Renal growth slope in children with congenital and acquired solitary functioning kidneys

Abbreviated title: Renal growth in solitary functioning kidneys

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Renal growth slope in children with congenital and acquired solitary functioning kidneys
Abstract

Purpose: To analyze the renal growth slope in children with congenital (unilateral renal agenesis as Agenesis group and multicystic dysplastic kidney [MCDK] as MCDK group) and acquired (nephrectomy associated with renal tumors as Nephrectomy group) solitary functioning kidneys.

Methods: This retrospective study included all renal ultrasonography examinations performed in children in the Agenesis, MCDK, or Nephrectomy group between September 2002 and February 2019. We reviewed the images and recorded the contralateral kidney size only when there was no focal lesion. Linear mixed model or piecewise linear mixed model analyses with a 24-month time point were performed to compare the groups.

Results: There were 132 patients, including 26 patients in the Agenesis group, 35 in the MCDK group, and 71 in the Nephrectomy group. The Nephrectomy group showed the largest baseline kidney size (7.4 cm vs. 5.3 cm in the Agenesis [p < 0.001] and 5.2 cm in the MCDK [p < 0.001] groups) and the smallest overall growth slope (0.04 cm/month vs. 0.06 cm/month in the Agenesis [p = 0.004] and 0.07 cm/month in the MCDK [p < 0.001] groups). However, considering the time point of 24 months reaching adult renal function, there were significant changes in slope, from 0.1 cm/month before 24 months of age to 0.03 cm/month after 24 months of age in all three groups (p < 0.001) without difference between the groups.

Conclusion: There are significant changes in renal growth slope before and after 24 months of age without difference between congenital and acquired solitary functioning kidneys during childhood follow-up.

Keywords: Solitary Kidney; Unilateral Renal Agenesis; Multicystic Dysplastic Kidney; Nephrectomy; Ultrasonography
Introduction

The kidneys are composed of three structures: the pronephros, mesonephric duct, and metanephric duct. A normal kidney contains approximately 1 million nephrons, even though the number varies widely, and no new nephrons are formed in human kidneys after approximately 36 weeks' gestation [1]. In normal renal growth after birth, renal length and volume are affected by overall body size of the individual, including age, height, weight, and body surface area [2,3]. The glomerular filtration rate (GFR) is considered the best overall indicator of renal function. In children, the GFR increases with age and is calculated with specific equations that are different from those used for adults. Adjusted for body surface area, the GFR reaches the adult level of ~120 mL/min/1.73 m^2 by approximately two years of age [4].

In pediatric patients, for some reasons, one has to live a life with a solitary functioning kidney which can be divided into two types: congenital or acquired. The congenital type includes unilateral renal agenesis and multicystic dysplastic kidney (MCDK), and the acquired type includes nephrectomy for various reasons, such as congenital anomalies, renal trauma, and renal malignancy [5,6].

Unilateral congenital renal agenesis is defined as unilateral congenital absence of renal tissue due to failure of embryonic kidney formation. This disease is associated with urological anomalies such as ureteropelvic junction obstruction or vesicoureteral reflux in the contralateral kidneys, hypertension, proteinuria, or impaired renal function, which can require dialysis in up to 50% of cases [7-9]. MCDK is the most common cystic renal disease in children. Patients with unilateral MCDK may also have anomalies such as vesicoureteral reflux, ureteropelvic junction obstruction, or vesicoureteral junction obstruction, which occurs in one-third of patients [10,11]. Therefore, identifying combined contralateral renal abnormalities is important for determining prognoses in children with unilateral renal agenesis or MCDK. Adequate length of the congenital solitary functioning kidney is a key parameter for renal function [12]. However, according to several theories and some evidence of remained functional renal tissue in MCDK [13], the renal growth slope can be different between renal
Nephroblastoma is the most common pediatric renal tumor and accounts for at least 90% of cases [15]. Treatment of unilateral nephroblastoma differs depending on inclusion of neoadjuvant chemotherapy, but complete resection is the main treatment approach [16]. Removal of one kidney leads to structural and functional changes in the remaining kidney, with creatinine elevation or microalbuminuria [17]. Therefore, after nephrectomy, surveillance of the contralateral kidney including renal growth is important, especially in children.

Previous studies have shown that the contralateral kidney in each of the three disease groups shows compensatory hypertrophy during follow-up [18]. However, most studies have suggested only compensatory renal hypertrophy, and only a few have suggested patterns of size change during follow-up [19-21]. In addition, no studies have assessed differences in growth slope between these three disease groups with different etiologies. Therefore, in this study, we analyzed the growth slope of congenital and acquired solitary functioning kidneys in children belonging to each disease group and assessed the differences between the groups.

Materials and Methods

Study design

This retrospective study was approved by the Institutional Review Board of our institution, and the requirement for informed consent was waived. All renal ultrasonography examinations performed between September 2002 and February 2019 in children (under 18 years of age at the time of examination) with congenital or acquired solitary functioning kidneys at our institution were included. Diseases categorized as congenital solitary functioning kidney included unilateral renal agenesis and MCDK, and diseases of acquired solitary functioning kidney included unilateral nephrectomy for primary renal tumor. We excluded examinations that showed abnormal parenchymal echogenicity or focal lesions, including renal cysts, scarring, or hydronephrosis in the contralateral kidney.
Patient data and images were retrospectively obtained from the electronic medical records and picture archiving and communication system. Sex, age at the time of each ultrasonography examination, and laboratory results on renal function, including serum creatinine, Cystatin C, and estimated GFR within two-week intervals of each ultrasonography examination, were recorded. The normal range of serum creatinine is 0.3-0.7 mg/dL for children under age 3 and 0.5-1.0 mg/dL for children ages 3-18 years. The normal range of Cystatin C is 0.59–1.97 mg/L for infants and 0.50–1.27 mg/L for children ages 1-18 years, and that of estimated GFR increases by age up to two years and is 90-160 mL/min/1.73 m³ for children ages 2-12 years and 110-170 mL/min/1.73 m³ for children ages 13-18 years. These biomarkers have different normal ranges depending on age in children [22], and the results of multiple follow-up tests in each patient were different. Therefore, we could not classify them as normal and abnormal. The presence of proteinuria was also assessed, if available within two weeks of the ultrasonography examinations during follow-up.

Renal ultrasonography and image review

Renal ultrasonography examinations were performed by pediatric radiologists using convex or linear transducers of HDI 5000 or IU-22 scanners (Philips Medical Systems, Bothell, WA, USA). The patients were in a supine position during the examinations. Although measurements of kidney size taken in a supine position can be 2 to 3 mm larger than those taken in a prone position [23], all patients were measured in the same position in order to allow for direct comparison. One radiologist reviewed the images and remeasured the kidney size as the maximum bipolar dimension in a longitudinal plane that displayed the best central sinus echoes in the blind status of the disease group. Any abnormalities in the renal parenchyma were recorded, and any kidneys with focal lesions were excluded from this study.

Statistical analyses
The patients were classified into three groups based on disease: Agenesis, MCDK, and Nephrectomy. Age at the time of each examination, laboratory findings, number of ultrasonography examinations, and size of the contralateral kidney were compared among the three groups. Baseline characteristics of the study populations in the three groups were compared using analysis of variance (ANOVA) for continuous variables and the chi-square test for categorical variables. Multiple comparison tests were performed for variables with significant differences among the three groups.

The size of the contralateral kidney without gross lesion was measured several times during the follow-up period, and longitudinal data analysis was implemented as follows. First, the size of contralateral kidney profiles in each patient over time was represented graphically using a spaghetti plot. Second, we investigated the associations between growth of the kidney and diseases using the linear mixed models with random effects. Pediatric GFR approaches adult levels by approximately 24 months of age [4], and the organ grows slowly after that time period [24]. To study the change associated with the critical time point, we implemented a piecewise linear mixed model to identify differences in renal growth slope before and after the age of 24 months. The piecewise linear mixed-effects models allow different linear functions of time corresponding to the periods before and after 24 months of age to obtain the data of renal growth slope in each time period [25,26]. Based on the change time point of 24 months of age, slope change was also evaluated. We then investigated whether sex was associated with change of renal growth slope across groups. Statistical analyses were performed with SPSS version 25 (IBM Corp., Armonk, NY) and SAS version 9.4 (SAS Institute Inc., Cary, NC). A p-value <0.05 was considered statistically significant, except for the multiple comparisons, which used a cutoff of 0.017.

Results

Demographics and clinical results

There were 1375 renal ultrasonography examinations of 193 pediatric patients during the study period.
Among these, 35 patients had unilateral renal agenesis, 62 patients had MCDK, and 96 patients had history of nephrectomy for primary renal tumor (95 nephroblastoma and 1 rhabdoid tumor of the kidney). From the review of images, 61 patients with 896 examinations were excluded due to combined diffuse or focal lesions in the contralateral kidney. The percentages of excluded patients were 25.7% from the Agenesis group, 43.5% from the MCDK group, and 26.0% from the Nephrectomy group. Therefore, a total of 479 ultrasonography examinations of contralateral kidneys without gross lesions from 132 pediatric patients were analyzed in this study (Figure 1).

There were 26 patients with 131 examinations in the Agenesis group, 35 patients with 171 examinations in the MCDK group, and 71 patients with 177 examinations in the Nephrectomy group. A summary of the demographics and laboratory findings of the three groups is presented in Table 1. There were 59 male and 73 female patients in total, and there were more female patients in the Nephrectomy group compared to the other groups (p ≤ 0.011). The mean age at the time of all ultrasonographic evaluations was 36.4 ± 39.4 months, with a range of 0-204 months. The mean age at the time of ultrasonography examinations was significantly older in the Nephrectomy group (60.6 ± 45.0 months) compared to the other two groups (23.1 ± 26.6 months in the Agenesis group and 21.6 ± 27.8 months in the MCDK group, p < 0.001). The mean age at the time of initial ultrasonography was also older in the Nephrectomy group than in the other two groups (p < 0.001 for both, Table 1).

Analysis of laboratory findings indicated that only serum creatinine level was significantly different between the Nephrectomy group and the MCDK group and was higher in the Nephrectomy group (mean, 0.43 ± 0.17 mg/dL vs. 0.36 ± 0.14 mg/dL; p < 0.001). The mean estimated GFR was 120.3 ± 44.0 mL/min/1.73 m² overall with a range of 26.2-241.7 mL/min/1.73 m². The estimated GFR was less than 90 mL/min/1.73 m² in 3 patients in the Agenesis group, 7 in the MCDK group, and 4 in the Nephrectomy group. Proteinuria was present in 5 patients in the Agenesis group, 6 in the MCDK group, and 11 in the Nephrectomy group.

Renal growth results
The mean number of follow-up visits for each patient was 5.0 in the Agenesis group, 4.9 in the MCDK group, and 2.5 in the Nephrectomy group. The follow-up visits were significantly fewer in the Nephrectomy group compared with the other two groups (p < 0.001, Table 1).

The baseline size of the contralateral kidney was 5.3 ± 1.4 cm in the Agenesis group, 5.2 ± 1.1 cm in the MCDK group, and 7.4 ± 1.3 cm in the Nephrectomy group. The baseline kidney size was larger in the Nephrectomy group than in the other two groups (p < 0.001, Table 1).

Figure 2 demonstrates the renal growth trends in the three groups with normal reference lines from a previous study [24]. Supplementary Figure 1 of scatter plots also shows the trends of renal growth of the three groups. While baseline kidney size was the largest in the Nephrectomy group, the increment of renal growth was smaller compared to the other two groups (p = 0.004 compared with the Agenesis and p < 0.001 compared with the MCDK groups, Table 2). When considering the renal growth slope separately before and after 24 months of age, we found that kidney size increased significantly in all three groups with the growth slope of 0.101-0.104 cm/month before 24 months of age and 0.025-0.032 cm/month after 24 months of age (p < 0.001). When compared between the groups (Table 2), the growth slope was not different between the groups before (p = 0.839-0.929) and after (p = 0.262-0.697) 24 months of age. The renal growth in boys and girls were not significantly different (Supplementary Table 1).

**Discussion**

For pediatric patients, kidney injury or disease can impact quality of life, and some patients live with only a solitary functioning kidney due to congenital or acquired reasons. This study included cases of unilateral renal agenesis, MCDK, and unilateral nephrectomy that were attributed to primary renal tumors, which are known to have compensatory renal growth. Renal growth slope was similar among the three groups, with a growth slope of about 0.1 cm/month before 24 months of age and about 0.03 cm/month after 24 months of age. The growth slope was similar to those of normal kidneys before 24
months of age (0.1 cm/month) but faster than those of normal kidneys after 24 months of age (0.02 cm/month) [27]. These growth slope can be useful in follow-up of kidney size assessment throughout childhood.

In this study, the Nephrectomy group was older with a larger kidney size, higher serum creatinine level, and lower overall renal growth slope. Because kidney size, renal growth slope and serum creatinine level are associated with age in children [22,28], we cannot say that it is a pathologic difference between the groups. Pediatric GFR increases to the adult level by two years of age [4], and pediatric kidneys show rapid growth during the first 24 months and slow down afterwards [24]. In addition, the Nephrectomy group had fewer ultrasonographic examinations. It may be due to the different workup pattern of imaging studies in the Nephrectomy group, which includes not only ultrasonography, but also CT and MRI for the evaluation of tumor progression, whereas patients with congenital solitary functioning kidneys only undergo ultrasonography during follow-up.

One of the key differences between congenital and acquired solitary functioning kidneys is the degree of nephron deficiency, which is generally more severe in acquired disease because it usually occurs after completion of nephrogenesis. Nephrogenesis is complete at approximately 34 to 36 weeks gestation, after which no new nephrons form. Therefore, in acquired solitary functioning kidneys, fewer nephrons are available to try to compensate for hyperfiltration and hypertrophy compared with in congenital conditions [29].

Unilateral renal agenesis causes intra-uterine compensatory renal growth, which can affect postnatal renal function [30]. MCDK can also cause compensatory hypertrophy of solitary functioning kidneys in utero [31]. In the postnatal period, 65-97% of solitary functioning kidneys show compensatory renal hypertrophy by 18-30 months of age [31-34]. However, the rate of compensatory hypertrophy can vary from 24-81% [35].

The reported rate of compensatory contralateral renal hypertrophy after nephrectomy in patients with nephroblastoma is 68-93% [36-38]. One study published in 1996 demonstrated that the frequency of contralateral renal hypertrophy was not related to age at nephrectomy, side of the solitary functioning
kidney, tumor stage, chemotherapy regimen, or treatment with radiation therapy [19]. However, another study showed that kidney size was inversely correlated with age at nephrectomy [39].

There are only a few studies that have compared contralateral renal hypertrophy in unilateral renal agenesis and nephrectomy from nephroblastoma. One study performed in 1976 showed that, in unilateral renal agenesis, the contralateral kidney was initially smaller than the bilateral normal mean but increased with a steeper slope than the standard, resulting in a larger size than normal [21]. In comparison, in the nephrectomy group associated with nephroblastoma, the preoperative contralateral normal kidney was larger than average and showed further compensatory growth after surgery. In addition, the overall growth slope tended to be steeper in nephrectomy associated with nephroblastoma compared with unilateral renal agenesis [21]. However, the report was from an old study in which the mean diagnostic patient age was 4 years and urography was used to measure kidney size. In 1988, another study showed no renal hypertrophy at the time of birth in the unilateral renal agenesis group compared to almost 190% of the volume of the healthy kidney due to hypertrophy by at least 4 years of age [40]. The Nephrectomy group showed similar renal hypertrophy up to 180% volume within 2-4 years after nephrectomy. However, the studies did not evaluate renal growth slope between the two groups.

In this study, the renal growth slope between congenital and acquired solitary functioning kidneys were similar when considering the age of 24 months. Figure 2 and supplementary Figure 1 also show similar patterns of growth in the three groups, even though the overall slope of renal growth was smaller in the Nephrectomy group. It could be the effect of older age of the Nephrectomy group compared to the congenital groups. To date, only one study has shown the renal growth rate of the contralateral kidney in patients with MCDK [41]. Contralateral hypertrophy was seen at birth and maintained during childhood, with a growth rate of 0.89 cm/year (0.07 cm/month) overall and 0.61 cm/year (0.05 cm/month) in two nephrectomy cases associated with MCDK, which was similar to our results. Although our research did not have pathological tests together, these growth slope require further verification of the existing hypotheses of nephrogenesis and renal growth in congenital and
acquired solitary functioning kidneys.

Additionally, glomerular hyperfiltration can lead to renal injury, which can result in hypertension, microalbuminuria, and chronic kidney disease [42,43]. Decreased size of the functioning kidney is also associated with risk of renal injury [6]. For this reason, follow-up assessment of contralateral renal growth is important, especially in children. Animal studies demonstrated an increased number of nephrons in congenital solitary functioning kidneys [44,45]. This indicates that patients with a congenital solitary functioning kidney might not be at increased risk for hyperfiltration-associated renal and cardiovascular disease due to a lower nephron number. However, in our study, 15-20% of the patients in each group and 16.7% overall experienced proteinuria during follow-up and estimated GFR was not different between the groups. Furthermore, it was difficult to classify abnormalities by assessing the normal ranges of blood pressure and GFR according to the age of the patients. Further research on the pathophysiologic status of congenital and acquired solitary functioning kidneys and the clinical impact is needed.

There were several limitations to this study. First, follow-up examinations in this study spanned more than 16 years. Depending on the timing of the examinations, there were variations in the ultrasonographic equipment used. In addition, several different examiners conducted the renal scanning, which can result in operator variations, even though one radiologist re-evaluated the kidney size to reduce inter-observer variability. However, follow-up renal growth assessment in pediatric patients is a long-term task, so long-term data can be more valuable and representative of reality. Second, the relationship between kidney size and renal function has not been clarified. The study identified only gross kidney size and did not pathologically identify any changes in glomeruli or interstitial tissue. Even though we excluded patients with gross renal lesions such as renal echo changes or cysts, it was not possible to guarantee that all kidneys in the patients involved were at a normal status. Therefore, future research will require modalities to distinguish earlier between normal kidneys and kidneys with impaired function in pediatric patients with congenital or acquired solitary functioning kidneys.
In conclusion, we analyzed renal growth slope in pediatric patients with congenital (agenesis and MCDK) and acquired (nephrectomy for renal tumors) solitary functioning kidneys. The baseline contralateral kidney size and overall growth slope were different. However, considering 24 months of age as the assumed time point for reaching adult renal function, the renal growth slope was similar among the three groups, faster before (about 0.1 cm/month) and slower after (about 0.03 cm/month) 24 months of age. This data on slope of renal growth can help guide follow-up and monitoring approaches for pediatric patients with congenital or acquired solitary functioning kidneys.
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# Tables

Table 1. Demographics, laboratory results, and renal ultrasonography examinations of patients in the Agenesis, Multicystic dysplastic kidney (MCDK), and Nephrectomy groups.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Agenesis group</th>
<th>MCDK group</th>
<th>Nephrectomy group</th>
<th>All three groups</th>
<th>p-values for differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>26</td>
<td>35</td>
<td>71</td>
<td>132</td>
<td>All groups</td>
</tr>
<tr>
<td>Sex (male: female)</td>
<td>7:19</td>
<td>11:24</td>
<td>41:30</td>
<td>59:73</td>
<td>0.005</td>
</tr>
<tr>
<td>Mean age at the time of initial examination in months (range)</td>
<td>9.4 ± 28.2 (0-109)</td>
<td>2.2 ± 4.6 (0-19)</td>
<td>40.0 ± 28.5 (0-122)</td>
<td>23.9 ± 30.0 (0-122)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean age among all examinations in months (range)</td>
<td>23.1 ± 26.6 (0-141)</td>
<td>21.6 ± 27.8 (0-130)</td>
<td>60.6 ± 45.0 (0-204)</td>
<td>36.4 ± 39.4 (0-204)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Laboratory results</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>0.38 ± 0.28</td>
<td>0.36 ± 0.14</td>
<td>0.43 ± 0.17</td>
<td>0.39 ± 0.20</td>
<td>0.012</td>
</tr>
<tr>
<td>Cystatin C (mg/L)</td>
<td>1.00 ± 0.25</td>
<td>1.06 ± 0.31</td>
<td>1.15 ± 0.42</td>
<td>1.06 ± 0.32</td>
<td>0.384</td>
</tr>
<tr>
<td>Estimated glomerular filtration rate (mL/min/1.73 m²)</td>
<td>128.7 ± 37.2</td>
<td>122.1 ± 44.2</td>
<td>105.4 ± 49.6</td>
<td>120.3 ± 44.0</td>
<td>0.274</td>
</tr>
<tr>
<td>Renal ultrasonography</td>
<td>Proteinuria</td>
<td>5 (19.2%)</td>
<td>6 (17.1%)</td>
<td>11 (15.5%)</td>
<td>22 (16.7%)</td>
</tr>
<tr>
<td>-----------------------</td>
<td>------------</td>
<td>-----------</td>
<td>-----------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>Total number of examinations</td>
<td>131</td>
<td>171</td>
<td>177</td>
<td>479</td>
<td></td>
</tr>
<tr>
<td>Examination number in each patient (range)</td>
<td>5.0 ± 2.4 (1-12)</td>
<td>4.9 ± 2.9 (1-12)</td>
<td>2.5 ± 2.8 (1-11)</td>
<td>3.6 ± 3.0 (1-12)</td>
<td>0.020</td>
</tr>
<tr>
<td>Baseline contralateral kidney size in cm (range)</td>
<td>5.3 ± 1.4 (3.4-10.2)</td>
<td>5.2 ± 1.1 (3.5-8.0)</td>
<td>7.4 ± 1.3 (4.5-9.9)</td>
<td>6.5 ± 1.7 (3.4-10.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overall contralateral kidney size in cm (range)</td>
<td>6.8 ± 1.7 (3.4-11.0)</td>
<td>7.0 ± 1.7 (3.5-12.0)</td>
<td>8.3 ± 1.7 (4.5-13.7)</td>
<td>7.4 ± 1.8 (3.4-13.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation (range) or number.
Table 2. Contralateral kidney growth slope in patients in the Agenesis, MCDK, and Nephrectomy groups.

<table>
<thead>
<tr>
<th></th>
<th>Agenesis group</th>
<th>MCDK group</th>
<th>Nephrectomy group</th>
<th>p-values for differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall*</td>
<td>0.062</td>
<td>0.006</td>
<td>0.070</td>
<td>0.006</td>
</tr>
<tr>
<td>Considering 24 months of age**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slope before 24 months of age</td>
<td>0.104</td>
<td>0.010</td>
<td>0.103</td>
<td>0.009</td>
</tr>
<tr>
<td>Slope after 24 months of age</td>
<td>0.029</td>
<td>0.005</td>
<td>0.032</td>
<td>0.005</td>
</tr>
<tr>
<td>Slope change at 24 months</td>
<td>-0.075</td>
<td>0.013</td>
<td>-0.071</td>
<td>0.011</td>
</tr>
</tbody>
</table>

*from the linear mixed model

**from a piecewise linear mixed model with consideration of the break time point at 24 months of age
**Figure Legends**

Fig. 1. Inclusion and exclusion criteria.

Fig. 2. Growth slope of contralateral kidneys according to age among the three groups: Agenesis, Multicystic dysplastic kidney (MCDK), and Nephrectomy.

Spaghetti plots demonstrate the growth slope of contralateral kidneys; the gray zone indicates the range of the contralateral kidney from our study, and the red line indicates the estimated mean value at each age time point. The blue line indicates the age of 24 months. The solid lines are the normal range of right kidney and the dotted lines are the normal range of left kidney as a reference from a previous study [24]. There was a significant difference in renal growth slope before and after 24 months of age, from 0.101-0.104 cm/month to 0.025-0.032 cm/month, and the results were similar for all three groups (p < 0.001).

Supplementary Fig. 1. Scatter plots of contralateral kidney size according to age in the three groups of Agenesis, Multicystic dysplastic kidney (MCDK), and Nephrectomy.

Scatter plots show the trends of renal growth slope of the three groups which were similar.
Fig. 1

Fig. 1. Inclusion and exclusion criteria.

Inclusion criteria
(193 patients with 1375 renal ultrasonography exams)
- Under 18 years of age at the examination
- Unilateral congenital renal agenesis (Agenesis group)
- Unilateral multicystic dysplastic kidney (MCDK group)
- Unilateral nephrectomy for primary renal tumor
  (Nephrectomy group)

Exclusion criteria
(61 patients with 896 renal ultrasonography exams)
- Diffuse or focal lesions in the contralateral kidney
- 9/35 in Agenesis, 27/62 in MCDK and 25/96 in
  Nephrectomy groups

Total 132 patients with 479 renal ultrasonography exams

Agenesis group
26 patients with 131 exam

MCDK group
35 patients with 171 exam

Nephrectomy group
71 patients with 177 exam
Fig. 2. Growth patterns of contralateral kidneys according to age among the three groups: Agenesis, Multicystic dysplastic kidney (MCDK), and Nephrectomy. Spaghetti plots demonstrate the growth pattern of contralateral kidneys, and the red line indicates the estimated mean value at each age time point. The blue line indicates the age of 24 months. The solid lines are the normal range of right kidney and the dotted lines are the normal range of left kidney as a reference from a previous study [24].

There was significant difference in renal growth slope before and after 24 months of age, from 0.101-0.104 cm/month to 0.025-0.032 cm/month, and the results were similar for all three groups (p<0.001).