

# What are the Optimal Renal Ultrasound Parameters for Detecting Small Kidney in Young Children?

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**Introduction:** Recent guidelines do not recommend routine screening of vesicoureteral reflux after a first febrile urinary tract infection in children without abnormal findings on ultrasound or atypical/recurrent urinary tract infection. Currently, there are no clear ultrasonographic parameters for detecting abnormalities in renal size, especially in young children. The aim of the present study was to determine an optimal cutoff value for detecting small kidney in children without apparent congenital anomalies except vesicoureteral reflux by retrospective chart review.

**Patients and Methods:** Children aged  $\leq 3$  years who had undergone nuclear renal scans and ultrasound were enrolled. Small kidney was defined as split renal function of  $<40\%$ . Optimal cutoff values of various ultrasonographic parameters for detecting small kidney were calculated.

**Results:** Of the 69 children included in the present study, small kidney was identified in 20. There was a significant difference in renal size between each kidney in patients with small kidney, whereas there was no significant difference in those without small kidney. With a ratio of estimated renal area of 74.26%, maximum area under the curve with the highest sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rate were obtained. In addition, simple measurement of renal length with a cutoff of 4.97 cm showed high specificity comparable with estimated renal area.

**Conclusion:** Small kidney may be screened by two-dimensional measurement on ultrasonographic examination, even in young children. With the cutoff described, risk stratification or an individualized approach may be possible.

**Keywords:** small kidney, ultrasound, screening, cutoff value

## Introduction

Primary vesicoureteral reflux (VUR) is the most common congenital anomaly of the urinary tract (UT). In infancy, VUR is commonly diagnosed following demonstration of prenatally detected dilatation of the UT or during investigation of UT infection (UTI). While routine voiding cystourethrography (VCUG) to detect VUR after the first febrile UTI was not recommended in recent guidelines, it is indicated when abnormal findings on ultrasound (US) are detected or when atypical or recurrent UTI is observed.<sup>1-3</sup>

Small kidney is a common finding in infants or young children with high-grade VUR, especially in boys. Small kidney is recognized as a hypo/dysplastic kidney resulting from disordered renal development<sup>4,5</sup> because of an abnormal origin of the

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ureteral bud, which interacts suboptimally with the metanephric mesenchyme,<sup>6,7</sup> or high-pressure voiding during gestation because of incomplete sphincter relaxation.<sup>5,8</sup> Renal abnormalities on US or nuclear renal scan have been reported in 12%–50% of patients with VUR detected in infancy.<sup>9–11</sup>

To date, no simple US parameters for detecting renal abnormalities, especially small kidney, have been reported, although VCUG is recommended when abnormal findings are observed on US. It has been demonstrated that volumetry on computed tomography or magnetic resonance imaging predicts the affected kidney's function, which is traditionally evaluated on nuclear renal scan.<sup>12,13</sup> We speculated that small kidney may be screened by measuring bilateral renal size, including length, area, and volume, on US.

We routinely perform <sup>99m</sup>Tc-DMSA renal scans and US of kidney and bladder for evaluation after a febrile UTI or US abnormality that is suspected to be a congenital anomaly of the kidney and UT. The aim of the present study was to determine an optimal cut-off value for detecting small kidney on US in young children without apparent congenital anomalies except VUR by retrospective chart review.

## Patients and Methods

### Patients

Medical charts of children aged  $\leq 3$  years who had undergone <sup>99m</sup>Tc-DMSA renal scans and US for the evaluation of UTI, VUR, or US abnormalities between September 2011 and May 2019 were retrospectively reviewed. Patients with grade 3 or grade 4 hydronephrosis were excluded from this study, because dilation of the renal pelvis may affect US evaluation of kidney size. Patients with congenital anomalies, such as ureterocele, posterior urethral valve, anorectal malformation, cloacal

anomaly, spina bifida, hypospadias, or fused kidney were also excluded. Informed consent was waived due to the retrospective nature of the study.

### Imaging Studies

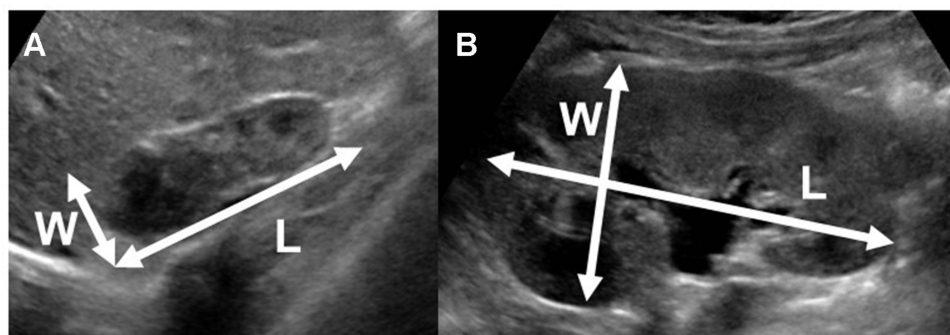
In patients who presented with febrile UTI, <sup>99m</sup>Tc-DMSA renal scans and US evaluation were performed at 3 months or later after UTI. US evaluations were performed without sedation. Renal length and width of each kidney were measured on US longitudinal scans (Figure 1). <sup>99m</sup>Tc-DMSA renal scans were performed under sedation. Small kidney was defined when split renal function (SRF) was  $<40\%$  on <sup>99m</sup>Tc-DMSA uptake.

Length, estimated renal area (eArea;  $\text{length} \times \text{width} \times \pi/4$ ), and estimated renal volume (eVol;  $\text{length} \times \text{width} \times \text{width} \times \pi/6$ ) in the smaller kidney were used to evaluate the optimal parameters for detection of small kidney in the present study. In addition, ratio of length, eArea, and eVol between both kidneys (smaller divided by larger kidney) were also calculated.

### Statistical Analyses

Mann–Whitney *U* and Chi-square tests were used to compare patients with or without small kidney. Wilcoxon signed-rank tests were for comparison of US parameters between each of the kidneys. A receiver-operating characteristic (ROC) curve was used to determine cutoff values of each parameter for detecting small kidney. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for each parameter.

The protocol for the present study was approved by the Ethics Committee of Hokkaido University Hospital (018-0346).



**Figure 1** Renal size measurement. Longitudinal scan of a small kidney (A) and contralateral kidney (B). Length (L) and width (W) of each kidney were measured.

**Table 1** Characteristics of patients

	All (n=69)	Patients with small kidney (n=20)	Patients without small kidney (n=49)	p
Boys/girls	41/28	18/2	23/26	0.001
Birth weight (g), median $\pm$ SD	3,030 $\pm$ 409	946 $\pm$ 281	3,066 $\pm$ 455, two unknown	0.7283
Presenting symptoms				
Febrile UTI	65	16	49**	
Hydronephrosis	8	4*	4**	
Renal abnormality in size on US	1	1*		
VUR <sup>+</sup>	51***	18 (90%)	33*** (68.8%)	0.0748
Grade 1–3	31	7	24	0.0342
Grade 4–5	20	11	9	
Hydronephrosis <sup>+</sup> (SFUI–2)	40	11 (55%)	29 (59.2%)	0.8703
Age at US (months), median $\pm$ SD	10.9 $\pm$ 8.3	11.7 $\pm$ 9.3	10.4 $\pm$ 8.0	0.9367
Age at DMSA (months), median $\pm$ SD	10.9 $\pm$ 8.5	11.8 $\pm$ 9.3	10.4 $\pm$ 8.2	0.9789

**Notes:** \*Three patients were referred due to mild hydronephrosis alone and one due to mild hydronephrosis on one side and abnormality in size on the other side. \*\*All were referred due to febrile UTI. Among them, mild hydronephrosis was detected in four before referral. \*\*\*VCUG was not performed in one patient. This patient was excluded from statistical analysis.

## Results

### Patient Characteristics

The present study enrolled 69 patients (41 boys and 28 girls), and their characteristics are summarized in Table 1. Median age at US and <sup>99m</sup>Tc-DMSA renal scan was 10.9 months. Small kidney was identified in 20 children (29%), and incidence in boys was significantly higher ( $p=0.001$ ). VCUG was performed in all, except one case without small kidney. VUR was identified more frequently in patients with small kidney had who received VCUG; however, the difference was not significant ( $p=0.0748$ ). However, the incidence of high-grade VUR (grade 4–5) was significantly higher in patients with small kidney ( $p=0.0342$ ). Age at US or <sup>99m</sup>Tc-DMSA renal scan or incidence of mild hydronephrosis (SFUI–2) were not significantly different between patients with or without small kidney.

### Comparison of Kidney Size Between Each Side

Median SRF of the lower uptake side on <sup>99m</sup>Tc-DMSA renal scan was 30.4% (13.0%–39.1%) in patients with small kidney compared to 47.7% (40.0%–49.9%) in those without small kidney. In 20 patients with small kidney, the kidney with lower SRF had a shorter length in all, whereas lower eArea or eVol was identified in 19 patients. Conversely, in 49 patients without small kidney, the kidney with lower SRF showed shorter length, lower eArea, or eVol in 25, 28, and 28, respectively. While length, eArea, and eVol were not significantly different between each side in patients without small kidney, these parameters were significantly different among patients with small kidney (Table 2).

**Table 2** Difference in parameters between kidneys in patients with or without small kidney

	Patients with small kidney (n=20)			Patients without small kidney (n=49)		
	Smaller SRF side*	Larger SRF side*	p	Smaller SRF side*	Larger SRF side*	p
SRF (%), median $\pm$ SD*	30.4 $\pm$ 8.8	69.6 $\pm$ 8.8		47.7 $\pm$ 2.1	52.3 $\pm$ 2.1	
Length (cm), median $\pm$ SD	5.06 $\pm$ 0.69	6.29 $\pm$ 0.80	<0.0001	5.84 $\pm$ 0.74	5.90 $\pm$ 0.77	0.6449
eArea (cm <sup>2</sup> ), median $\pm$ SD	9.49 $\pm$ 3.03	15.90 $\pm$ 2.58	<0.0001	12.68 $\pm$ 3.08	12.89 $\pm$ 3.13	0.1281
eVOL (mL), median $\pm$ SD	15.70 $\pm$ 7.87	33.31 $\pm$ 8.48	<0.0001	23.24 $\pm$ 9.28	23.81 $\pm$ 9.70	0.1555

**Note:** \*Split renal function.

**Table 3** Impact of each parameter on detecting small kidney

	Cutoff	AUC*	Sensitivity	Specificity	PPV**	NPV***	Accuracy rate
Length	4.97 cm	0.71327	0.5	0.8776	0.6250	0.8113	0.7681
eArea	11.02 cm <sup>2</sup>	0.70918	0.7	0.7143	0.5000	0.8537	0.7101
eVol	17.42 mL	0.69388	0.6	0.7755	0.5217	0.8261	0.7246
Ratio of length	90.85%	0.82347	0.8	0.7959	0.6154	0.9070	0.7971
Ratio of eArea	74.26%	0.88061	0.8	0.8980	0.7619	0.9167	0.8696
Ratio of eVol	63.84%	0.85102	0.8	0.8367	0.6667	0.9111	0.8261

Notes: \*Area under the curve; \*\*positive predictive value; \*\*\*negative predictive value.

## Impact of Each Parameter for Detecting Small Kidney

Cutoff values for detection of small kidney estimated by the ROC curve was 4.97 cm length, 11.02 cm<sup>2</sup> eArea, 17.42 mL eVol, 90.85% ratio of length, 74.26% ratio of eArea, and 63.84% ratio of eVOL. Among these parameters, maximum area under the curve (AUC) was obtained using a ratio of eArea of 74.26%, with the highest sensitivity (80.0%), specificity (89.8%), positive predictive value (76.2%), negative predictive value (91.67%), and accuracy rate (86.96%) when compared with other parameters. Simple measurement of length showed high specificity (87.76%) comparable with the ratio of eArea (Table 3).

## Discussion

In this retrospective study, we report that small kidney may be screened by two-dimensional measurement of renal US in patients aged  $\leq 3$  years. By using a ratio of eArea of 74.26%, we obtained maximum AUC with highest sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rate. In addition, simple measurement of renal length with a cutoff of 4.97 cm showed high specificity, followed by ratio of eArea.

UTI is one of the most common bacterial infections in children. Its incidence in infants and young children aged between 2 months and 2 years is reported to be about 15%.<sup>14</sup> While recurrent febrile UTI is bothersome and there is a risk of renal impairment, recent guidelines do not recommend routine VCUG to detect VUR after the first febrile UTI in patients without abnormal findings on US or atypical or recurrent UTI.<sup>1-3</sup>

US is the preferred tool to evaluate the kidneys and UT in pediatric patients because it is safe, readily available, non-ionizing, and cost-effective. While it is credited with low sensitivity and positive and negative predictive value in detecting renal scars,<sup>15</sup> it is the accepted method for assessment of renal size in children.<sup>16</sup> Nomograms of renal size using US in healthy children with normal renal function have

been reported;<sup>17,18</sup> however, accepted cutoff values for evaluating abnormal renal size have not been reported. While SRF in children was estimated by measuring kidney size on US in a limited number of studies, those that focused on infants or very young children were scarce.<sup>19,20</sup>

Kidney length is the simplest and most commonly used approach to evaluate renal size. In the present study, a cutoff of 4.97 cm showed high specificity, indicating that a kidney longer than this is less likely to be small kidney. In a previous study investigating kidney length in normal healthy children in an Australian population, Coombs et al found that mean kidney lengths among infants were 5.6 (95% CI 5.5–5.8) cm for the left and 5.5 (95% CI 5.3–5.6) cm for the right.<sup>18</sup> Furthermore, Luk et al reported that mean kidney lengths among infants were 5.67 cm for the left and 5.55 cm for the right kidney.<sup>17</sup> According to these values, a cutoff of 4.97 cm is suitable for screening for small kidney by US. Although racial variation in renal size has been reported,<sup>17,21</sup> our data were based on a Japanese population, whereas the studies by Coombs et al<sup>18</sup> and Luk et al<sup>17</sup> were based on an Australian population with diverse ethnicity and an Asian population, respectively. On the other hand, Farhat et al demonstrated that sonographic findings of decreased renal length (<50th percentile for age) were strongly correlated with renal hypoplasia on renal scans.<sup>19</sup> Comparison with age-related renal size would be a reasonable approach to define the cutoff, because kidney size in children changes with their growth. However, development of a referenced normal size across various races at each age would be relatively complex.

The maximum AUC with the highest sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rate were obtained by using a ratio of eArea of 88.06% in the present study. Comparison with the contralateral kidney would be a promising approach to screen the unilateral small kidney. Weitz et al demonstrated that relative renal volume (evaluated by three-dimensional measurements) in 85 children with primary VUR was significantly correlated with SRF, which was estimated using <sup>99m</sup>Tc-

MAG3 renal scans.<sup>20</sup> A similar finding was reported by Sargent et al, who calculated the mean difference between relative volume and SRF in 19 children with various renal disorders using <sup>99m</sup>Tc-DMSA renal scans.<sup>16</sup> The present study demonstrated that the ratio of eVol showed the same sensitivity as the ratio of eArea and similar but slightly lower positive predictive value, negative predictive value, and accuracy rate. As only two-dimensional measurements of renal size were obtained on US evaluations in the present study due to its retrospective nature, eVol was calculated from these. This may be the reason that the ratio of eArea was slightly superior to the ratio of eVol in detecting small kidney. However, as previous studies have identified a good correlation between renal function and renal volume, as well as renal area,<sup>22,23</sup> evaluation of eArea may be another choice for renal size measurement. Furthermore, two-dimensional measurements may be performed using only a single image on the longitudinal scan section, which is a simple procedure.

Renal abnormality on <sup>99m</sup>Tc-DMSA renal scans has been reported to be a risk factor of recurrent UTI or breakthrough UTI.<sup>24–27</sup> Accordingly, risk stratification may be possible by detection of small kidney using screening US, even in initial febrile UTI episodes. In addition, incidence of high-grade VUR was significantly higher in patients with small kidney. High-grade VUR has also been reported as a risk factor of recurrent UTI or breakthrough UTI.<sup>27–29</sup> Therefore, an individualized approach that includes indication of VCUG or <sup>99m</sup>Tc-DMSA renal scan, or administration of continuous antibiotic prophylaxis, may be necessary even after the first febrile UTI by screening for small kidney on US.

The limitations of the present study include the retrospective design, the small sample (n=69), and single institutional experience. To clarify our findings, a multi-institutional prospective study on a larger number of patients is necessary.

In conclusion, small kidney may be screened by two-dimensional measurements on US examination in small children. By using the cutoff value demonstrated in the current study (ratio of eArea of 74.26% or maximum renal length of 4.97 cm), risk stratification or an individualized approach may be possible.

## Ethics Approval

This study was approved by the institutional review board (protocol 018-0346). The need for written informed consent was waived, because this study was conducted by retrospective chart review. Data were gathered from the institution database with permission. Patient data were

anonymized and maintained with confidentiality throughout the study. This study was performed in accordance with the Declaration of Helsinki.

## Author Contributions

Masafumi Kon contributed to conception and design, data analysis, and manuscript writing/editing. Michiko Nakamura collected and analyzed the data. Kimihiko Moriya was involved in conception and design, data collection, data analysis, and critical revision of the manuscript for scientific and factual content. Yoko Nishimura, Yurie Hirata, and Mutsumi Nishida collected and analyzed the data. Madoka Higuchi and Takeya Kitta critically revised the manuscript for scientific and factual content. Nobuo Shinohara supervised the study. All authors contributed to data analysis, drafting, or revising the article, have agreed on the journal to which the article will be submitted, gave final approval to the version to be published, and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare that they have no competing interests.

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