Multicystic dysplastic kidney: is an initial voiding cystourethrogram necessary?

Adam C. Calaway, MD,[1] Benjamin Whittam, MD,[1]
Konrad M. Szymanski, MD,[1] Rosalia Misseri, MD,[1] Martin Kaefer, MD,[1]
Richard C. Rink, MD,[1] Boaz Karymazn, MD,[2] Mark P. Cain, MD[1]

[1]Division of Pediatric Urology, Riley Hospital for Children at Indiana University School of Medicine, Indianapolis, Indiana, USA
[2]Division of Pediatric Radiology, Riley Hospital For Children at Indiana University School of Medicine, Indianapolis, Indiana, USA

CALAWAY AC, WHITTAM B, SZYMANSKI KM, MISSERI R, KAEFER M, RINK RC, KARYMAZN B, CAIN MP. Multicystic dysplastic kidney: is an initial voiding cystourethrogram necessary? *Can J Urol* 2014; 21(5):7510-7514.

Introduction: *Traditionally, a voiding cystourethrogram (VCUG) has been obtained in patients diagnosed with multicystic dysplastic kidney (MCDK) because of published vesicoureteral reflux (VUR) rates between 10%-20%. However, with the diagnosis and treatment of low grade VUR undergoing significant changes, we questioned the utility of obtaining a VCUG in healthy patients with a MCDK. We reviewed our experience to see how many of the patients with documented VUR required surgical intervention.*

Materials and methods: *We performed a retrospective review of children diagnosed with unilateral MCDK from 2002 to 2012 who also underwent a VCUG.*

Results: *A total of 133 patients met our inclusion criteria. VUR was identified in 23 (17.3%) children. Four patients underwent ureteral reimplant (3.0%). Indications for surgical therapy included breakthrough urinary tract infections (2 patients), evidence of dysplasia/scarring (1 patient) and non-resolving reflux (1 patient). All patients with a history of VUR who are toilet trained, regardless of the grade or treatment, are currently being followed off antibiotic prophylaxis. To date, none have had a febrile urinary tract infection (UTI) since cessation of prophylactic antibiotics. Hydronephrosis in the contralateral kidney was not predictive of VUR ($p = 0.99$).*

Conclusion: *Routine VCUG in healthy children diagnosed with unilateral MCDK may not be warranted given the low incidence of clinically significant VUR. If a more conservative strategy is preferred, routine VCUG may be withheld in those children without normal kidney hydronephrosis and considered in patients with normal kidney hydronephrosis. If a VCUG is not performed the family should be instructed in signs and symptoms of urinary tract infection.*

Key Words: multicystic dysplastic kidney, voiding cystourethrogram, vesicoureteral reflux

Introduction

Voiding cystourethrograms (VCUG) have traditionally been a part of the initial imaging evaluation of children diagnosed with multicystic dysplastic kidney (MCDK) due to previously reported vesicoureteral reflux (VUR) rates between 10%-20%.[1-3] However, the degree of VUR in this patient population has been shown to be predominantly low grade with rates of low grade VUR (I-III) between 80%-90%.[3,4] In recent years, the management of low grade VUR has become increasingly more conservative with fewer patients undergoing surgical intervention. With this shift in the management of low grade VUR, coupled with high rates of low grade VUR in patients with MCDK, we questioned the necessity of obtaining a VCUG in healthy patients with a MCDK. We reviewed our experience to determine how many patients with documented VUR and MCDK required therapy and to identify risk factors for VUR requiring intervention.

Accepted for publication August 2014

Address correspondence to Dr. Adam C. Calaway, Indiana University School of Medicine, 705 Riley Hospital Drive, Suite 4230, Indianapolis, IN 46202 USA

Materials and methods

Patient selection and data abstraction

We retrospectively reviewed the charts and images of 220 children with a diagnosis of MCDK, identified via ICD-9 code (753.19), from January 2002 to December 2012. Children who had other significant congenital

abnormalities, other genitourinary abnormalities or incomplete clinical data were excluded. The Institutional Review board of Indiana University School of Medicine approved this study.

Diagnosis of MCDK

The diagnosis of MCDK on renal bladder ultrasound (RBUS) was made according to a radiology report with the following criteria: multiple non-communicating cysts of size and non-medial location of the largest cyst, absence of normal renal sinus and absence of normal renal parenchyma.[5] The normal kidney was assessed on every ultrasound. The degree of normal kidney hydronephrosis, if present, was graded per Society of Fetal Urology (SFU) grading system. Absence of renal function on 99m Tc-mercaptoacetyletriglycine (Mag3) or 99m Tc-dimercaptosuccinic acid (DMSA) nuclear medicine studies was used to confirm the diagnosis of MCDK but was not universally required. Diagnostic imaging tests were ordered based on physician preference.

Diagnosis and treatment of VUR

VCUG's were obtained in all patients to investigate VUR. VUR grade was based on the radiology reports, which were graded by the International Reflux Study Committee classification.[6] All patients with VUR were initially treated with antibiotic prophylaxis.

Statistical analysis

The Fisher's exact test was used to test for an association between hydronephrosis and VUR on the side contralateral to the MCDK.

Results

A total of 133 patients with MCDK met our inclusion criteria. There were 76 males (57.1%) and 57 females (42.9%) in the study population. MCDK was diagnosed in the left kidney in 69 children (51.8%) and in the right kidney in 64 patients (48.1%). All patients had RBUS evidence of MCDK. Nuclear medicine renal scans were ordered to confirm the diagnosis in all but five patients. All patients that had nuclear medicine renal scans confirmed absent function of the MCDK.

VUR was identified in 23 patients (17.3%) with a total of 28 refluxing units. Fourteen patients had VUR into the normal kidney, 4 had VUR into the MCDK and 5 had bilateral VUR. Non-dilating VUR (I-II) was seen in 11 patients and 15 renal units and dilating VUR (III-V) was seen in 12 patients and 13 renal units, Table 1. One patient with unilateral grade 3 VUR into the MCDK was lost to follow up. Patients with VUR were followed for an average of 3.6 years (range 1.0-9.5 years). None of the five patients without a confirmatory renal scan had evidence of VUR.

Ultimately, 4 of 22 (18.2%) of patients with VUR who had adequate follow up failed conservative therapy and underwent ureteral reimplantation. Two patients (1 male, 1 female) had breakthrough urinary tract infections (UTIs). The male had grade 4 VUR and the female had grade 5 VUR. One patient (female) had evidence of dysplasia/scarring on routine RBUS and therefore underwent ureteral reimplantation. She had grade 3 reflux prior to the operation. The last patient (male) who underwent reimplantation had grade 4 nonresolving reflux. In this subgroup, two patients had evidence of renal scarring prior to the ureter reimplantation. One patient previously mentioned had increased renal echogenicity and evidence of dysplasia/scarring which was an indication for surgical therapy. This finding continued to be observed on follow up ultrasounds. The second patient had evidence of renal scaring on nuclear medicine renal scan. Postoperatively, normal renal parenchyma was observed on RBUS. All patients treated with ureteral reimplantation had VUR into the normal kidney.

Resolution of VUR was seen in seven patients who had a VCUG during follow up. Four additional patients had VUR into the MCDK and underwent upper tract surgery in the form of a nephrectomy (2) or nephroureterectomy (2). In all of these patients, the indication for upper tract surgery was enlarging MCDK. In the seven patients who resolved without surgery, 5 patients had VUR into the normal kidney and 2 had VUR into the MCDK. There were seven patients who did not have surgery or follow up

TABLE 1. **Number of refluxing renal units based on vesicoureteral reflux (VUR) grade**

Grades of VUR	**Grade I**	**Grade II**	**Grade III**	**Grade IV**	**Grade V**
No. refluxing units* (%)	7 (25)	8 (28.6)	8 (28.6)	4 (14.3)	1 (3.6)

*there were 23 total patients with VUR. Five of these patients had bilateral VUR. There were a total of 12 patients with dilating VUR (III-V) with one of these patients having bilateral grade IV VUR.

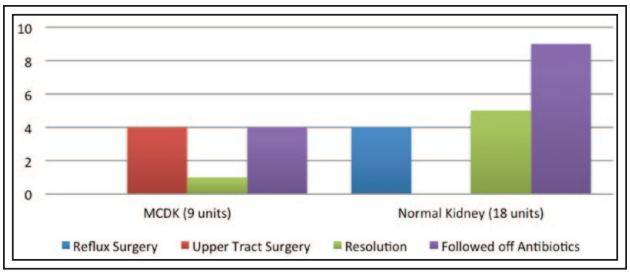

Figure 1. Fate of the refluxing renal unit based on laterality of vesicoureteral reflux (VUR).
There were a total of 28 refluxing units. Fourteen patients have VUR into the normal kidney, 4 into the MCDK, and 5 with bilateral reflux. One patient with grade III VUR into the normal kidney was lost to follow up.

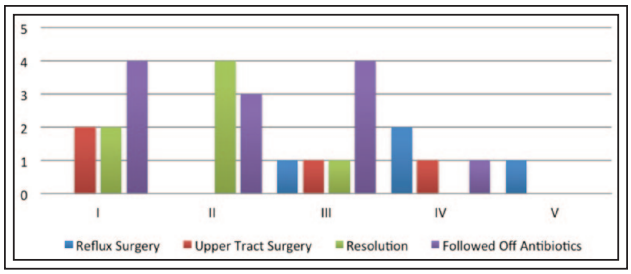

Figure 2. Fate of the refluxing renal unit based on degree of vesicoureteral reflux (VUR).
There were a total of 15 renal units with non-dilating VUR and 13 units with dilating VUR. As expected patients with low grade VUR were more likely to resolve and patients with high grade VUR were more likely to undergo surgical intervention.

imaging. All of these patients are currently toilet trained and are being followed off of antibiotics. The fate of the refluxing renal units over time based on laterality and by grade of VUR is represented in Figures 1 and 2, respectively. Finally, Figure 3 represents a flow chart of all the patients in the study cohort to better visualize the fate of the refluxing renal units.

Overall, 6 of 133 (4.5%) had febrile UTIs (fUTI). Two of these patients had VUR. These patients had grade 4 and 5 reflux, respectively, and progressed to surgical management as mentioned above.

High grade VUR (grade 4-5) was documented in four patients with one patient having bilateral grade 4 VUR. Three of these patients progressed to surgical management of the VUR. Two of these patients with high grade reflux had UTIs. The last patient had downgrading of their VUR and has been followed without antibiotics since toilet training.

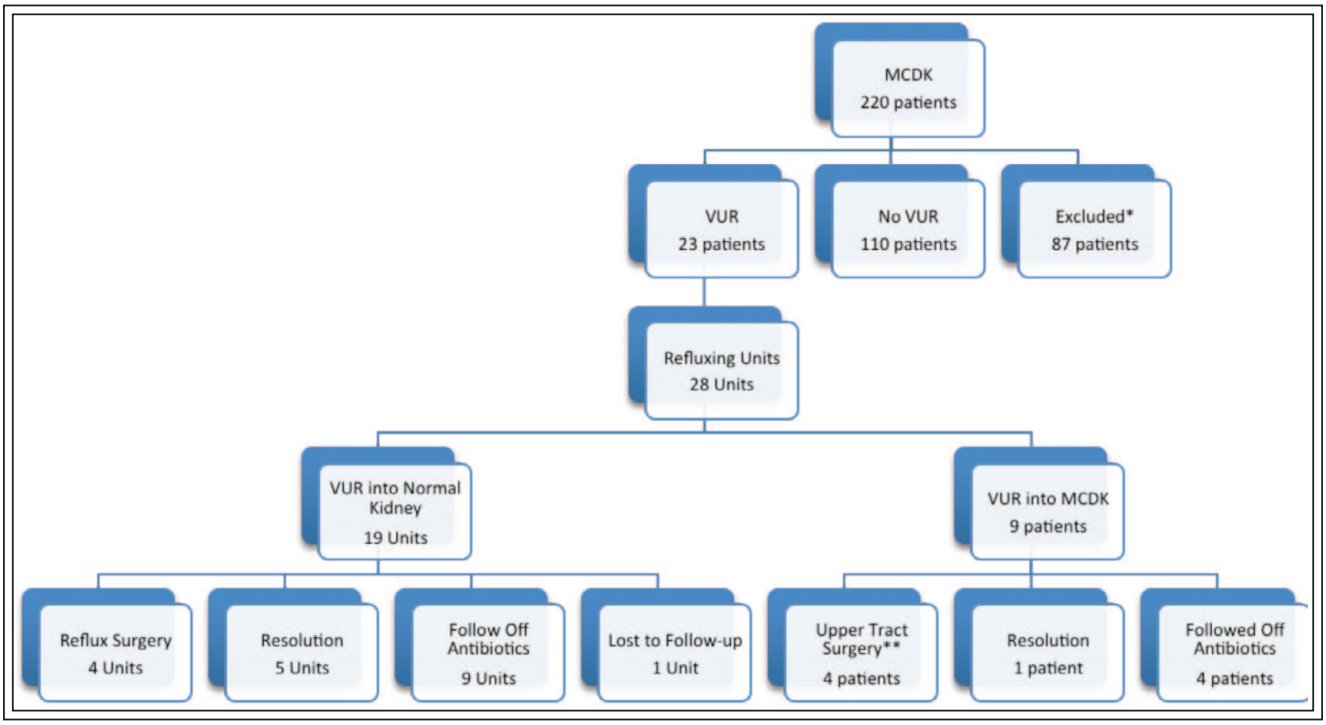

Figure 3. Flow chart representing fate of vesicoureteral reflux (VUR) in patients with multicystic dysplastic kidney (MCDK).

Hydronephrosis of the normal kidney was found in 38/133 patients (28.6%) of whom eight had VUR. All patients had grade 1 or 2 hydronephrosis except for three patients who had grade 3 hydronephrosis. In this patient population, 2 patients had VUR into the MCDK kidney, 4 had VUR into the normal kidney and 2 had bilateral VUR. Of the six children with VUR into the normal kidney, one patient had grade 2-3 VUR, two had grade 3 VUR, two had grade 4 VUR and one had grade 5 VUR. Three of these patients (grade 3 VUR with evidence of dysplasia/scarring and grade 4 and grade 5 with breakthrough UTIs) were treated with surgical correction of the reflux. Hydronephrosis of the normal kidney was not predictive of reflux ($p = 0.99$). Hydronephrosis resolved in 22 patients on follow up ultrasound.

All patients with a history of VUR who are toilet trained, regardless of the grade or treatment, are currently being followed off antibiotic prophylaxis. To date, none have had a febrile UTI since cessation of prophylactic antibiotics.

Discussion

Historically, children with MCDK were thought to have an increased risk of contralateral urinary tract abnormalities.[1-3] VUR is the most common reported abnormality, seen in approximately 10%-20% of normal kidneys. Therefore, many have advocated for routine VCUG's to screen for VUR in these patients.[7-9] In addition to a VCUG, patients with MCDK typically undergo a postnatal renal bladder ultrasound (RBUS) for initial evaluation and then repeat RBUS serially to check for involution and neoplastic transformation. Nuclear medicine scans have also been used to confirm absent function of the MCDK.

However, this paradigm has begun to shift. Given the benign nature of MCDK and the lack of association with hypertention and neoplastic transformation, the use of serial RBUS has significantly decreased.[10] Advancements in ultrasound technology along with more specialized radiologists and technicians have similarly improved the diagnostic ability of RBUS thus limiting the utility of a confirmatory NM scan in otherwise healthy children.

Given the trend towards conservative management for MCDK, and in light of recent changes in management of VUR, we sought to evaluate the current practice of obtaining a routine VCUG to screen for VUR in patients with MCDK.

In this cohort, all patients with VUR were initially treated conservatively with prophylactic antibiotics and of the 22 patients with adequate follow up just four patients underwent ureteral reimplantation. Two patients had high grade VUR (4 and 5) and developed breakthrough fUTI, while the third had evidence of renal dysplasia/scarring of the normal kidney on follow up RBUS. The final patient had persistent grade 4 VUR and underwent ureteral reimplantion for nonresolving VUR per parental preference. Overall, only 4 patients of the 133 patients with MCDK (3.0%) had VUR that resulted in surgical correction. Interestingly, if routine screening VCUGs would have been withheld in this patient population, 3 of the 4 who underwent surgical correction would have met current indications for evaluation with a VCUG (2 with febrile UTIs, 1 with renal dysplasia/scarring). Thus, in the majority of cases, a preemptive VCUG is unnecessary and does not impact the final outcome.

Recent literature suggests that prophylactic antibiotics are of little or no benefit, particularly in low to moderate grade VUR.[11-14] In our population 11 patients had non-dilating grade (1-2) VUR and 12 patients had dilating grade (3-5) VUR, in whom evidence supports antibiotic prophylaxis. Therefore, by current standards, only 12 of 133 (9.0%) patients management were impacted by VCUG results.

Hypothetically, if routine VCUGs were not performed in this patient population, none of these patients would have been placed on prophylactic antibiotics. Previously, the PRIVENT trial documented that antibiotic prophylaxis had a 5% absolute risk reduction (ARR) of future fUTIs in patients with non-dilating VUR.[15] Extrapolating this data to our patient cohort, less than one patient with non-dilating VUR would have benefitted from diagnosis of VUR and antibiotic prophylaxis. For patients with dilating VUR, the Swedish Reflux Trial showed that antibiotic prophylaxis reduced future fUTIs by 38.5%.[11] Using this data in our patient cohort, three patients would have benefitted from initial VCUG for diagnosis of VUR and antibiotic prophylaxis. This corresponds quite well with our actual review of our cohort of patients with dilating VUR as two patients developed a fUTI.

Previously, Ismaili et al investigated if screening VCUG was needed for a patient with MCDK and a normal appearing contralateral kidney on RBUS.[4] When the contralateral kidney was normal on two successive RBUS completed post-natally, VCUG revealed reflux in only 7% of children, with predominately low-grade reflux. This low percentage of low-grade reflux arguably is of no clinical significance thus severely limits the utility of screening VCUG in this population. A similar study by Miller et al reviewed 75 patients with MCDK and found 19 patients with VUR, predominantly low grade, and found no detrimental effects of this VUR on renal growth.[3]

These results, coupled with the results of our current study, argue for judicious use of VCUG in patients with a normal contralateral kidney on RBUS. We believe that routine VCUG in healthy children diagnosed with MCDK may not be necessary given the low incidence of clinically significant VUR. In the current era of medical reform, necessitated by rising costs of medical care, this is a significant area of possible savings for our patients and healthcare system without a significant increased risk of a missed diagnosis. Excluding routine VCUG will additionally avoid radiation exposure and patient discomfort secondary to catheter placement. Currently, we are not performing VCUGs uniformly on all patients with MCDK.

We were unable to identify any RBUS findings predictive of VUR. In particular, normal kidney hydronephrosis was not predictive of the presence of VUR ($p = 0.99$). Only 34.7% of patients with VUR had normal kidney hydronephrosis. In patients with normal kidney hydronephrosis, we recommend following SFU guidelines for management. If a more conservative management strategy is preferred in these patients with a solitary functioning renal unit, we suggest limiting routine VCUG to patients with any degree of hydronephrosis of the normal kidney. This measure would still drastically reduce the use of VCUG in patients with MCDK while ensuring the normal kidney was not at risk. If a VCUG is not performed as part of an initial evaluation, the family should be instructed on signs and symptoms of a urinary tract infection.

Our study is not without limitations. The retrospective nature and relatively small patient cohort, are limitations of our study. Our study group is one of the largest cohorts of patients with MCDK diagnosed and treated at a single institution, which contributes in the homogeneity of our results, but does limit the power of the analysis. As shown above, 4 of the 12 patients with dilating VUR progressed to surgical therapy. It is unclear what the fate of the remaining eight patients with dilating VUR would have been if they were not placed on antibiotic prophylaxis. Despite these flaws, we believe that our results provide initial insight to further reduce unnecessary imaging studies in patients with a relatively benign condition. We hope to reproduce our results with a prospective clinical trial.

Conclusion

Routine VCUG in healthy children diagnosed with unilateral MCDK may not be warranted given the low incidence of clinically significant VUR. If a VCUG is not performed the family should be instructed in signs and symptoms of urinary tract infection. □

References

1. Schreuder MF, Westland R, van Wijk JA. Unilateral multicystic dysplastic kidney: a meta-analysis of observational studies on the incidence, associated urinary tract malformations and the contralateral kidney. *Nephrol Dial Transplant* 2009;24(6): 1810-1818.
2. Onal B, Kogan BA. Natural history of patients with multicystic dysplastic kidney-what followup is needed? *J Urol* 2006;176 (4 Pt 1):1607-1611.
3. Miller DC, Rumohr JA, Dunn RL, Bloom DA, Park JM. What is the fate of the refluxing contralateral kidney in children with multicystic dysplastic kidney? *J Urol* 2004;72(4 Pt 2):1630-1634.
4. Ismaili K, Avni FE, Alexander M, Schulman C, Collier F, Hall M. Routine voiding cystourethrography is of no value in neonates with unilateral multicystic dysplastic kidney. *J Pediatr* 2005;146(6): 759-763.
5. Rabelo EA, Oliveira EA, Silva GS, Pezzuti IL, Tatsuo ES. Predictive factors of ultrasonographic involution of prenatally detected multicystic dysplastic kidney. *BJU Int* 2005;95(6): 868-871.
6. Medical versus surgical treatment of primary vesicoureteral reflux: report of the International Reflux Study Committee. *Pediatrics* 1981;67(3):392-400.
7. Atiyeh B, Husmann D, Baum M. Contralateral renal abnormalities in multicystic-dysplastic kidney disease. *J Pediatr* 1992;121(1):65-67.
8. Flack CE, Bellinger MF. The multicystic dysplastic kidney and contralateral vesicoureteral reflux: protection of the solitary kidney. *J Urol* 1993;150(6):1873-1874.
9. al-Khaldi N, Watson AR, Zuccollo J, Twining P, Rose DH. Outcome of antenatally detected cystic dysplastic kidney disease. *Arch Dis Child* 1994;70(6):520-522.
10. Narchi H. Risk of Wilms' tumour with multicystic kidney disease: a systematic review. *Arch Dis Child* 2005;90(2):147-149.
11. Brandstrom P, Jodal U, Sillen U, Hansson S. The Swedish reflux trial: review of a randomized, controlled trial in children with dilating vesicoureteral reflux. *J Pediatr Urol* 2011;7(6):594-600.
12. Montini G, Rigon L, Zucchetta P et al. Prophylaxis after first febrile urinary tract infection in children? A multicenter, randomized, controlled, noninferiority trial. *Pediatrics* 2008; 122(5):1064-1071.
13. Pennesi M, Travan L, Peratoner L et al. Is antibiotic prophylaxis in children with vesicoureteral reflux effective in preventing pyelonephritis and renal scars? A randomized, controlled trial. *Pediatrics* 2008;121(6):e1489-e1494.
14. Roussey-Kesler G, Gadjos V, Idres N et al. Antibiotic prophylaxis for the prevention of recurrent urinary tract infection in children with low grade vesicoureteral reflux: results from a prospective randomized study. *J Urol* 2008;179(2):674-9;discussion 679.
15. Craig JC, Simpson JM, Williams GJ et al. Antibiotic prophylaxis and recurrent urinary tract infection in children. *N Engl J Med* 2009;361(18):1748-1759.