%) abnormal DBP, based on the consensus guidelines for diagnosis of hypertension.\[19\] However, no significant differences were observed in systolic and diastolic BP at baseline and end of study (P>0.05).

There was no significant difference in mean weight, height, WC, HC, WHR, WHtR, and BMI at baseline and at the end of the study (P\textsubscript{baseline} > 0.05, P\textsubscript{end of study} > 0.05).

In total, the mean ± SD of U\textsubscript{cre}, S\textsubscript{cre}, eGFR, and 24-h U\textsubscript{pro} were 139.3 ± 1.05 mg/dl, 1.9 ± 0.05 mg/dl, 110.8 ± 1.2 mL/min/1.73 m\textsuperscript{2}, and 320.9 mg/day, respectively, at baseline. No significant differences were observed in U\textsubscript{cre}, S\textsubscript{cre}, eGFR, and 24-h U\textsubscript{pro} between different grades at baseline (P>0.05), but there was a significant difference in U\textsubscript{cre} and 24-h U\textsubscript{pro} between grade 1 and grade 4 of the disease at baseline and end of study (P<0.05). In total, the mean ± SD of U\textsubscript{cre}, S\textsubscript{cre}, eGFR, and 24-h U\textsubscript{pro} were 141.5 ± 3.16 mg/dl, 1.9 ± 0.08 mg/dl, 110.7 ± 1.3 mL/min/1.73 m\textsuperscript{2}, and 401.9 mg/day, respectively, at the end of the study. No significant differences were observed in U\textsubscript{cre} and 24-h U\textsubscript{pro} between different grades at the end of the study (P>0.05). There was no significant difference in mean U\textsubscript{cre}, S\textsubscript{cre}, eGFR, 24-h U\textsubscript{pro}/U\textsubscript{cre}, spot U\textsubscript{pro}/U\textsubscript{cre}, and Hb level at baseline and end of study (P\textsubscript{baseline} > 0.05, P\textsubscript{end of study} > 0.05). There was a trend toward higher U\textsubscript{cre} concentration and 24-h U\textsubscript{pro} along with increasing the grades of the tumor, so that U\textsubscript{cre} concentration and 24-h U\textsubscript{pro} in WT-IV were more than WT-I, WT-II, and WT-III [Table 1].

Thirty-nine patients (81.2%) at baseline and 41 patients (85.4%) at the end of the study had a high spot U\textsubscript{pro}/U\textsubscript{cre} >0.7 mg/mg which indicates proteinuria. Patients with higher grades had more severe proteinuria (data not shown). No significant differences were observed in spot U\textsubscript{pro}/U\textsubscript{cre} ratio between grade 1 and grade 4 of the disease at baseline (P = 0.074) and end of study (P = 0.132).

Forty-one patients (85.5%) at baseline and 42 patients (87.5%) at the end of the study had a high U\textsubscript{cre}/U\textsubscript{pro} ratio which indicates hypercalciuria. Patients with higher grades had more severe hypercalciuria (data not shown). There was a significant difference in U\textsubscript{cre}/U\textsubscript{pro} ratio between grade 1 and grade 4 of the disease at baseline (P = 0.024) and end of study (P = 0.038).

Analysis of kidney size showed a statistical association with tumor grade (P<0.05). The size of the kidney in WT-IV was
### Table 1: Demographic and anthropometric characteristics of patients with Wilms tumor

| Variables       | Minimum | Maximum | Baseline | Grade* | After follow-up |
|-----------------|---------|---------|----------|--------|-----------------|
|                 |         |         | I  | II  | III | IV  | P      | I  | II  | III | IV  | P      |
| Age (years)     | 2.6     | 9.4     | 4.1 (0.12) | 5.4 (0.03) | 3.5 (2.14) | 5.7 (3.01) | 0.563 | 0.687 | 5.2 (0.32) | 6.1 (0.13) | 5.3 (1.61) | 6.6 (2.91) | 0.324 | 0.568 |
| Weight (kg)     | 9.3     | 29.6    | 16.2 (1.20) | 18.0 (0.33) | 15.3 (2.47) | 14.6 (1.51) | 0.358 | 0.536 | 19.5 (1.61) | 20.0 (1.19) | 16.6 (0.93) | 17.0 (1.53) | 0.128 | 0.456 |
| Height (cm)     | 85.6    | 11.7    | 99.1 (1.35) | 95.0 (1.78) | 97.3 (0.32) | 96.5 (2.34) | 0.430 | 0.741 | 106.2 (1.23) | 102.1 (2.31) | 104.1 (0.47) | 103.5 (2.36) | 0.398 | 0.854 |
| BMI Z-score     | 0.71    | 0.79    | 0.74 | 0.72 | 0.76 | 0.73 | 0.897 | 0.874 | 0.74 | 0.73 | 0.77 | 0.74 | 0.568 | 0.787 |
| WC (cm)         | 43.5    | 60.7    | 51.5 (0.10) | 50.8 (1.23) | 52.3 (1.45) | 52.9 (2.78) | 0.374 | 0.852 | 52.2 (1.58) | 51.2 (0.32) | 53.0 (1.89) | 54.5 (2.41) | 0.421 | 0.769 |
| HC (cm)         | 61.7    | 70.1    | 63.4 (1.78) | 63.5 (0.23) | 64.9 (1.98) | 65.0 (1.82) | 0.572 | 0.368 | 64.7 (1.84) | 64.8 (1.43) | 65.7 (1.05) | 66.3 (2.31) | 0.380 | 0.438 |
| WHR             | 0.70    | 0.86    | 0.81 | 0.79 | 0.80 | 0.81 | 0.857 | 0.987 | 0.80 | 0.79 | 0.80 | 0.82 | 0.877 | 0.957 |
| WHRr            | 0.50    | 0.52    | 0.52 | 0.53 | 0.53 | 0.54 | 0.645 | 0.889 | 0.50 | 0.50 | 0.50 | 0.52 | 0.357 | 0.897 |
| SBP (mmHg)      | 90.1    | 11.58   | 90.5 (0.02) | 90.5 (0.01) | 91.0 (0.11) | 90.3 (0.27) | 0.877 | 0.877 | 91.3 (0.14) | 90.9 (0.31) | 91.9 (0.03) | 91.3 (0.25) | 0.612 | 0.979 |
| DBP (mmHg)      | 45.3    | 56.7    | 51.3 (0.12) | 51.0 (1.03) | 50.2 (0.05) | 51.3 (1.05) | 0.831 | 0.995 | 51.5 (1.25) | 51.3 (0.38) | 51.6 (1.96) | 51.5 (1.65) | 0.990 | 0.905 |
| UCr (mg/dl)     | 78.2    | 356.1   | 120.1 (32.3) | 131.7 (41.2) | 149.5 (29.3) | 168.9 (26.8) | 0.083 | 0.041 | 125.3 (29.8) | 133.6 (32.2) | 156.4 (20.3) | 171.4 (30.6) | 0.074 | 0.038 |
| Serum Cr (mg/dl)| 1.8     | 2.5     | 1.8 (1.01) | 1.9 (1.12) | 1.9 (1.30) | 2.0 (1.54) | 0.158 | 0.657 | 1.9 (0.09) | 1.9 (1.02) | 1.9 (0.64) | 2.1 (1.37) | 0.141 | 0.753 |
| 24 h UPro (mg/day)| 94.1  | 960.8   | 239.4 (16.1) | 283.8 (29.6) | 366.8 (35.3) | 475.7 (31.6) | 0.093 | 0.021 | 270.4 (18.6) | 294.0 (20.2) | 375.3 (26.3) | 513.2 (34.9) | 0.081 | 0.011 |
| UCa/Ucr ratio (mg/mg)| 0.04 | 1.09 | 0.98 (0.01) | 0.10 (0.17) | 0.34 (0.06) | 0.50 (0.44) | 0.215 | 0.024 | 0.10 (0.32) | 0.11 (0.09) | 0.38 (1.81) | 0.81 (0.08) | 0.138 | 0.038 |
| UPro/Ucr ratio (mg/mg)| 0.01 | 0.51 | 0.15 (0.01) | 0.32 (0.10) | 0.35 (0.08) | 0.39 (0.05) | 0.412 | 0.074 | 0.17 (0.03) | 0.33 (0.13) | 0.36 (0.21) | 0.41 (0.09) | 0.403 | 0.132 |
| Hb (g/dl)       | 13.4    | 15.9    | 13.9 (0.02) | 14.6 (0.01) | 14.3 (0.12) | 14.1 (0.32) | 0.970 | 0.988 | 14.2 (0.07) | 14.7 (0.71) | 14.5 (0.36) | 14.2 (1.21) | 0.865 | 0.965 |
| eGFR (mL/min/1.73 m²)| 109.1 | 112.4   | 111.1 (1.45) | 110.9 (0.38) | 111.2 (1.58) | 109.6 (1.76) | 0.385 | 0.567 | 111.5 (0.12) | 111.0 (0.85) | 110.9 (1.01) | 109.3 (1.52) | 0.771 | 0.387 |
| Kidney size (cm)| 7.3     | 9.3     | 7.5 (0.32) | 7.8 (1.03) | 8.0 (1.74) | 8.9 (1.55) | 0.048 | 0.036 | 7.7 (0.56) | 8.2 (1.25) | 8.7 (0.36) | 9.0 (1.28) | 0.045 | 0.047 |

*Data are presented as mean±SD. **Compared the values in Grade 1 and Grade 4 of the disease at baseline. ***Compared the values in Grade 1 and Grade 4 of the disease after follow-up. BMI: Body mass index, DBP: Diastolic blood pressure, HC: Hip circumference, SBP: Systolic blood pressure, WC: Waist circumference, WHR: Waist-to-hip ratio, WHtR: Waist-to-height ratio, eGFR: Estimated glomerular filtration rate, Cr: Creatinine, Hb: Hemoglobin level, Ca: Calcium, UPro: Total urinary protein, UCa: 24 h urinary calcium excretion, U: Urine, Pro: Protein, SD: Standard deviation.
larger than other grades at baseline and after follow-up [Table 1]. Comparison of the kidney size in patients showed that there is a statistically significant difference ($P < 0.0001$) at baseline and duration of the study [Figure 2]. Therefore, there was a significant difference in kidney size between grade 1 and grade 4 of the disease at baseline ($P = 0.048$) and end of study ($P = 0.047$).

**Discussion**

This study revealed that the most frequent grade of the disease in children was WT-II. Our result showed that BMI, systolic-diastolic BP, urine protein, urine Cr, serum Cr, urine Ca, serum Ca, UCa/UCr ratio, Hb level, and eGFR in baseline and during the study did not change significantly. However, the kidney size increased significantly in patients. In the other words, patients with WT are greatly predisposed to the increase of kidney size over time and it seems that the first renal symptom in these patients is an oversized kidney. It can be effective in the patient’s follow-up with WT who are being treated. Given that patients with WT are at risk for renal impairment during treatment with nephrectomy, chemotherapy, or radiation, it is important to find a marker to indicate a renal function in these patients. In this study, we showed that as WT progressed, the size of the kidneys increases without any renal dysfunction. Therefore, it seems that urinalysis of patients with WT along with sonography is necessary to determine renal dysfunction and the use of ultrasound alone to determine kidney dysfunction is not recommended.

In a study about evaluating renal function in 75 patients with WT, the authors found that most patients were in grades I and II and none of the patients had eGFR less than 60. They also showed that 6.7% of patients had hypertension, and patients with WT who had undergone surgery and had not received nephrotoxic chemotherapy or radiotherapy were less likely to have renal dysfunction. However, monitoring is necessary to assess renal function (to identify a limited group of patients with impaired renal function).[20]

Mullen *et al.* evaluated the role of sonography in the diagnosis of WT recurrence in patients with WT recurrence and found that follow-up using regular sonography showed major abdominal recurrences.[21]

Monastyrskyi *et al.* evaluated the changes in kidney size after nephrectomy in mice and found that animals undergoing nephrectomy had a significant increase in kidney size.[22] In our study, we found that based on sonography, the kidney size increased significantly during the study, but no changes in the variables related to renal function including eGFR, creatinine, urine Ca/Cr, and urine Pr/Cr were seen. Therefore, according to the study by Monastyrski *et al.* in which an increase in kidney size had been seen following nephrectomy and also because the main treatment is involved in patients with WT surgery and renal nephrectomy, it seems that the use of ultrasound and kidney size assessment of all patients during the disease in the diagnosis possible renal dysfunction has no role and due to the increased response in kidney size, ultrasound is not a suitable method to follow-up patients. However, to investigate the relationship between increased kidney size and the occurrence of renal dysfunction in patients with WT, more studies are needed over a long time.

Furthermore, several studies have shown an intimate relationship between kidney size and its function, though, concerning the results of our study, there is no relationship between sonographic findings and renal dysfunction in patients with WT.

In a study, Antoniewicz *et al.* evaluated renal function (serum level of creatinine and eGFR) in patients (mean age ± SD, 62.2) with kidney tumor who had undergone surgery and found that from 3 months after surgery, the serum level of creatinine increased, but the level of eGFR decreased.[23] However, in our study, the mean of creatinine and eGFR did not change significantly during the study. One of the reasons for the difference between the results of the present study and the above study could be the difference in the age range of the patients studied. Furthermore, differences in tumor type can be another reason for differences in the results of the two studies. Due to the few studies on renal dysfunction in patients with WT, there could not compare the results of the variables in patients with WT with the other studies.

**Conclusion**

The present study showed that as WT progressed, the size of the kidneys increases without any renal dysfunction. Therefore, it seems that urinalysis of patients with WT along with sonography is necessary to determine renal dysfunction and the use of ultrasound alone to determine kidney dysfunction is not recommended.

**Acknowledgment**

The authors acknowledge the staff of the Blood and Oncology Department of Amirkabir Hospital, Arak, Iran.
Financial support and sponsorship

This study is under the Arak University of Medical Sciences grant with Grant No. 3167.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Berthold F, Spix C, Kaatsch P, Lampert F. Incidence, survival, and treatment of localized and metastatic neuroblastoma in Germany 1979-2015. Paediatr Drugs 2017;19:577-93.
2. Gooskens SL, Segers H, Pritchard-Jones K, Graf N, Dome JS, van den Heuvel-Eibrink MM. The clinical relevance of age at presentation in nephroblastoma. Exon Publications; 2016. p. 23-30.
3. Chaussy Y, Vieille L, Lacroix E, Lenoir M, Marie F, Corbat L, et al. 3D reconstruction of Wilms’ tumor and kidneys in children: Variability, usefulness and constraints. J Pediatr Urol 2020;16:830.e1-8.
4. Pritchard-Jones K, Kelsey A, Vujanic G, Imeson J, Hutton C, Mitchell C, et al. Older age is an adverse prognostic factor in stage I, favorable histology Wilms’ tumor treated with vincristine monochemotherapy: A study by the United Kingdom Children’s Cancer Study Group, Wilm’s Tumor Working Group. J Clin Oncol 2003;21:3269-75.
5. Sayed HA, Ali AM, Hamza HM, Abdalla MA. Long-term follow-up of infantile Wilms tumor treated according to International Society of Pediatric Oncology protocol: Seven years’ follow-up. Urology 2011;77:446-51.
6. Spreadico F, Fernandez CV, Brok J, Nakata K, Vujanic G, Geller JI, et al. Wilms tumour. Nat Rev Dis Primers 2021;7:75.
7. Green DM, Wang M, Krasin MJ, Davidoff AM, Sivastava D, Jay DW, et al. Long-term renal function after treatment for unilateral, nonsyndromic Wilms tumor. A report from the St. Jude lifetime cohort study. Pediatr Blood Cancer 2020;67:e28271.
8. Interiano RB, Delos Santos N, Huang S, Sivastava DK, Robison LL, Hudson MM, et al. Renal function in survivors of nonsyndromic Wilms tumor treated with unilateral radical nephrectomy. Cancer 2015;121:2449-56.
9. Mullen EA, Chi YY, Hibbitts E, Anderson JR, Steacy KJ, Geller JI, et al. Impact of surveillance imaging modality on survival after recurrence in patients with favorable-histology Wilms tumor: A report from the children’s oncology group. J Clin Oncol 2018;36:JCO1800076.
10. Riis P. Thirty years of bioethics: The Helsinki declaration 1964-2003.

New Rev Bioeth 2003;3:1:15-25.
11. Blössner M, Siyam A, Borghi E, Onyango A, De Onis M. WHO AnthroPlus for Personal Computers Manual: Software for Assessing Growth of the World’s Children and Adolescents. Geneva, Switzerland: World Health Organization; 2009.
12. Kjeldsen SE. Hypertension and cardiovascular risk: General aspects. Pharmacol Res 2018;129:95-9.
13. Baker-Smith CM, Flynn SK, Flynn JT, Kaelber DC, Blowey D, Carroll AE, et al. Diagnosis, evaluation, and management of high blood pressure in children and adolescents. Pediatrics 2018;142:e20182096.
14. Robertson J, Shilkofski N. The Harriet Lane handbook: A manual for pediatric house officers. Mosby; 2005.
15. Foley KF, Boccuzzi L. Urine calcium: Laboratory measurement and clinical utility. Lab Med 2010;41:683-6.
16. Al Ghali R, El-Mallah C, Obeid O, El-Saleh O, Smail L, Haroun D. Urinary minerals excretion among primary schoolchildren in Dubai – United Arab Emirates. PLoS One 2021;16:e0255195.
17. Siu WK, Mak CM, Lee HC, Tam S, Lee J, Chan TM, et al. Correlation study between spot urine protein-to-creatinine ratio and 24-hour urine protein measurement in 174 patients for proteinuria assessment. Hong Kong J Nephrol 2011;13:51-4.
18. Schwartz GJ, Work DF. Measurement and estimation of GFR in children and adolescents. Clin J Am Soc Nephrol 2009;4:1832-43.
19. de Ferranti SD, Steinberger J, Amoduri R, Baker A, Gooding H, Kelly AS, et al. Cardiovascular risk reduction in high-risk pediatric patients: A scientific statement from the American Heart Association. Circulation 2019;139:e603-34.
20. Wenzel M, Yu H, Uhrig A, Würschimmel C, Wallbach M, Becker A, et al. Cystatin C predicts renal function impairment after partial or radical tumor nephrectomy. Int Urol Nephrol 2021;53:2041-9.