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ORIGINAL ARTICLE

Simple multicystic dysplastic kidney disease: end points for subspecialty follow-up

Adam Weinstein · T. Rob Goodman · Sandra Iragorri

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Abstract Simple multicystic dysplastic kidney (MCDK) disease, defined as unilateral MCDK without other genitourinary tract involvement, portends an excellent prognosis. Nevertheless, its long-term management remains undefined. This study aims to provide subspecialty discharge recommendations for these patients. We identified eighty patients with simple MCDK disease by renal ultrasound between 1996 and 2006. Their charts were reviewed for growth of the contralateral kidney, involution of the MCDK, and incidence of complications, specifically hypertension, chronic renal insufficiency (CRI), urinary tract infection (UTI), and malignancy. Mean follow-up was 5 years. At approximately 1 year, 59% of unaffected kidneys were hypertrophied (≥95th percentile for age/height) and 100% were >50th percentile. With continued follow-up, 80.3% of unaffected kidneys were hypertrophied. Likewise, at 1 year, 71.2% of MCDKs assessed were either involuting or had disappeared; on further follow-up, this increased to 89.6%. No patient had hypertension, CRI, or malignancy. Four patients (5%) developed nonrecurrent UTIs, none leading to renal scarring or growth impairment. These data suggest that subspecialty follow-up may be discontinued once contralateral hypertrophy and ipsilateral involution occur, assuming that the patient has not experienced hypertension, CRI, or UTI. These criteria are often met by 1 year of age, which would preclude repeated visits, uncomfortable investigations, and unnecessary costs.

A. Weinstein (✉) · S. Iragorri
Pediatric Nephrology, Yale University School of Medicine,
333 Cedar Street, 3105 LMP,
New Haven, CT 06520, USA
e-mail: adam.weinstein@yale.edu

T. R. Goodman
Pediatric Radiology, Yale New Haven Hospital,
New Haven, CT, USA

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Introduction

Multicystic dysplastic kidney (MCDK) disease is an increasingly recognized diagnosis, with an estimated rate of 1 in 4,000 live births [1]. Classically, it was identified during the workup of a neonatal abdominal mass. Currently, improved imaging techniques and the evolution of routine prenatal ultrasonography have resulted in more frequent asymptomatic and otherwise incidental prenatal diagnosis [1, 2]. This has led to new challenges for pediatric nephrologists and urologists with respect to its ideal management and follow-up. MCDK is believed to be due to abnormal branching of the ureteric bud into the metanephric mesenchyme during kidney development [3, 4]. This results in a cystic mass, without normal renal appearance or function, often resembling a bunch of grapes [4].

In the past, standard management included nephrectomy of the involved kidney due to concerns for hypertension, infection, and malignant degeneration [5–7]. However, recent experience demonstrates spontaneous involution of the dysplastic kidney, compensatory hypertrophy of the unaffected kidney, and an overall excellent prognosis with a very low incidence of complications [2, 6, 8–12]. Although hypertension and malignancy are rare and infection is infrequent, their true risk remains undefined. A systematic literature review of 1,115 patients with MCDK disease suggests that the risk for hypertension may be no greater than that of the general pediatric population [11]. Furthermore, concerns for potential malignant degeneration are not supported by the many more current reviews, including a

systematic review that included 1,041 eligible patients. No cases of Wilms tumor or renal malignancy were identified in these cohorts [10, 12, 13].

Feldenberg and Siegel divided MCDK into simple [unilateral MCDK with no other associated genitourinary (GU) abnormalities] and complex forms. They found that patients with complex MCDK (defined as either unilateral MCDK with other GU anomalies or bilateral MCDK with or without other GU anomalies) had a higher incidence of urinary tract infections (UTI) and chronic renal insufficiency compared with those with simple MCDK. Simple MCDK had a favorable prognosis with respect to risk of hypertension, chronic renal insufficiency, and UTI—the latter irrespective of the presence or absence of vesicoureteral reflux (VUR) at the time of diagnosis [14]. A similar approach with respect to VUR was confirmed by Aslam and Watson in their analysis of MCDK disease. They concluded that a voiding cystourethrogram is an invasive and unnecessary procedure unless the contralateral unaffected kidney shows ultrasonographic abnormalities or the young patient develops a febrile UTI [12].

Nevertheless, the long-term management of patients with simple MCDK disease, particularly with regard to the frequency and duration of clinical and radiological follow-up, is yet to be defined. The purpose of this study was to establish recommendations in terms of discharge criteria from subspecialty follow-up and diagnostic investigations for simple MCDK disease. We aimed to determine a safe and effective follow-up regimen, which continues to emphasize the early detection of potential complications, such as renal insufficiency, UTI, hypertension, or malignancy, while minimizing repeated and uncomfortable investigations, health care costs, and missed days from school and work.

Methods

Patients were identified via a retrospective analysis from the Yale New Haven Hospital radiology information system. This data search included all radiology reports containing the words “multicystic dysplastic kidney” or the initials “MCDK” from January 1996 to June 2006. Patients diagnosed with MCDK were identified from these records, and their imaging diagnosis was confirmed by an attending pediatric radiologist. The diagnosis of MCDK was made based on the established ultrasound criteria: multiple cysts of various sizes, without communication, and without normal renal parenchyma [14]. Only those patients with simple MCDK as defined above were included. Any patient with other cystic diseases of the kidney, such as polycystic kidney disease, renal dysplasia with cysts, nephronophthisis, or medullary cystic disease, and those with complex MCDK, as defined by Feldenberg and Siegel, were excluded. As in their study, VUR was not included in the definition of associated abnormalities [14].

Eighty patients qualified for the study. Clinical data was obtained from charts from the Yale Pediatric Nephrology office records and/or Yale Pediatric Urology records. A retrospective review was conducted using clinical charts and laboratory data from these records to determine whether any complications, in particular high blood pressure, proteinuria, renal insufficiency, or UTI, ensued despite appropriate compensatory hypertrophy (≥95th percentile) of the contralateral kidney by the age of 1 year and/or at the most recent follow-up visit. We also recorded the incidence and degree of involution of the dysplastic kidney by 1 year of age and at the most recent follow-up visit. Sixty-six out of the 80 patients in the study had ultrasounds at approximately 1 year of age (range 6–18 months). Coincidentally, 66 also had ultrasounds beyond 18 months of age, up to 15 years (some of the original 66 were not followed beyond 18 months; conversely, others were referred to us after they were 2 years or older). Contralateral kidney size percentile was determined using the published standard pediatric kidney growth curves used by the Yale Pediatric Radiology department [15].

Of the 80 patients included in the analysis, 31 had blood pressure measurements followed to 1 year of age, whereas 34 had blood pressure follow-up beyond 1 year in the pediatric nephrology clinic. Blood pressure percentiles were determined using the tables presented by the 2004 Pediatric High Blood Pressure Working Group [16]. Data for proteinuria was available on 29 patients. Glomerular filtration rate (GFR) was estimated using the Schwartz formula [17]. Data for such calculations was available on 24 of the patients at approximately 1 year (range 6–18 months) and 23 patients on further follow-up. We assessed clinical and laboratory records on all 80 patients during their respective periods of follow-up to determine the incidence of UTI via urine culture. No patients were contacted, and all data was obtained by direct review of our clinical charts and laboratory and radiological records. Prior to initiating the study, permission was obtained from the Human Investigation Committee at Yale University School of Medicine.

Results

The demographic characteristics of our 80 patient samples are displayed in Table 1. The mean follow-up was 5.3 years, and the median follow-up was 3.9 (range 0.25–15.3) years. Notably, more than 85% of our patients were followed for at least 1 year. There was no clear increased prevalence in gender, 53% boys and 47% girls, but as has been previously reported in the MCDK literature, the left kidney

Table 1 Characteristics of simple multicystic dysplastic kidney (MCDK) patients

Total patients	$n=80$
Follow-up (years)	
Mean	5.3
Median	3.9
Range	0.25–15.3[a]
Gender	53% boys; 47% girls
Affected kidney	42% right MCDK; 58% left MCDK

[a] > 85% followed for 1 year or more

was more commonly affected than the right, 58% vs 42%, in our patient sample [2, 8].

As demonstrated in Fig. 1, all of our patients with simple MCDK had a contralateral kidney that was at least at the 50th percentile for age (and length/height, if available) as early as 1 year of age. Remarkably, at 1 year, 59 (89.4%) of 66 patients had contralateral kidneys that were at least "approaching" the 95th percentile, defined as being well above the 50th percentile but not quite at the 95th percentile. Thirty-nine (59.1%) of these patients had unaffected kidneys that were at or larger than the 95th percentile. Beyond 1 year, 65 (98.5%) of the contralateral kidneys at least approached the 95th percentile, with 53 (80.3%) of these at or larger than the 95th percentile. Once a patient's unaffected kidney approached or reached the 95th percentile, there were no cases in which it regressed in size or percentile.

Regarding dysplastic kidneys (Fig. 2), 11 of the 66 (16.7%) MCDKs assessed at our 1-year time point had already disappeared, and an additional 36 (54.5%) had begun to involute. Ultimately, we were able to assess dysplastic kidney regression on 77 of our 80 patients (one patient had their MCDK nephrectomized prior to referral to our clinic; two others only had a single ultrasound, so no comparison was available). On latest follow-up, 35 (45.4%) MCDKs had completely involuted, and 34 (44.2%) had begun involuting. Only eight (10.4%) were stable in size. None were enlarging. Notably, when analyzing the subgroup of 39 patients whose unaffected kidneys were greater than the 95th percentile by the 1-year time point, they demonstrated an increased tendency toward disappearance or involution than did the entire population (see Fig. 2).

Similarly, we revealed reassuring trends in evaluating the subgroup of patients whom we followed for 6.5 years or more (see Figs. 1 and 2). With respect to their contralateral kidneys, 26 (92.9%) of 28 reached the 95th percentile. Of their dysplastic kidneys, one was removed by nephrectomy (the same one as noted above), 15 (55.6%) had disappeared, nine (33.3%) were involuting, and three (11.1%) were stable in size. Interestingly, with regards to 13 patients whom we followed for at least 10 years, all of their contralateral kidneys hypertrophied, and all but one of their MCDKs were either no longer visualized (66.7%) or were involuting (25%); one had been removed.

Our simple MCDK patients' outcomes with respect to many of the potential complications thought to be associated with MCDK are shown in Table 2. First, there were no MCDK or renal-associated malignancies in our population.

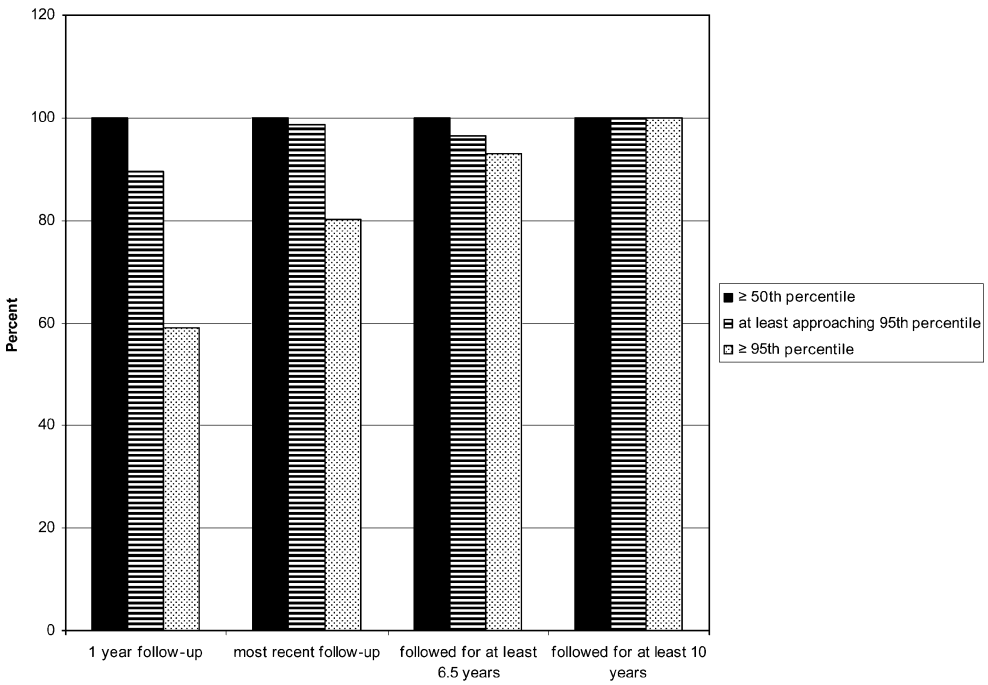

Fig. 1 Measurement of contralateral kidney hypertrophy by renal ultrasound

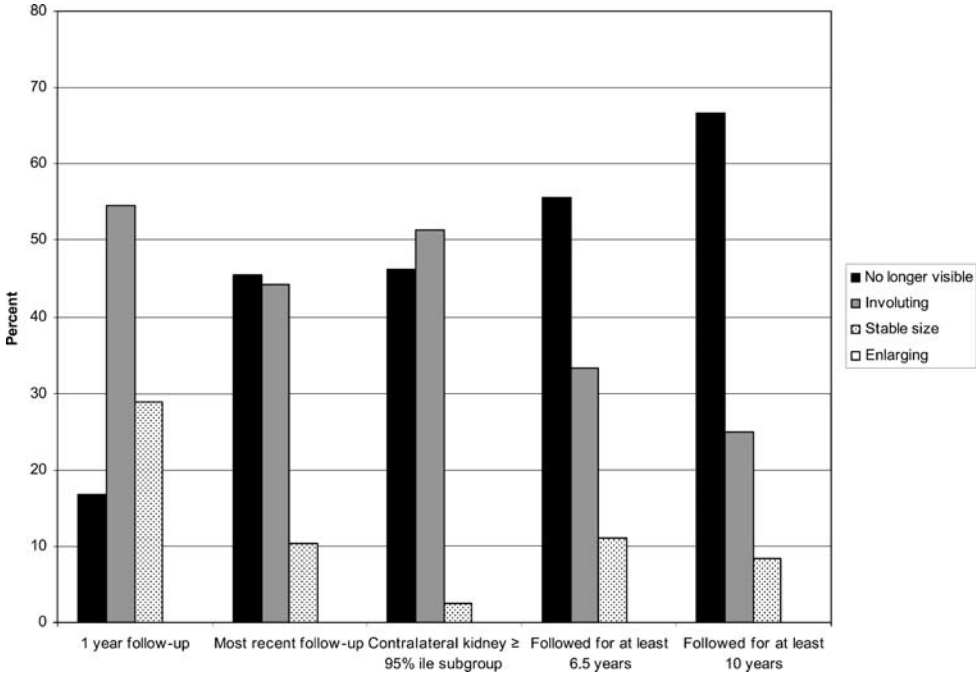

Fig. 2 Multicystic dysplastic kidney (MCDK) involution by renal ultrasound

As noted above, a single patient had a nephrectomy. This was done "per protocol" at an outside center prior to referral to our clinic. She had no documented clinical symptoms or complications prior to the surgery.

Next, none of our patients were identified as having high blood pressure. All 31 with blood pressure records at 1 year and all 34 with blood pressure records beyond that time had blood pressures below the 95th percentile for age, height, and gender. Similarly, our patients with simple MCDK had excellent outcomes with respect to kidney function based on estimated glomerular filtration rate (eGFR) [17]. In all patients in whom we were able to assess eGFRs, it was > 80% of what would be expected had they had two normal functioning kidneys. At the 1-year follow-up, the average eGFR was 84.3 ml/min per 1.73 m^2, which is within the normal range for otherwise healthy 1-year-olds. Notably, the only three patients who had eGFRs < 70 at this time point were between 6 and 8 months old. Given their younger ages, these eGFRs wre similarly at least 80% of the normal value [18]. It is worth mentioning that all three of these patients had contralateral kidneys approaching the 95th percentile at this time point. At the most recent follow-up, our tested population's mean eGFR continued to be > 80% of the expected rate. Of significance, only four patients had eGFRs < 90. Even so, these were still > 80% of their expected rate based on age and gender. In all four, their contralateral kidneys were, at a minimum, approaching the 95th percentile. Two were at or above the 95th percentile. Furthermore, as of last follow-up, none of the 29 patients examined with urinalysis demonstrated proteinuria.

Lastly, four (5%) of our 80 patients had documented UTIs during the follow-up period. None of these patients had recurrent UTIs, and only one had documented VUR. Three were girls, who had their UTIs at age 1 month, 18 months, and 14 years, respectively. The other was a boy who was circumcised and was 21 months old at the time of the UTI. Three of four had contralateral kidneys that were at or larger than the 95th percentile as of last follow-up; the

Table 2 Outcomes of patients with simple multicystic dysplastic kidney (MCDK)

	1-year follow-up	Most recent follow-up
Blood pressure ≥ 95% for age, gender, and height	0/31 (0%)	0/34 (0%)
eGFR ≥ 80% for age and gender	24/24 (100%)	23/23 (100%)
Average eGFR	84.3	108.9
Range of eGFR	48.6–126[a]	73–158[b]
Proteinuria > 1+ on urinalysis		0/29 (0%)
UTI		4/80 (5.0%)
Recurrent UTI		0/4 (0%)

eGFR estimated glomerular filtration rate, *UTI* urinary tract infection
[a] All but three > 70, and those three were 6–8 months old [b] all but four > 90

fourth was approaching the 95th percentile. Likewise, three of four affected kidneys had disappeared; the fourth was involuting after 2 years of follow-up. These patients have been followed for 2, 4, 11 (boy), and 14 years.

Discussion

For the past few decades, the natural history of simple MCDK disease has demonstrated an extremely favorable prognosis [2, 6–14]. Our findings in this review of 80 patients with simple MCDK are consistent with these reports. With respect to contralateral kidney growth and function, we found that the large majority of unaffected kidneys developed compensatory hypertrophy, with all at least larger than the 50th percentile. Remarkably, more than half (59.1%) had already developed 95th percentile hypertrophy by the 1-year time point, and nearly 90% were at least approaching this level of hypertrophy. Likewise, all had normal renal function for age despite having only one functional kidney. This illustrates that effective compensatory growth and function of the unaffected kidney is often established within the first year of life. These results are reassuring that with adequate growth of the normal kidney, simple MCDK patients have a favorable prognosis with respect to kidney function.

Malignant potential represents a major concern regarding the persistent ultrasonographic identification of the cystic kidney. In our series, dysplastic kidney regression demonstrated similar trends to previously reported cohorts [2, 6, 8, 10, 12]. Of note, in those whose contralateral kidneys had already reached the 95th percentile at 1 year, all but one affected kidney has either involuted or had begun involution. A clear association between MCDK disease and renal malignancy has not been established. Given the low incidence of such malignancies in childhood, an extremely large cohort of MCDK patients would need to be recruited and observed to determine the true incidence of renal malignancy in MCDK patients and to evaluate whether these patients appear to be at increased risk [12, 13]. Despite the unclear risk, most experts feel that once the cystic kidney has either begun or completed involution, this potential complication becomes much less of a concern. Our study suggests that simple MCDK patients have excellent outcomes in this regard, especially those individuals who demonstrate early contralateral hypertrophy.

No one in our simple MCDK cohort developed hypertension. This is consistent with other similar cohorts in which few or no patients developed high blood pressure during their childhood follow-up [11]. The infrequency of childhood hypertension in this population compared with the general pediatric population would suggest that if it is not identified by the time the MCDK begins to involute and the contralateral kidney hypertrophies, then routine blood pressure monitoring at general pediatric well child care should be sufficient.

Additionally, as of our last follow-up, no patient demonstrated proteinuria. This result is reassuring, as it suggests that our simple MCDK patients' good compensating kidney was not affected by hyperfiltration injury. Nevertheless, our patients have only been followed, on average, for just over 5 years, and such injury may not become apparent until later.

Only 5% of our patients developed a UTI. This rate is consistent with the general pediatric incidence of UTI in an otherwise healthy population [19]. Few retrospective or prospective studies have separated simple MCDK from more complex forms of the disease, which carry an increased risk for UTI [14]. Our data supports the conclusion that patients with simple MCDK disease are not at the same risk for contralateral kidney or GU tract infection to the same extent that complex MCDK patients are and suggests this risk may be no higher than that of an otherwise healthy child.

This study has a number of limitations. Due to its retrospective nature, the specific management and follow-up of our patient sample was not consistent. Some patients were followed by pediatric nephrology, others by pediatric urology, and others by both services. Depending on which service took care of the patient and when, they may have had repeat ultrasounds, serum creatinines, and/or blood pressures measured at different times. This variation, in addition to new patient referrals after 18 months of age, explains why only 66 of our 80 patients had ultrasounds at the 1-year time point, even though 71 were followed beyond 1 year of age and all but three beyond 6 months. Similarly, this variation explains why only certain patients from our sample had documented blood pressures and serum creatinines measured.

Another limitation is in respect to length of follow-up. We study a pediatric-aged population, similar to previous reviews and cohorts. Hypertension, proteinuria, renal insufficiency, and even malignant transformation may not occur for many years. A future study that identifies and follows simple MCDK patients well into adulthood would be important to clearly determine whether these patients are at increased risk for these and/or other complications as adults.

Due to the small sample size, it is difficult to ascertain whether a subset of patients—for example, those whose unaffected kidneys never reached the 95th percentile—were more at risk for a particular complication. Nevertheless, it is clear from the trends of our study that pediatric patients with simple MCDK disease whose contralateral kidneys demonstrated substantial hypertrophy are at extremely low or no risk compared with otherwise healthy children for any of these complications.

Our findings support previous reports that the clinical course and prognosis for patients with simple MCDK is excellent. After confirmation of the diagnosis of simple MCDK, we would suggest periodic follow-up visits at 6 months, 1 year, and then yearly to carefully monitor for the potential clinical complications discussed above. Ultrasounds could be repeated at 1 year, 2 years, and then every subsequent 2 or 3 years to assess for MCDK involution and contralateral growth. Provided there are no signs of renal insufficiency, proteinuria, or hypertension and the patient has been free from UTIs, once the contralateral kidney has reached or grown beyond the 95th percentile and the affected kidney has begun or completed involution, routine subspecialty and radiologic follow-up would no longer be necessary. The general pediatric provider, however, should continue to screen for high blood pressure and proteinuria as well as plot growth and development at yearly well-child visits. When indicated, the provider should have a high index of suspicion to test for UTI. Likewise, such periodic well visits and screenings should continue through adulthood due to the potential long-term consequences from reduced nephron number.

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