

## Temporary Renal Enlargement in Children with A First Episode of Febrile Urinary Tract Infection is A Significant Risk of Recurrent Infection

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**Purpose:** Although morphological renal abnormalities in children with febrile urinary tract infection (fUTI) have shown a predictive factor for recurrent infection, there are no available data on recurrence regarding sonographic renal enlargement at the first fUTI episode, especially focusing on whether renal enlargement is temporary or not.

**Materials and Methods:** This cohort study reviewed the medical records of children who underwent renal ultrasound during their first fUTI during 2005–2013 and who aged < 15 years at diagnosis. We defined a kidney as temporary enlarged when the kidney length was  $\geq 2$  standard deviation above normal renal length for that age on sonography or a difference of  $\geq 1$  cm in sonographic length between the right and left kidneys, following normal renal length after antibiotic treatment.

**Results:** A total of 132 children were enrolled, of whom 11 had sonographic temporary renal enlargement during their first fUTI. After completing antibiotic therapy for a first fUTI episode, 20 (15%) children had fUTI recurrence. The clinical characteristics at the first episode of fUTI were not significantly different between renal enlargement and nonrenal enlargement groups. Children with temporary renal enlargement at a first fUTI episode had significantly lower fUTI recurrence-free survival proportion than those with nonrenal enlargement according to the Kaplan–Meier method ( $p = 0.003$ ).

**Conclusion:** Identification of temporary renal enlargement as a predictor of recurrent fUTI may help identify children with the first episode of fUTI who will be warned of close monitoring.

**Keywords:** children; febrile urinary tract infection; recurrence; renal sonography, temporary renal enlargement

### INTRODUCTION

In the long-term follow-up, the clinical sequela of febrile urinary tract infection (fUTI) in children is renal dysfunction, which is associated with recurrent fUTI, hypertension, and renal scarring<sup>(1)</sup>. Approximately 10% of children with the first experience of fUTI are known to have at least one episode of recurrent infection<sup>(2-4)</sup>. Recurrent episodes of fUTI are also associated with progression of renal scarring, which is a critical factor for long-term renal prognosis<sup>(5-10)</sup>. It has been reported to identify the risk of recurrence of fUTI. One of the prognostic factors is morphological abnormality of the kidney and urological systems<sup>(5)</sup>. Vesicoureteral reflux (VUR) has been reported to be the most common congenital anomaly of the kidney and urinary tract (CAKUT) that causes the risk for recurrence<sup>(7,11-13)</sup>. However, it is important to evaluate the voiding cystourethrography (VCUG) using contrast medium for making a definitive diagnosis of VUR. Although guidelines recommend the use of diagnostic imaging in only a limited group of children with an initial fUTI<sup>(12,14,15)</sup>, it is essential to prioritize the avoidance of invasive procedures.

Sonographic examination is a noninvasive procedure and can be used even for younger children. The Amer-

ican Academy of Pediatrics suggests that infants aged between 2 and 24 months with fUTI should undergo renal and bladder ultrasonography (RBUS)<sup>(14)</sup>. The most commonly identified findings of RBUS in infants are CAKUT, such as hydronephrosis, solitary kidneys, and ectopic kidneys. Although few in number, some children with fUTI have temporary renal enlargement, which is manifested as increased renal length on their renal ultrasound during the acute phase of fUTI following a normal renal length after antibiotic treatment<sup>(16)</sup>. Most of them showed a reduction to normal range within 2 weeks in the follow-up renal sonographic examination<sup>(17)</sup>. Temporary renal enlargement during the occurrence of fUTI can be a consequence of interstitial edema attributable to direct bacterial infection or local swelling reaction<sup>(18)</sup>. Although studies have reported that increased renal length is associated with renal scarring<sup>(18-20)</sup>, no data are available on the recurrence of fUTI related to temporary renal enlargement. Identifying whether renal enlargement is relatively associated with the recurrence of fUTI, focusing on temporary or permanent increased renal length on renal ultrasound not only at the acute period of fUTI but also after the antibiotic treatment, is considered to be useful in managing children with a first episode of fUTI. In the present

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**Table 1.** Characteristics of studied patients

	All (n=132)	Renal enlargement (n=11)	Nonrenal enlargement (n=121)	P value
Male : Female	88:44	7:4	81:40	1
Age at onset of a first fUTI (months)	3 (2-9)	3 (2-56)	3 (2-9)	0.98
Observation period (months)	16 (9-34)	27 (8-69)	16 (9-34)	0.58
Characteristics at first fUTI				
Bacteremia	5 (4 %)	0 (0 %)	5 (4 %)	1
Microorganisms in the urine culture				
E. coli	107 (81 %)	9 (82 %)	98 (81 %)	1
other than E. coli	78 (59 %)	7 (64 %)	71 (59 %)	1
Blood examination				
WBC counts (/μL)	16500 (12560-19950)	20600 (14400-23300)	16300 (12530-19235)	0.13
CRP (mg/dL)	4.3 (1.4-9.5)	8.0 (2.2-11.5)	3.8 (1.3-9.3)	0.17
Urine examination				
Pyuria	109 (83 %)	9 (82 %)	100 (83 %)	1
Hydronephrosis				
Bilateral	41 (32 %)	5 (45 %)	36 (30 %)	0.32
Unilateral	6 (5 %)	0 (0 %)	6 (5 %)	1
	35 (27 %)	5 (45 %)	30 (25 %)	0.16

study, we conducted a retrospective cohort analysis of the data of children with an initial fUTI who underwent RBUS during the acute phase, with a focus on recurrent fUTI concerning temporary renal enlargement at a first episode of fUTI.

## MATERIALS AND METHODS

### Patients and study design

We retrospectively reviewed all files of pediatric patients with fUTI who were diagnosed at Kakogawa Central City Hospital and Takatsuki General Hospital during 2005–2013. The inclusion criteria were patients who underwent prompt RBUS within 72 hours after the commencement of antibiotic therapy for a first episode of fUTI and were aged <15 years at the time of fUTI diagnosis. The exclusion criteria were patients who were not subjected to RBUS during a first episode of fUTI and those who have been managed with less than 2 months of follow-up at the hospital after the diagnosis of fUTI. We considered that 2 months follow-up was too short to evaluate whether children with a first episode of fUTI experience recurrent fUTI after antibiotic treatment. The other exclusion criteria were patients with bladder and bowel dysfunction, hypoplastic kidney, cystic kidney, ectopic kidney, solitary kidney, horseshoe kidney, duplex kidney, obstructed kidney, or severe hydronephrosis of urinary tract dilation (UTD) P3 according to the new classification<sup>(21)</sup>. We also excluded children with permanent enlarged kidney, because they might have cystic kidney, renal lymphoma, and renal involvement of acute lymphoblastic leukemia, if they are not diagnosed with any kidney disease at the time of detection of the enlargement. There were no male infants with circumcision. Children with sonographic enlarged kidney at a first episode of fUTI were also excluded, unless they underwent a repeat RBUS after the termination of antibiotic treatment. Moreover, patients who were known to have VUR before the development of a first fUTI episode and those who had a genetic abnormality, epilepsy, or abnormality of the central nervous system were excluded. This study was conducted according to the Declaration of Helsinki and the ethical guidelines for medical and health research involving human subjects formulated by the Ministry of Health, Labor and Welfare in Japan. Study approval was obtained from the institutional ethics review board of Kakogawa Central City Hospital (approval number:

30-49). According to institutional ethics, no informed consent was obtained from the patients or their parents. In compliance with the guidelines and the institutional ethics review board for the patients' benefit, the study protocol was displayed publicly in a poster at both institutions, so that each patient could have opportunities to refuse to participate in this study.

Definitions and imaging examinations

In this study, fUTI was defined as fever of  $\geq 38^{\circ}\text{C}$ , with the urine culture yielding a growth of only one microorganism at 10,000 colony-forming units/ml or two microorganisms at 100,000 colony-forming units/ml from a catheter specimen or midstream urine. If children have fUTI within 14 days after the termination of antibiotic treatment for the first episode of fUTI, this fUTI was defined as not a new episode of fUTI but a relapse of fUTI. Therefore, we defined the second episode of fUTI as that occurring more than 14 days after the termination of antibiotic treatment for the first episode of fUTI. In addition, the timing of the first fUTI recovery was defined as the termination day of antibiotic treatment for fUTI without a relapse of fUTI. The initiation timing of follow-up was the termination day of antibiotic treatment for the first episode of fUTI, and the end of follow-up was the last day visited to our hospital. All sonographic examinations were performed within 72 hours after the commencement of antibiotic therapy. Mild hydronephrosis was defined as UTD P1 or P2 according to the new classification<sup>(21)</sup>. Renal length measurements were the longest length measurements recorded at any location. We considered a kidney as enlarged when the kidney length was  $\geq 2$  standard deviation above normal renal length for that age on RBUS according to a previous report<sup>(22)</sup> or a difference of  $\geq 1$  cm in sonographic length between the right and left kidneys. Permanent enlargement was defined as enlarged kidney that was observed not only during the acute phase of fUTI but also after the completion of treatment for acute fUTI. Temporary enlargement was defined as enlarged kidney observed only at the acute phase and with normal length (between  $-2$  and  $2$  standard deviations) or a difference of  $<1$  cm in sonographic length between the right and left kidneys after the termination of antibiotic treatment. Hypoplastic kidney was defined as  $<-2$  standard deviation of the kidney length on RBUS. The proportion of children

**Table 2.** Detailed microorganism in the urine culture

	Number
Escherichia coli	107
Enterococcus faecalis	35
Extended-spectrum $\beta$ -lactamase Escherichia coli 5	
Streptococcus agalactiae	5
Klebsiella pneumoniae	3
Citrobacter amalonaticus	3
Staphylococcus epidermitis	2
Staphylococcus haemolyticus	1
Staphylococcus aureus	1
Methicillin-resistant Staphylococcus aureus	1
Klebsiella oxytoca	1
Pseudomonas aeruginosa	1
Enterobacter aerogenes	1
Yersinia enterocolitica	1
Streptococcus lugdunensis	1
Serratia marcescens	1

with renal enlargement was defined as the percentage of those with enlarged kidney of either the right or left side. The operator was not aware of the results of other clinical examinations. We adopted the traditional radiography for VCUG and classified to five degrees of VUR according to the International Reflux Study<sup>(23)</sup> in a proportion of children who were not known to have VUR before the development of a first fUTI episode. In our centers, we have the policies of administering VCUG to children with first fUTI episode depending on the presence of bacteremia and their microorganism in the urine culture. If they have the bacteremia during the acute phase of fUTI or the microorganism other than Escherichia coli in the urine culture, VCUG is administered. Renal scarring was defined as decreased uptake with distortion of the contours or cortical thinning with loss of parenchymal volume on 99 mTc-dimercaptosuccinic acid (DMSA) scintigraphy. We administer DMSA scintigraphy 6 to 12 months after acute fUTI to detect the formation of renal scarring<sup>(24,25)</sup>. None of the children underwent continuous antibiotic prophylaxis after the first episode of fUTI.

### Statistical analysis

The calculated sample size was 150 children. We needed approximately 15 events (recurrent fUTI) in our analysis, because approximately 10% of children with a first episode of fUTI have at least one episode of recur-

rent infection. The number of inpatients with fUTI aged <15 years in each of our institutions is 30 per year. If the proportion of children with fUTI who were administered RBUS at an acute episode and have been managed for more than 2 months was approximately 40%, the estimated number during a year is 24 in two institutions (40%: 24 divided by 60). We assumed that 30-40 children would be subtracted from 192 (24 children times 8 years equals 192), because it would be very difficult to determine the correct data for some children managed more than 10 years earlier. Hence, the sample size was set as 150 children, which was calculated to satisfy these assumptions. Statistical analysis was conducted using the JMP 9.0 software (SAS Institute Japan Ltd., Tokyo, Japan). All data were expressed as median (interquartile range) or number (percentage). We expressed age at onset of a first fUTI, observation period, blood examination (white blood cell count, C-reactive protein), and clinical course during treatment (duration of fever, total duration of intravenous combined oral antibiotics, duration of intravenous antibiotics and duration of oral antibiotics) as median (interquartile range) and rate of bacteremia, microorganisms in the urine culture, rate of pyuria, rate of hydronephrosis, initial antibiotic therapy at first fUTI, and prognosis as number (percentage). The Wilcoxon rank sum test was used for the association between categorical values and continuous values, and Fisher's exact test was used for two categorical values. Time to recurrence of fUTI (the period between the time of the first episode of fUTI and the second episode of fUTI) based on the presence or absence of temporary renal enlargement at a first episode of fUTI was estimated using the Kaplan-Meier method and Wilcoxon test. The hazard ratio for recurrent fUTI was calculated with 95% confidence intervals using Cox proportional hazard regression adjusted for the factors that showed significance in the univariate analysis. A *p* value of < 0.05 was considered to be statistically significant.

## RESULTS

### Characteristics during the first episode of fUTI

A total of 227 children with a first episode of fUTI were treated at our hospital (**Figure 1**). 26 children who did not undergo RBUS examination during the episode of first fUTI and 69 who met any other exclusion criteria were excluded. Therefore, a total of 132 children

**Table 3.** Comparison of therapy, clinical course, and prognosis between the renal enlargement group and the nonrenal enlargement group.

	All (n=132)	Renal enlargement (n=11)	Nonrenal enlargement (n=121)	<i>P</i> value
Initial antibiotic therapy of first fUTI				
Cefotaxime	83 (63 %)	4 (36 %)	79 (65 %)	0.1
Ampicillin combined Cefotaxime	3 (2 %)	1 (9 %)	2 (2 %)	0.23
Cefotiam	8 (6 %)	2 (18 %)	6 (5 %)	0.13
Ceftriaxone	2 (2 %)	1 (9 %)	1 (1 %)	0.16
Sulbactam ampicillin	17 (13 %)	1 (9 %)	16 (13 %)	1
Oral antibiotics	1 (1 %)	0 (0 %)	1 (1 %)	1
Clinical course during treatment				
Duration of fever (Day)	2 (2-4)	2 (2-4)	2 (1-2)	0.51
Total duration of intravenous combined				
oral antibiotics (Day)	11 (8-14)	13 (8-14)	11 (8-14)	0.35
Duration of intravenous antibiotics (Day)	6 (4-7)	6 (6-7)	6 (4-7)	0.28
Duration of oral antibiotics (Day)	5 (3-7)	7 (3-9)	5 (3-7)	0.19
Prognosis				
Recurrent fUTI	20 (15 %)	5 (45 %)	15 (12 %)	0.01
Vesicoureteral reflux †	8/53 (15 %)	0/8 (0 %)	8/45 (18 %)	0.33

fUTI; febrile urinary tract infection, †; Evaluated 53 children who were performed voiding cystourethrography

**Table 4.** Detailed characteristics of 11 children with temporary renal enlargement

No	Sex	Age (months)	Bacteremia	Microorganism in the urine culture	Duration of fever (Day)	Characteristics at first episode of fUTI			Prognosis after first episode of fUTI					
						Total duration of IV + oral antibiotic treatment (Day)	Total duration of IV antibiotic treatment (Day)	Side of renal enlargement	Hydrocele (UTD)	Recurrent fUTI	Time to recurrent fUTI (months)	VCUG	VUR	<sup>99m</sup> Tc-DMSA scintigraphy
1	F	158	-	<i>E. coli</i>	3	10	6	Left	-	+	10	-	NA	NA
2	M	2	-	<i>E. coli</i> , <i>E. faecalis</i>	5	4	4	Left	-	+	1	+	-	NA
3	F	81	-	<i>E. coli</i>	4	21	7	Left	-	-	-	+	-	NA
4	F	5	-	<i>E. coli</i> , <i>Streptococcus agalactiae</i>	2	13	5	Right	Right (UTD P1)	-	-	+	-	NA
5	M	3	-	<i>E. coli</i>	2	11	4	Left	-	+	1	+	-	NA
6	M	1	-	<i>Klebsiella pneumoniae</i>	2	6	6	Left	-	-	-	+	-	NA
7	M	3	-	<i>E. coli</i>	3	8	8	Left	Left (UTD P1)	-	-	+	-	NA
8	M	3	-	<i>E. coli</i>	3	14	6	Left	Left (UTD P1)	-	-	-	NA	NA
9	F	2	-	<i>E. coli</i>	1	14	7	Left	Left (UTD P1)	+	3	+	-	NA
10	M	3	-	<i>E. coli</i>	1	14	7	Left	Left (UTD P2)	-	69	-	NA	NA
11	M	56	-	<i>E. coli</i> , <i>E. faecalis</i>	8	21	14	Left	-	+	8	+	-	Scarring

fUTI; febrile urinary tract infection, *E. coli*; Escherichia coli, IV; Intravenous, DMSA; dimercaptosuccinic acid, VCUG; voiding cystourethrography,

VUR; vesicoureteral reflux, UTD; urinary tract dilatation, *E. faecalis*; Enterococcus faecalis, NA; not available

(88 boys and 44 girls) were included in this study. As shown in Table 1, we divided the children into those who had temporary renal enlargement at a first episode of fUTI (renal enlargement group: 11 children) and those who did not have enlarged kidney (nonrenal enlargement group: 121 children). In comparison with the renal enlargement and nonrenal enlargement groups, the observation period showed no significant differences. The duration of the observation period in more than half of children was less than 1 year. The most common microorganism in the urine culture was Escherichia coli (Table 2). The results of blood and urine examinations showed no significant differences in both the renal enlargement and nonrenal enlargement groups. Similar proportions of children in both groups had mild hydronephrosis at a first fUTI episode.

#### Therapy, clinical course, and prognosis

Except for a child who was treated orally without intravenous antibiotics, the majority of all children received intravenous antibiotics as initial therapy for a first fUTI episode following oral antibiotics (Table 3). After the completion of antibiotic therapy for a first episode of fUTI, 20 (15%) children had recurrence of fUTI. Comparison between the renal enlargement and nonrenal enlargement groups indicated a significantly higher proportion of children with recurrent fUTI in the renal enlargement group. No significant differences were observed among children who had VUR between the two groups, although only a part of the patients were examined by VCUG.

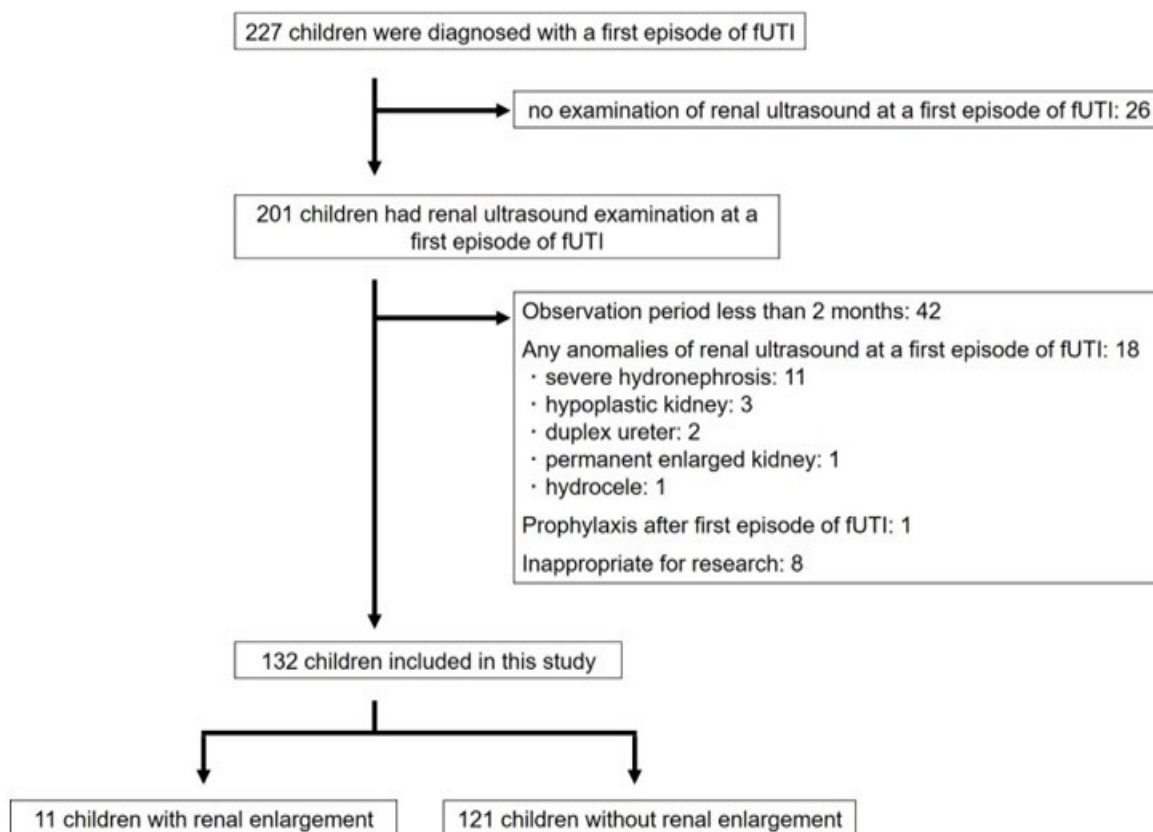
Table 4 shows the detailed characteristics of children with temporary renal enlargement. Among five patients with recurrent fUTI, four progressed to recurrence within a year from a first episode of fUTI. Four of the five children who had recurrence underwent VCUG, and no child was found to have VUR. Of three children

who underwent <sup>99m</sup>Tc-DMSA scintigraphy, one had renal scarring.

#### Outcome

The fUTI recurrence-free survival time based on temporary renal enlargement at a first episode of fUTI assessed using the Kaplan–Meier method is shown in Figure 2. The fUTI recurrence-free survival proportion in children with nonrenal enlargement was 89.2% at 12 months from a first episode of fUTI. The fUTI recurrence-free survival proportion in children with temporary renal enlargement was 47.7% at 12 months from a first episode of fUTI. A significant difference was observed between the renal enlargement and nonrenal enlargement groups ( $p = 0.003$ ). A significant difference was observed between the renal enlargement and nonrenal enlargement groups ( $p = 0.003$ ). Moreover, we divided the children into those who had recurrent fUTI (recurrent group: 20 children) and those who did not have recurrent fUTI (nonrecurrent group: 111 children). Compared with the nonrecurrent group, the level of serum CRP at the first episode of fUTI was higher, and the duration of intravenous antibiotics was longer in the nonrecurrent group with statistical significance. The proportion of children with renal enlargement at the first episode of fUTI and VUR was significantly higher than that of children without renal enlargement or VUR (data not shown). We calculated the hazard ratio for recurrent fUTI using Cox proportional hazard regression adjusted for renal enlargement or nonrenal enlargement, the level of serum CRP at the first episode of fUTI, and the duration of intravenous antibiotics with or without VUR, because not all 132 children received the VCUG management. The results of our recalculated analysis showed that there was no significant independent factor for recurrent fUTI using the multivariate Cox regression analysis.





Flow chart of our retrospective cohort study.

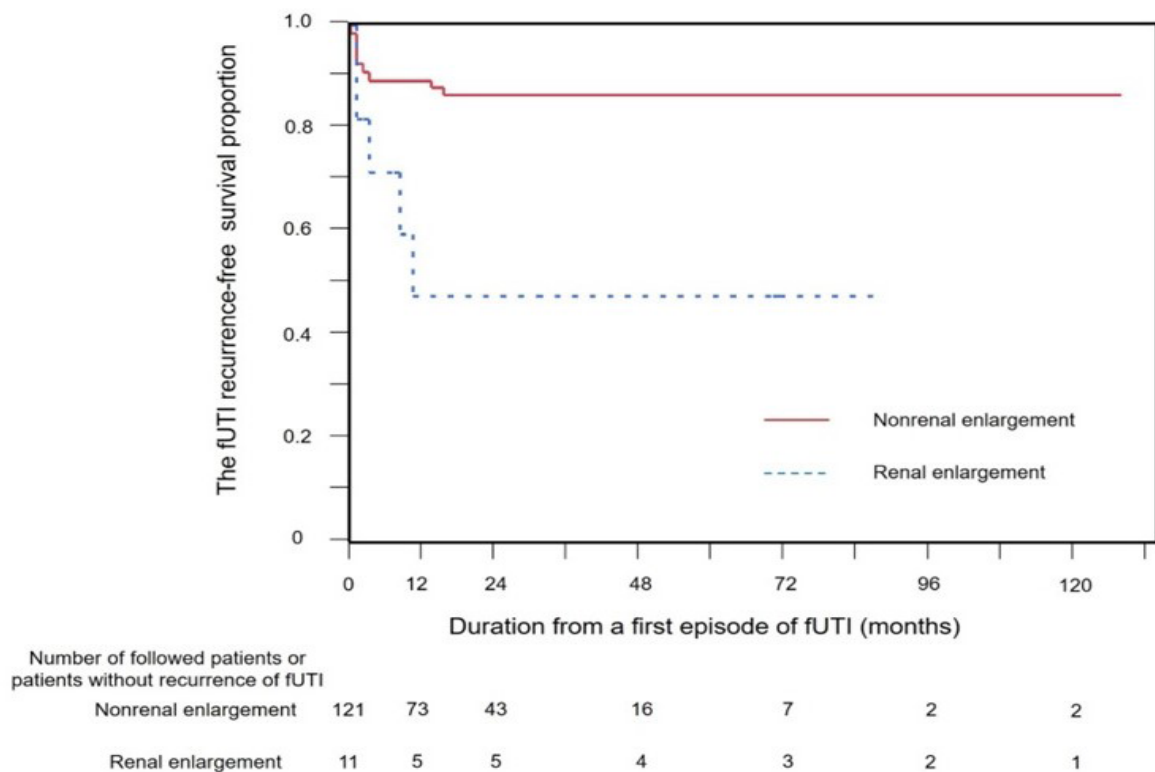
## DISCUSSION

Our study results showed that children with temporary renal enlargement at a first episode of fUTI had a significantly high risk for recurrent infection, and approximately 12% of children required antibiotics for recurrent fUTI among our patients comparable with previous reports<sup>(3,4)</sup>, wherein approximately half of the children with temporary renal enlargement progressed to a second episode of fUTI.

In our cohort, we evaluated the relationship between temporary renal enlargement and clinical characteristics during the acute phase of fUTI and after the completion of treatment for fUTI. Compared with children without renal enlargement at an initial fUTI episode, the proportion of patients with recurrent infection was significantly higher among those with renal enlargement. In recent studies, enlarged kidney during an initial episode of fUTI has been believed to be associated with permanent renal damage. Muller et al. reported that the maximum renal longitudinal diameter on RBUS correlated with the degree of 99 mTc-DMSA scintigraphic uptake<sup>(20)</sup>. Bouissou et al. demonstrated that increased renal diameter at initial fUTI significantly correlated with the risk of renal scarring<sup>(19)</sup>. Two hypotheses can be used for interpreting these analyses wherein renal enlargement was significantly associated with permanent renal damage. First, children with increased renal diameter at an fUTI episode could already have irreversible renal damage at the time of first fUTI episode, which would appear as the finding of permanent renal enlargement

on RBUS. Second, these children could carry multiple risks for renal scarring, although increased renal length during the acute phase of fUTI indicates a temporary renal swelling reaction of interstitial edema and following normal renal length after antibiotic treatment<sup>(18)</sup>. Our present result show that temporary renal enlargement during an episode of fUTI is a predictor of recurrent fUTI as a risk of renal scarring and might match with the latter hypothesis.

Although more than half of children with an initial fUTI have never had recurrence, an increase in the number of recurrences increases the risk for renal scarring<sup>(26)</sup>. Following several studies focusing on a first episode of pediatric fUTI have been concerned with protecting the kidney function from further damage to avoid recurrence of fUTI and manage dilating reflux. The American Academy of Pediatrics recommends that children should receive medical evaluation to confirm fUTI and to intervene promptly if they have high fever or urinary symptoms<sup>(14)</sup>. For children with initial fUTI, it is essential to identify valuable clinical and radiological indicators of recurrences and VUR. Panaretto et al. found that an age of <6 months, dilating reflux, and abnormality on 99 mTc-DMSA scintigraphy at the initial fUTI were the risk factors for recurrent infection<sup>(7)</sup>. Carpenter et al. demonstrated that nondetection of *Escherichia coli* in urine culture during fUTI correlated with a high grade of VUR<sup>(27)</sup>. Although our study results showed no significant relationship between temporary renal enlargement and VUR, identification of temporary enlargement as a predictor of recurrent fUTI may



**Figure 2.** The febrile urinary tract infection (fUTI) recurrence-free survival time based on temporary renal enlargement. The solid line indicates children with nonrenal enlargement at a first episode of fUTI; the fUTI recurrence-free survival proportion was 89.2% at 12 months from a first episode of fUTI. The dashed line indicates children with temporary renal enlargement at a first episode of fUTI; the fUTI recurrence-free survival proportion was 47.7% at 12 months from a first episode of fUTI. A significant difference was observed between the renal enlargement and nonrenal enlargement groups ( $p = 0.003$ ).

help identify patients for whom closer monitoring may be warranted or early intervention considered as previous study recommended<sup>(14,28)</sup>. Children with recurrent episode of fUTI, not detecting VUR, may have some other triggers of recurrence. While we did not evaluate further investigation, patients with temporary renal enlargement without VUR in our cohort have intrarenal reflux which plays an important role in the pathogenesis of reflux associated fUTI<sup>(29,30)</sup>. In addition, male infants without circumcision have an increased risk of fUTI than circumcised boys<sup>(31,32)</sup>. There were no male infants with circumcision in our cohort study, and three among seven boys with temporary renal enlargement had recurrence of fUTI. Their recurrence of fUTI may relate to non-circumcision. Moreover, children without VUR who have recurrent fUTI are recommended antimicrobial prophylaxis<sup>(33)</sup>. With further details, evaluating the effect of antimicrobial prophylaxis for children with temporary renal enlargement at an initial episode of fUTI, we might be able to conclude that detecting of temporary enlargement could prevent recurrence in terms of management of children without VUR.

In general, RBUS is a sensitive and noninvasive procedure for detecting morphological renal anomalies, but it is insensitive for diagnosing acute pyelonephritis. Some children with acute fUTI were reported to have focal or diffuse renal sonographic enlargement<sup>(10)</sup>. Previous studies have estimated the degree and radiological change of renal enlargement based on sonographic

imaging measurements of renal length in patients with fUTI. One cohort study indicated that kidneys with scintigraphic defects such as acute pyelonephritis were longer than kidneys without defects, but they returned to normal size range within 11 days of starting treatment<sup>(16)</sup>. Johansson et al. showed that children with acute pyelonephritis had an average increase of 150% of the normal renal volume in control subjects<sup>(34)</sup>. In the first 2 weeks, the most prominent decrease in renal length was detected in the follow-up ultrasound. Dinkel et al. reported an average increase in renal volume of 176% in 51 children with acute pyelonephritis<sup>(17)</sup>. They showed a reduction in renal volume of 50–60% within 2 weeks in the follow-up renal sonographic examination. In the present cohort analysis, RBUS at a first episode of fUTI could be suggested as an important procedure for detecting enlarged kidney as a risk factor for recurrent fUTI.

There were several limitations in our study. First, the duration of the observation period in more than half of children was less than 1 year. This duration may be too short to appropriately analyze the rate of recurrence in children with initial fUTI. Some children may experience episodes of recurrent fUTI within a time range beyond our observation period. Second, we excluded patients who did not undergo sonographic evaluation at an initial fUTI episode. Moreover, unless children underwent a repeat renal ultrasound after the antibiotic treatment for fUTI, they were excluded even if they had

sonographic increased renal length at an initial fUTI episode. Third, our study had sparse data bias because the sample size was too small. Finally, as our study was a retrospective cohort analysis, imaging examinations for the evaluation of CAKUT and renal scarring after the completion of treatment for an initial fUTI were performed in some but not all children. Although recurrent fUTI was significantly associated with the increase of kidney size in the acute phase of infection, no significant relationships were detected between renal enlargement and morphological abnormality of the kidneys, including VUR. The strategy for contrast imaging in children with fUTI in our center was to evaluate CAKUT according to the protocol of a published guidelines<sup>(14)</sup>. If we were to evaluate follow-up imaging examinations for all patients with fUTI with an interval of several months after an acute infection, we might obtain different results on the risk factors for recurrence.

### CONCLUSIONS

In conclusion, temporary renal enlargement on ultrasonography at a first episode of fUTI in pediatric patients was significantly associated with the recurrence of fUTI in a limited study with small sample size and no confounding adjustment. Identification of temporary temporal renal enlargement as a predictor of recurrent fUTI may help identify children with a first episode of fUTI who will be warned of close monitoring.

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### CONFLICT OF INTEREST

The authors report no conflicts of interest relevant to this article.

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