



Necessity of performing voiding cystourethrography for children with unilateral multicystic dysplastic kidney

Kazuna Yamamoto^{1,2} · Koichi Kamei¹ · Mai Sato¹ · Masao Ogura¹ · Mari Suzuki³ · Yuichi Hasegawa³ · Katsuhiko Ueoka³ · Shuichi Ito^{1,4} · Kenji Ishikura¹

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Abstract

Background The purpose of this study was to resolve the clinical question as to whether all patients with unilateral multicystic dysplastic kidney (MCDK) should receive voiding cystourethrography (VCUG).

Methods This is a retrospective study using cross-sectional analysis. Seventy-five children with unilateral MCDK were enrolled, excluding patients with other genetic or chromosome abnormalities, spinal cord diseases, or anal atresia. We reviewed their records from medical charts and calculated risk factors for abnormal VCUG using multivariate logistic regression analysis.

Results Abnormal VCUG findings were present in 24 of 75 patients (32.0%), specifically, vesicoureteral reflux (VUR) in 8 (10.6%), including high-grade VUR in 2 (2.7%), and only lower urinary tract or bladder disease in 16 (21.3%). In multivariate analysis, only abnormal findings by ultrasonography was an independent risk factor for abnormal VCUG findings with statistical significance in multivariate analysis (OR 6.57; 95% CI 1.99–26.26; $P = 0.002$). When we excluded five patients who showed similar findings by ultrasonography and VCUG, abnormal findings by ultrasonography were again calculated as an independent risk factor (OR 4.44; 95% CI 1.26–28.42; $P = 0.02$). Sensitivity, specificity, positive predictive value, and negative predictive value of abnormal findings by ultrasonography to predict urologic anomalies by VCUG in these children were 83%, 59%, 49%, and 88%, respectively. Two children required a third ultrasonography to detect abnormal findings.

Conclusions We can select, using only abnormal findings by ultrasonography, children with unilateral MCDK who should undergo VCUG. We would also like to emphasize that ultrasonography should be performed repeatedly to detect congenital anomalies of the urinary tract.

Keywords Multicystic dysplastic kidney (MCDK) · Voiding cystourethrography (VCUG) · Vesicoureteral reflux (VUR) · Congenital anomalies of the kidney and urinary tract (CAKUT) · Ultrasonography · Children

Introduction

Multicystic dysplastic kidney (MCDK) is often associated with other congenital anomalies of the kidney and urinary tract (CAKUT) and genital abnormalities. The most common anomaly in patients with unilateral MCDK is vesicoureteral reflux (VUR). As some studies showed that the rates of VUR in patients with unilateral MCDK range from 5 to 43% [1], they traditionally underwent voiding cystourethrography (VCUG) as initial imaging for the evaluation of VUR or other lower urinary tract anomaly.

However, the issue as to whether VCUG should be conducted for all children with MCDK remains controversial. In recent years, there have been some reports stating that VCUG should not be performed for all patients with MCDK for several reasons. First, patients are exposed to radiation with

✉ Koichi Kamei
kamei-k@nchd.go.jp

¹ Division of Nephrology and Rheumatology, National Center for Child Health and Development, 2-10-1 Okura, Setagaya-ku, Tokyo 157-8535, Japan

² Division of Pediatrics, Shiga University of Medical Science, Setatsukinowa-cho, Otsu, Shiga 520-2192, Japan

³ Division of Urology, National Center for Child Health and Development, 2-10-1, Okura, Setagaya-ku, Tokyo 157-8535, Japan

⁴ Department of Pediatrics, Graduate School of Medicine, Yokohama City University School of Medicine, 3-9, Fukuura, Kanazawa-ku, Yokohama, Kanagawa 236-0004, Japan

VCUG. Second, VCUG is painful for children. Third, the medical strategy for patients with unilateral MCDK is not affected by the result of VCUG in many cases. Although VUR was reported to be detected in 19.7% of patients with unilateral MCDK, most VUR in patients with MCDK is of low grade (I-II) [2]. Moreover, the treatment for VUR is changing and fewer patients with low-grade VUR (I-II) require surgical treatment. Most of them are followed conservatively. Some other findings detected by VCUG, such as ureterocele, posterior urethral valve, and urethral obstruction, can also be detected by ultrasonography. Some guidelines recommend that we should carefully select patients with VUR to whom we administer continuous antibiotic prophylaxis [3, 4]. According to these guidelines, antibiotic prophylaxis is unnecessary for low-grade VUR, although no evidence has been established concerning antibiotic prophylaxis for low-grade VUR for solitary functional kidney.

The purpose of this study was to help resolve the clinical question as to whether all patients with unilateral MCDK have to receive VCUG. We reviewed the VCUG findings from their medical charts, analyzed risk factors for positive findings by VCUG, and evaluated whether routine VCUG is necessary for them.

Materials and methods

Study design and patient population

There were 117 patients with the diagnosis of unilateral MCDK who were followed at the National Center for Child Health and Development from November 2003 to May 2016. As we excluded 42 children who had incomplete clinical data, other genetic or chromosome abnormalities, spinal cord diseases, or anal atresia, 75 patients were enrolled in this study.

We retrospectively reviewed the records of patients with MCDK. We evaluated clinical parameters of gender, VCUG findings, ultrasonography findings, history of urinary tract infection (UTI), renal function (serum creatinine levels), and other factors. We compared baseline data between patients with normal VCUG findings and those with abnormal VCUG findings. We also analyzed risk factors for abnormal VCUG findings with multivariate analysis.

Clinical strategy for MCDK and criteria

The diagnosis of MCDK was made according to ultrasonography confirmed by pediatric radiologists. The diagnosis was based on the following established ultrasound criteria: (1) multiple cysts of varying size, (2) absence of normal renal sinus echoes, and (3) absence of normal renal parenchyma [5]. The absence of renal function on ^{99m}Tc -mercaptoacetyl triglycine (MAG3) renogram

or ^{99m}Tc -dimercaptosuccinic acid (DMSA) scintigraphy was used to confirm the diagnosis of MCDK.

Voiding cystourethrography was performed by pediatric radiologists. VUR was graded according to the International Reflux Study Committee classification [6]. We started antibiotic prophylaxis for patients who showed VUR. Antibiotic prophylaxis was continued until VUR resolved in the follow-up VCUG or they finished toilet training. In this study, abnormal findings by ultrasonography meant signs of congenital anomalies that were found by abdominal ultrasound. We examined the liver, biliary system, genital organs, and CAKUT by abdominal ultrasonography. Abnormal findings by ultrasonography were defined as anomalies of the kidney, urinary tract, or genital organs other than MCDK. Anomalies of genital organs included visceral organs, such as ovary and uterus, and we did not include external anomalies. Pediatric radiologists performed abdominal ultrasonography and made the diagnoses. Decreased renal function was defined as over twice the median level of serum creatinine [7]. If patients had suspected UTI, we collected urine samples by clean catheterization. UTI was diagnosed by $\geq 10^4$ colonies in urine culture.

Statistical analysis

For statistical analysis, data were analyzed with JMP version 11.0 (SAS Institute Japan Ltd., Tokyo, Japan). Clinical characteristics were compared between children with normal VCUG and those with abnormal VCUG findings using the Mann-Whitney *U* test for continuous variables and the Fisher's exact test for categorical variables. Univariate and multivariate analyses for abnormal findings by VCUG were performed using logistic regression analysis. Statistical significance was established at $P < 0.05$.

Results

Among 75 children, 71 had a diagnosis of MCDK by fetal ultrasonography, 2 children had UTI, and 2 children underwent chance ultrasonography or magnetic resonance imaging. Six patients showed slight function ($< 5\%$) on the MCDK side by DMSA. Table 1 shows clinical characteristics stratified by VCUG findings. Abnormal VCUG findings were present in 24 of 75 patients (32.0%). Abnormal findings by ultrasonography consisted of congenital anomalies of the kidney, urinary tract, and genital organs. The abnormal findings by ultrasonography were hydronephrosis, hydroureter, ectopic ureter, renal duplex kidney, ureterocele, contralateral simple renal cyst, dysplastic kidney, cysts in the pelvis, double uterus, and bicornuate uterus. No children had congenital anomalies of the liver or biliary system. In 41 children with abnormal findings by ultrasonography, two children required a third ultrasonography to detect abnormal findings. Patients with

Table 1 Patient characteristics stratified by VCUg findings

Characteristics	All patients (n = 75)	Abnormal VCUg (n = 24)	Normal VCUg (n = 51)	P value
Gender				
Male	29 (38.7%)	11 (45.8%)	18 (35.3%)	0.45
Female	46 (61.3%)	13 (54.2%)	33 (64.7%)	
Laterality of MCDK				
Left	35 (46.7%)	15 (62.5%)	20 (39.2%)	0.08
Right	40 (53.3%)	9 (37.5%)	31 (60.8%)	
Age at diagnosis (months)	0 (0–83)	0 (0–83)	0 (0–54)	0.95
Age at last observation (months)	67 (0–283)	61 (9–212)	67 (0–283)	0.66
Period of observation (months)	58 (0–283)	62 (0–212)	49 (0–283)	0.61
Findings by ultrasonography ^a				
Abnormal findings	41 (54.7%)	20 (83.3%)	21 (41.2%)	0.001
Normal findings	34 (45.3%)	4 (16.7%)	30 (58.8%)	
History of urinary tract infection				
Yes	12 (16.0%)	7 (29.2%)	5 (9.8%)	0.045
No	63 (84.0%)	17 (70.8%)	46 (90.2%)	
Decreased renal function				
Yes	6 (8.0%)	2 (8.3%)	4 (7.8%)	1.00
No	69 (92.0%)	22 (91.7%)	47 (92.2%)	

Data are expressed as number (percent) or mean (min-max)

VCUg voiding cystourethrography, MCDK multicystic dysplastic kidney

^aHydronephrosis, n = 14; hydroureter, n = 14; ectopic ureter, n = 11; renal duplex kidney, n = 2; ureterocele, n = 6; contralateral simple renal cyst, n = 3; dysplastic kidney, n = 1; cysts in the pelvis, n = 3; double uterus, n = 3; bicornuate uterus, n = 1

abnormal VCUg findings showed higher rates of abnormal findings by ultrasonography and history of UTI compared with those with normal VCUg findings (with statistical significance). Of six children with decreased renal function, two children had hydronephrosis and four children had suspected dysplastic kidney in the contralateral kidney to the MCDK.

Table 2 shows abnormal VCUg findings. VUR was identified in 8 patients (10.6%), and congenital anomalies of the lower urinary tract were identified in 20 patients (26.7%). Four children had both VUR and abnormal findings in the lower urinary tract. Only two children had VUR of high grade (III-V) in the contralateral ureter to the MCDK, and six children had VUR of low grade (I-II).

Risk factors for abnormal VCUg findings using logistic regression analysis are shown in Table 3. In univariate analysis, two factors (abnormal findings by ultrasonography [OR 7.14; 95% CI 2.31–27.34; P = 0.0004] and history of UTI [OR 3.79; 95% CI 1.07–14.39; P = 0.04]) were calculated as statistically significant risk factors for abnormal VCUg findings. In multivariate analysis, only abnormal findings by ultrasonography (OR 6.57; 95% CI 1.99–26.26; P = 0.002) were an independent risk factor for abnormal VCUg findings (with statistical significance). As five patients showed the same abnormal findings by ultrasonography and VCUg, we analyzed risk factors for newly detected abnormal findings by VCUg by excluding these five patients. Abnormal findings by ultrasonography was again calculated as an independent risk factor with statistical significance

in multivariate analysis (OR 4.44; 95% CI 1.26–28.42; P = 0.02) (Table 4). Sensitivity, specificity, positive predictive value, and negative predictive value of abnormal findings by ultrasonography to predict urologic anomalies on VCUg in these children were 83%, 59%, 49%, and 88%, respectively (Table 1). In four

Table 2 Abnormal findings by VCUg in 24 cases

VUR	Unilateral (n = 6)	Grade	Ipsilateral	Contralateral
		I	1	2
		II	1	1
		III	0	0
		IV	0	1
		V	0	0
		Total	2	4
	Bilateral (n = 2)	Cases	Ipsilateral	Contralateral
		1	II	I
		2	I	IV
Abnormal findings in lower urinary tract (n = 20) (One patient might show more than one finding.)				
	Suspected urethral stricture		7	
	Ureterocele		6	
	Bladder diverticulum		5	
	Bladder malformation		3	
	Ectopic ureter		2	
	Urethral dilatation		1	

VCUg voiding cystourethrography, VUR vesicoureteral reflux

Table 3 Risk factors for abnormal findings by VCUG ($n = 75$)

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% Confidence interval	<i>P</i> value	Odds ratio	95% Confidence interval	<i>P</i> value
Male gender	1.55	0.57–4.19	0.38	1.53	0.50–4.75	0.45
Abnormal findings by ultrasonography	7.14	2.31–27.34	0.0004	6.57	1.99–26.26	0.002
History of UTI	3.79	1.07–14.39	0.04	3.25	0.71–18.32	0.13
Decreased renal function	1.07	0.14–5.91	0.94	0.27	0.03–1.90	0.19

VCUG voiding cystourethrography, UTI urinary tract infection

children with normal ultrasound findings, the findings by VCUG were grade I VUR, mild urethral stricture, and bladder diverticulum; none of them required surgical intervention. All of these four children were boys. They did not experience UTI over 48 months of follow-up. On the other hand, one of 31 children who showed normal ultrasound and normal VCUG findings experienced UTI. Eleven of 41 children with abnormal ultrasound findings suffered from UTI.

Discussion

In this study, we examined whether it was possible to select, by abdominal ultrasonography, patients who should receive VCUG. Some authors evaluated whether VUR can be detected by ultrasonography of the kidney and urinary tract in patients with MCDK. To date, there have been apparently no reports concerning the relationship between lower urinary tract disorders, including VUR, and ultrasonography findings, including congenital anomalies of the genital organs. We examined risk factors associated with the presence of urinary tract abnormalities for 75 children in our hospital. MCDK is complicated by congenital urinary tract abnormalities and abnormalities of the genital organs. In our study, 8 of 75 children (10.6%) with MCDK had VUR and 2 of 8 children (25.0%) had high-grade VUR (III–V). Seven of 75 children (9.3%) had congenital abnormalities of the genital organs. Our results are compatible with past reports [1, 2, 8]. According to the results of our study, we show that abnormal findings by ultrasonography were an independent risk factor for abnormal VCUG findings in patients with unilateral MCDK.

Only four children (5.3%) had abnormal findings by VCUG that we could not detect by abdominal ultrasonography. In these four children, only one patient showed grade 1 VUR, for which antibiotic prophylaxis is usually unnecessary. No evidence was established about antibiotic prophylaxis for low-grade VUR in solitary kidney. Actually, the VCUG findings in these four children did not affect the treatment strategy. This study demonstrated that we could select, by the use of ultrasonography, patients who should undergo routine VCUG.

Whether routine VCUG is necessary in all patients with unilateral MCDK at the time of diagnosis is still debated in the literature. Some authors have advocated for routine VCUG to screen for VUR in children with MCDK, as high-grade VUR of the contralateral kidney may cause pyelonephritis and scarring in the normal kidney, when UTI occurs [9–11]. Flack and Bellinger studied 29 patients with MCDK [12]. Eight of 29 patients showed VUR on VCUG, and 7 patients had normal ultrasound findings. This study suggested that single ultrasounds may be unreliable predictors of VUR; however, the ultrasound criteria used were not specified.

On the contrary, some authors have argued that routine VCUG for children with unilateral MCDK might not be necessary given the low incidence of clinically significant VUR [13–16]. These results support our strategy. Ismaili et al. concluded that two successive normal neonatal renal ultrasound scans would rule out clinically significant contralateral anomalies [14]. When the contralateral kidney was normal on two successive renal bladder ultrasounds, only 7% of children presented with low-grade VUR on VCUG. They consider the neonatal ultrasound criteria to be important, defining abnormal

Table 4 Risk factors for newly detected abnormal findings by VCUG ($n = 70$)

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% Confidence interval	<i>P</i> value	Odds ratio	95% Confidence interval	<i>P</i> value
Male gender	2.03	0.70–6.04	0.19	2.00	0.62–6.69	0.25
Abnormal findings by ultrasonography	5.36	1.68–20.90	0.004	4.44	1.26–18.42	0.02
History of UTI	4.24	1.11–17.00	0.03	3.72	0.75–22.13	0.11
Decreased renal function	1.38	0.18–7.77	0.73	0.37	0.03–2.76	0.34

VCUG voiding cystourethrography, UTI urinary tract infection

contralateral kidney to include pelvic anteroposterior diameter ≥ 7 mm, calyceal or ureteral dilation, pelvic or ureteral wall thickening, absence of corticomedullary differentiation, and signs of renal dysplasia (small kidney, thinned or hyperechoic cortex, and cortical cysts). Kuwertz-Broeling et al. reviewed 89 patients with MCDK and indicated that the low rate of reflux made routine VCUG unnecessary if the contralateral upper urinary tract and kidney appeared to be normal on ultrasound [15]. Hayes et al. reviewed 323 patients with unilateral MCDK, and they did not perform routine VCUG unless the ultrasonography showed dilated ureters, calyces or small or abnormal appearance of the contralateral kidney in the investigation protocol [16]. Calaway et al. supported the view that in the majority of cases with unilateral MCDK, routine VCUG was unnecessary and did not impact the final outcome [17]. Furthermore, it is not clear whether undetected VUR leads to higher frequency of UTI or places the contralateral kidney at higher risk for injury in children with MCDK [18]. However, Ismaili et al. and Calaway et al. pointed out that it is important that families should understand the symptoms of UTI, if routine VCUG is not performed [14, 17].

Our study has some limitations. First, this study is a retrospective cohort study. Age at the VCUG procedure was not decided as the protocol and the observation periods varied. Moreover, antibiotic prophylaxis might affect development of UTI. Second, some patients did not receive repeat ultrasonography. We believe that to detect abnormal findings of the urinary tract, patients have to receive ultrasonography more than once. Third, reliability of ultrasonography may be dependent on the examination skills of the ultrasound technician and the availability of a trained pediatric radiologist. Therefore, we recommend that the ultrasounds be performed by technicians with experience imaging small children and be interpreted by experienced pediatric radiologists. However, if adequate pediatric radiology resources are not available, VCUG should be considered regardless of ultrasound findings.

In conclusion, we can select, using only abnormal findings by ultrasonography, children with unilateral MCDK who should undergo VCUG. However, if routine VCUG is not performed, patients should receive repeat ultrasonography and the family should be instructed about the signs and symptoms of UTI.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The design and execution of this study were in accordance with the ethical standards of the Declaration of Helsinki. The protocol was approved by the Ethics Committee of the National Center for Child Health and Development (No. 1372).

Informed consent For this type of study, formal informed consent is not required.

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