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Multicystic dysplastic kidney – treat each case on its merits☆,☆☆

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ABSTRACT

Objectives: To assess outcomes of unilateral multicystic dysplastic kidney (MCDK) managed at an Australasian centre over a 15 year period. To assess if MCDK involution could be predicted based on change noted between first two postnatal ultrasound scans 6 months apart.
Subjects and Methods: A retrospective study was performed.
Results: One-hundred-and-six cases of unilateral MCDK were studied. Eighty-four of these presented antenatally. Twenty-two MCDK cases presented postnatally.
Urological anomalies associated with MCDK included vesicoureteric reflux (VUR), ureterocele and contralateral pelviureteric junction obstruction (PUJO). Children undergoing surgical intervention for these anomalies were offered concurrent MCDK nephrectomy. Morbidity associated with MCDK under surveillance included febrile culture-positive urinary tract infection in 20 cases (20.7%), hypertension in four (3.7%) and Wilms' tumor in one (0.9%). Thirty-six cases (34%) underwent complete involution, 32 (30.2%) were in the process of involuting and 38 cases (35.8%) underwent nephrectomy because of failure of involution or associated morbidity.
If the MCDK reduced in cranio-caudal interpolar length by 20% or more between the first postnatal USS and the next one 6 months later, then it was very likely to involute spontaneously. If the MCDK did not reduce in cranio-caudal interpolar length by 20% between the first postnatal scan and the next one 6 months later, then it was highly likely to fail to involute, and in our study, correlated with the outcome of nephrectomy.
Conclusion: Although MCDK is a benign condition, it should be carefully investigated and followed-up, as involution may not occur in over a third. In some cases, morbidity may occur. Each case of MCDK should be managed on its own merits.
Level of Evidence: Level II – Prognosis study, Retrospective.

Multicystic dysplastic kidney (MCDK) is characterized by non-communicating renal cysts and the absence of a functioning pyeloureteral system. The incidence of MCDK is estimated to be one in 1000–4300 live births [1].

1. Objectives

We aimed to review the management and outcome of all cases of MCDK managed at our institution over a 15-year period. We aimed to determine if future involution could be predicted based on MCDK cranio-caudal length changes on early postnatal scans.

2. Methods

A retrospective study was performed of all cases of MCDK managed at our institution from January 1, 2001, to December 31, 2015. Institutional approval was obtained (GEKO 9981). Medical records of all MCDK cases managed at our institution, the only tertiary level pediatric hospital serving the population of an entire state, were reviewed, with no exclusions, with follow-up data of all cases current until June 2018 (follow-up range 2.5–17.5 years).

Baseline demographic data included antenatal and postnatal renal ultrasound (USS) information, postnatal micturating cystourethrogram (MCU) and nuclear imaging data (Mag 3 or DMSA scan). Data was collected into an SPSS data spreadsheet. All analyses were performed with SPSS 22 software.

The chi-squared test was used for bivariate analyses, specifically to calculate the ability to predict future spontaneous involution of MCDK. Statistical significance was defined as $p < 0.05$.

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3. Results

There were 106 cases of MCDK in our cohort (Table 1), of which two (1.8%) were segmental upper pole MCDK in a duplex.

3.1. Antenatal presentation

Eighty-six cases were antenatally suspected to have unilateral MCDK. The commonest gestational age at first detection of possible MCDK was 20–24 weeks (23%), with suspicion of MCDK in some cases as early as 13 weeks of gestation. Of the 86 cases, three were found to have function within the affected kidney on postnatal imaging. These three cases are examined in brief detail in our discussion, as they raise an important point about postnatally confirming antenatally suspected MCDK. Of these three cases, two were excluded from further study as they were found not to be MCDK. The third was found to be a segmental upper pole MCDK with a functioning lower moiety undetected on antenatal or postnatal USS. This case was included in the 84 cases (79.3%) that were confirmed to be antenatally detected MCDK and studied in our series.

3.2. Postnatal presentation

Twenty-two cases (20.7%) presented postnatally. Of these 22, 13 had normal antenatal scans at 18–20 weeks of gestation. In nine cases presenting postnatally, antenatal scan information was unavailable.

All 106 cases had characteristic appearances of MCDK on postnatal USS, and were confirmed to have no ipsilateral function on nuclear imaging.

The average maximal cranial to caudal interpolar length of MCDK on the initial postnatal scan was 43 mm (range 13–110 mm).

Ipsilateral vesicoureteric reflux (VUR) was detected in 9 cases (8.4%), all grade I. Contralateral VUR was detected in 4 cases and was dilating VUR in all cases (Grade III–V). There were five ipsilateral ureteroceles and one contralateral ureterocele, all over 1 cm in maximal diameter. The most common contralateral renal tract anomaly was pelviureteric junction obstruction (PUJO) in 6 cases (5.6%) (Table 1).

Associated MCDK morbidity occurred in 25 cases (23.5%) overall (Table 2). Febrile urinary tract infection (UTI), temperature 38 °C or higher and culture-positive, occurred in 20 cases (20.7%). Sixteen of the 20 cases (75%) had ipsilateral or contralateral anomalies that are known risk factors for UTI, such as VUR in 6 cases (37%) or ureterocele in 4 cases (25%). The remaining fFour had no known associated UTI risk factors. Six children with febrile UTI (30%) were admitted for intravenous antibiotics; the rest were treated with oral antibiotics. The commonest culture-positive UTI was *E. coli* in 7 (35%).

Table 1
Demographics.

Variables		
Gender	Males = 63 (59.4%)	Females = 43 (40.5%)
Site	Right = 51 (48.1%)	Left = 55 (51.8%)
Antenatal diagnosis	Yes = 84 (79.2%)	No = 22 (20.7%)
Mean MCDK cranio-caudal length	43 mm	Range (13–110 mm)
Mean max dominant cyst diameter	17 mm	Range (2–70 mm)
Ipsilateral renal anomalies		
	VUR	9 (8.4%)
	Ureterocele	5 (4.7%)
	Renal Duplication	2 (1.8%)
Contralateral renal anomalies		
	PUJO	6 (5.6%)
	VUR	4 (3.7%)
	Ureterocele	1 (0.94%)
Grades of VUR		
Ipsilateral (09)	Grade 1–3: 9	Grade 4–5: 0
Contralateral (04)	Grade 1–3: 1	Grade 4–5: 3

Table 2
Morbidity Associated with MCDK.

Morbidity	%	Had nephrectomy
UTI	20 (18.8%)	09 (45%)
Hypertension	04 (3.7%)	02 (50%)
Wilms tumor	01 (0.94%)	01 (100%)

Hypertension (HTN) was recorded in four cases of MCDK (3.7%). Median blood pressure in this group was 142/75 mmHg. Three (75%) had a normal contralateral kidney on imaging, and one (25%) had a primary megaureter in the contralateral kidney. All four were on medication, including propranolol and captopril. Two were successfully managed medically, but the hypertension remained difficult to manage in the other two. They were referred by pediatric nephrology for MCDK nephrectomy.

One child developed Wilms' tumor in the involuting MCDK. He was undergoing surveillance for an antenatally-detected right MCDK, with annual USS, by the pediatric nephrologists. Surveillance USS at age 29 months showed a 7 cm solid soft tissue mass in the right renal bed (Fig. 4). The child had no symptoms and was normotensive. He underwent open radical nephrectomy as per Children's Oncology Group (COG) protocols. Histopathology confirmed blastematous triphasic nephroblastoma with favorable histology, with peripheral residual MCDK tissue compressed by the tumor. (Fig. 4). The child completed post-surgical chemotherapy for Stage 2 Wilms' as per COG protocols, and remains recurrence-free.

Sixty-eight cases (64.2%) showed signs of complete (34%) or on-going (30.2%) MCDK involution during the study and follow-up period. Thirty-eight cases (35.8%) ultimately underwent nephrectomy. Median age at MCDK nephrectomy was 25 months (range 1 month–79 months).

Indications for MCDK nephrectomy in this series included failure of involution of MCDK in 15 (39.5%); concurrent with surgery for ureterocele or contralateral dilating VUR in 10 (26.3%), of whom 5 had already had a previous febrile UTI; concurrent with surgery for associated contralateral PUJO in 6 (15.8%); and recurrent UTI with no other urological anomaly in 4 (10.5%). Two cases (5.2%) were referred for nephrectomy for HTN persisting despite medical management, of whom, blood pressure normalized post-nephrectomy in one case.

Out of 38 (35.8%) who underwent nephrectomy, 12 were by open technique. Twenty-six were by laparoscopic approach, 17 transperitoneal and nine retroperitoneal. Chosen surgical technique was dependent upon the operating surgeon's training and preference. No post-operative complications were recorded in our series.

In this series, children with MCDK underwent an average of 4 (range 1–9) prenatal USS per patient. Postnatally, children whose MCDK spontaneously involuted completely had a median six ultrasound scans (range 1–15). Mean age at final USS in this group was 23 months (range 3–65 months). Those who eventually underwent nephrectomy had median seven ultrasound scans (range 2–12) during MCDK surveillance. Each of these scans was followed by an outpatient clinic appointment for clinical review.

It was routine protocol for the pediatric urologists to arrange the second post-natal surveillance USS 6 months after the initial postnatal USS. Seventy-two of the 106 MCDK cases (67.9%) had their second postnatal scan 6 months after the first postnatal scan. We reviewed these 72 cases, and measured change in the cranio-caudal pole to pole maximal MCDK length between the initial two postnatal USS done 6 months apart. Statistical analysis showed that we could reliably predict future likelihood of MCDK involution based on these two USS. If there was more than 20% reduction in cranio-caudal MCDK length between the two scans, we could reliably predict that the MCDK would involute ($p = 0.0003$). If there

Table 3
Predicting MCDK outcome.

MCDK cranio-caudal length reduction of >20% at 6 months after initial postnatal ultrasound leads to natural involution (N = 72)				
		Involution	*No Involution*	p Value
MCDK length Stable/Increase		08	27	<0.003
MCDK length Decrease >20%		24	13	
Total	72	32	40	

MCDK cranio-caudal length reduction of < 20% at 6 months after initial postnatal ultrasound correlates with outcome of Nephrectomy (N = 72)				
		Nephrectomy	*No nephrectomy*	p Value
<20% length Decrease		20	14	<0.01
>20% length Decrease		01	37	
Total	72	21	51	

was less than 20% reduction in cranio-caudal MCDK length between the two scans, then the MCDK was unlikely to involute, and in our series, correlated with outcome of nephrectomy ($p < 0.01$) (Table 3).

4. Discussion

Majority of MCDK are now suspected on antenatal scans, but there is a rate of misdiagnosis, and the diagnosis may change postnatally [2]. There are publications questioning the value of nuclear imaging to confirm lack of function in the MCDK, given the characteristic appearance of the MCDK on USS [1]. Whilst ultrasound appearances alone are generally characteristic and likely to be correct, caution is advised. We describe 3 out of 86 cases (3.5%) of antenatally suspected MCDK that had good renal function worth preserving. Two were excluded from our cohort as they were not MCDK - one had a severe pelviureteric junction obstruction (PUJO) with 49% ipsilateral split function on Mag3 and underwent pyeloplasty (Fig. 1). The second case had a dysplastic, dilated duplex kidney, with cystic change in both moieties. Mag3 afforded 25% split function to the dysplastic kidney, spread between both moieties (Fig. 2). The upper moiety ureter was ectopic, so conjoined ureteric reimplantation was performed. The third case was included in our cohort as a segmental MCDK. A large 5 cm cystic dysplastic upper pole of a duplex masked a functioning lower moiety with 54% split renal function. The functioning lower moiety was undetected on either antenatal or postnatal USS. This functioning moiety was noted on Mag3, and confirmed on MRI (Fig. 3). In all these cases, postnatal nuclear imaging guided renal preservation and avoided erroneous assumption that the kidney was non-functioning.

In this series, we performed an MCU routinely as work-up for MCDK. Some centres recommend selective use of MCU in the initial assessment of children with MCDK [3]. We consider an early MCU to be important to obtain good baseline information about co-existing anomalies such as VUR, and to facilitate timely and informed medical decision-making to manage the solitary functioning kidney [4].

For all 106 confirmed MCDK cases, USS surveillance was commenced. Our centre follows the general consensus of conservative management and surveillance of MCDK, to allow spontaneous involution to occur and to monitor the single functioning kidney. However, it is well known that not all MCDK will involute. The rate of MCDK involution is usually greatest during the first 2 years of life [5]. A recent large study showed that even at 10 years follow up, 59% of MCDK had involuted but the rest had not [6]. Another study showed the probability of MCDK involution to be 53.5% by 10 years [7]. Guidelines about how often to monitor with USS, how long to monitor for and the indications for surgical intervention with MCDK nephrectomy are not concise and can vary between centres, as well as between specialties.

This study documented multiple ipsilateral and contralateral renal tract abnormalities associated with MCDK. VUR was the most common associated abnormality in our study, occurring in nine (8.4%) ipsilateral (all Grade 1) and four (3.7%) contralateral (all Grade V) renal units. The association between VUR and MCDK is known in the literature [8].

Ipsilateral large ureterocele in the bladder, a lower urinary tract anomaly that is known to be associated with MCDK [9], was seen in five cases (4.7%). Our clinical experience and data from the literature would support that ureterocele is a known risk factor for UTI [10]. Large ureteroceles may also result in mechanical problems like prolapse or bladder outflow obstruction. Some centres advocate for endoscopic puncture of ureteroceles as a possible definitive long term treatment, but note a significant number of patients still require secondary surgery and have persistent UTI [11, 12]. In our centre, children with MCDK and

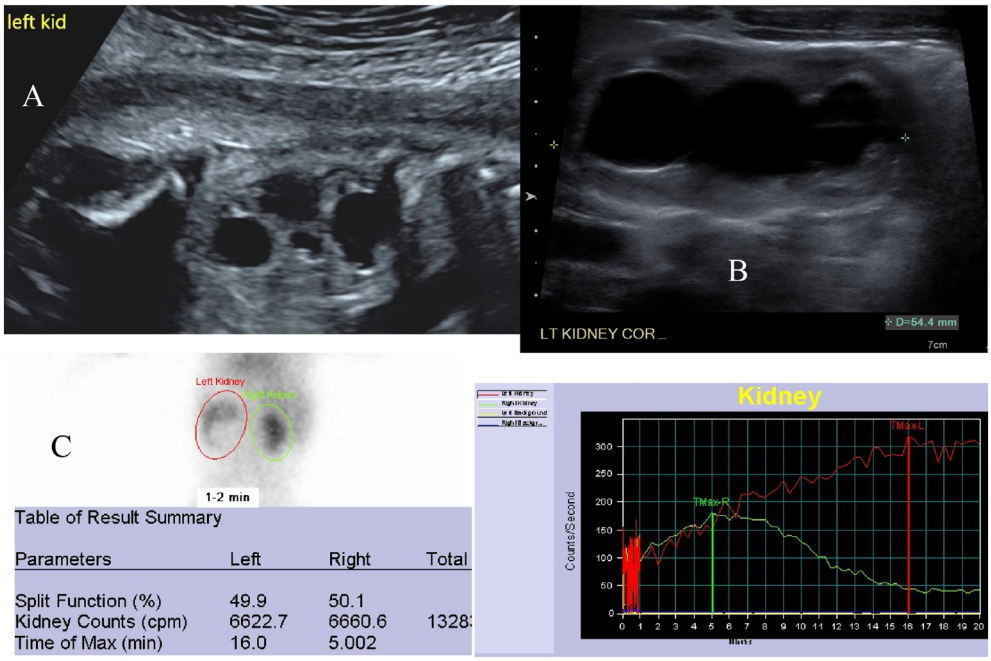


Fig. 1. Antenatally suspected left MCDK, postnatally left PUJO. A: Appearance of left kidney at 22 weeks of gestation on USS, reported as MCDK. B: Postnatal appearance of left kidney on USS highly suggestive of PUJO. C: Mag 3 scan shows preserved left kidney function but no drainage.

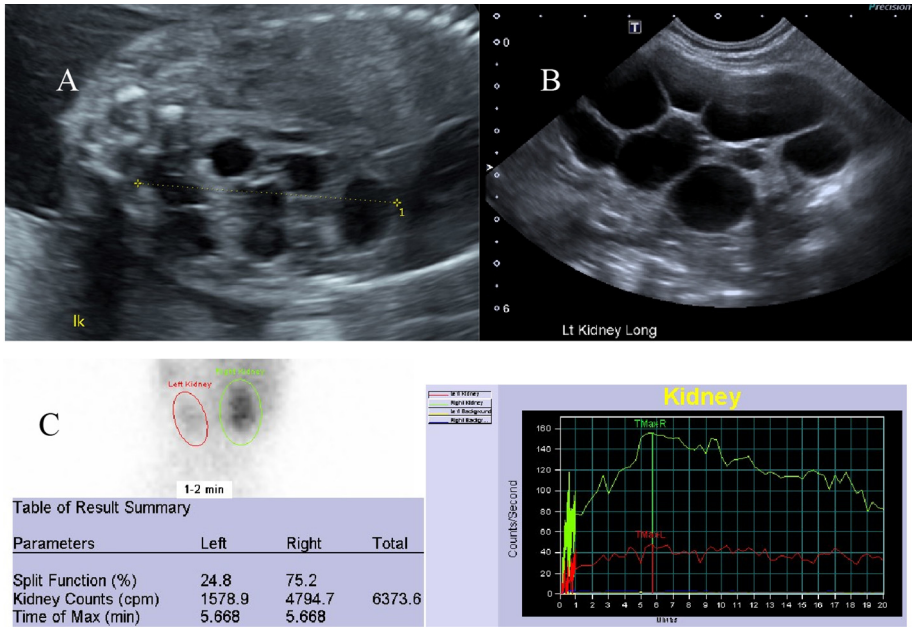


Fig. 2. Antenatally suspected left MCDK, postnatally duplex dilated left kidney with dysplasia but 25% split function. A: Antenatal left kidney appearance on USS at 32 weeks gestation. B: Postnatal USS appearance of left kidney. C: Mag 3 showing 25% split function in dilated dysplastic left kidney.

associated ureterocele are offered elective ureterocele excision by 6 months of age, due to the high risk of UTI posed by ureteroceles. If the MCDK is still present, then associated MCDK excision is offered concurrently.

PUJO was the commonest contralateral anomaly, occurring in six cases (5.6%). Literature reports of contralateral PUJO suggest this association occurs in 1.5–5% of children with MCDK [1]. In our centre, if the MCDK is still present at the time of pyeloplasty for the contralateral PUJO, elective MCDK nephrectomy is offered concurrently.

There were two cases of segmental MCDK affecting the upper pole of the duplex. Segmental MCDK comprises about 4% of MCDK reported in the literature and may involute spontaneously [13, 14].

Conservative management of MCDK with USS surveillance is currently standard practice and in a good majority, the MCDK will involute, and children will have no associated morbidity. There is, however, clear documentation that MCDK may be associated with morbidity of UTI, HTN and tumor formation, although rates and experiences vary [4, 15, 16].

UTI was the most common associated morbidity in our series. Literature-reported UTI rates associated with MCDK range from 15% to 20%, as in our series [15, 17]. Nine of 20 (45%) underwent subsequent MCDK nephrectomy for recurrent UTI. Most children with MCDK who had UTI had associated anomalies such as ureterocele and VUR, known risk factors for UTI. In four cases with UTI, there were no

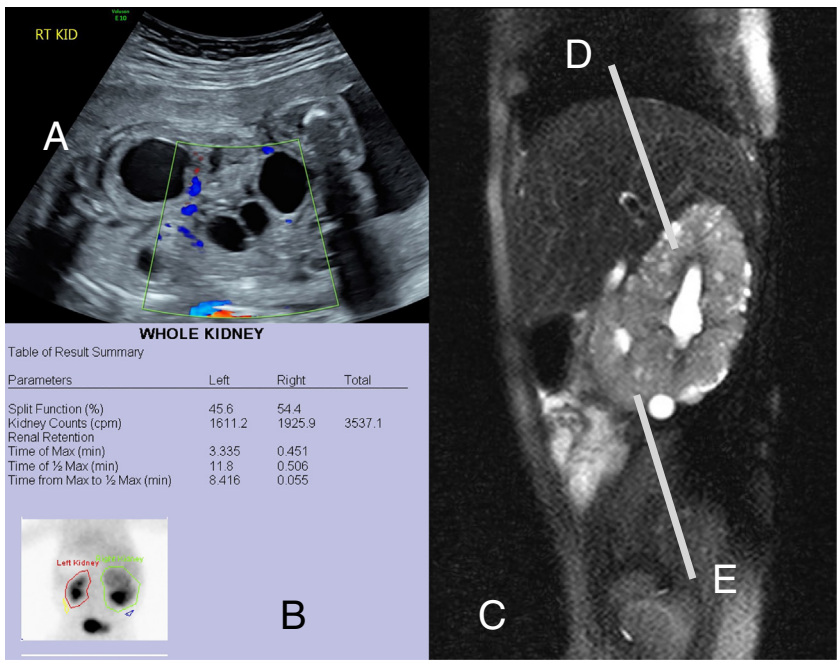


Fig. 3. Antenatally suspected large right MCDK, postnatally large upper moiety MCDK with hidden lower moiety with preserved function. A: Antenatal USS appearance of right suspected MCDK at 30 weeks gestation. B: Mag 3 shows previously undetected lower moiety with 54% split renal function. C: MRI confirms large upper moiety segmental MCDK (D) and small lower moiety with functioning parenchyma (E).

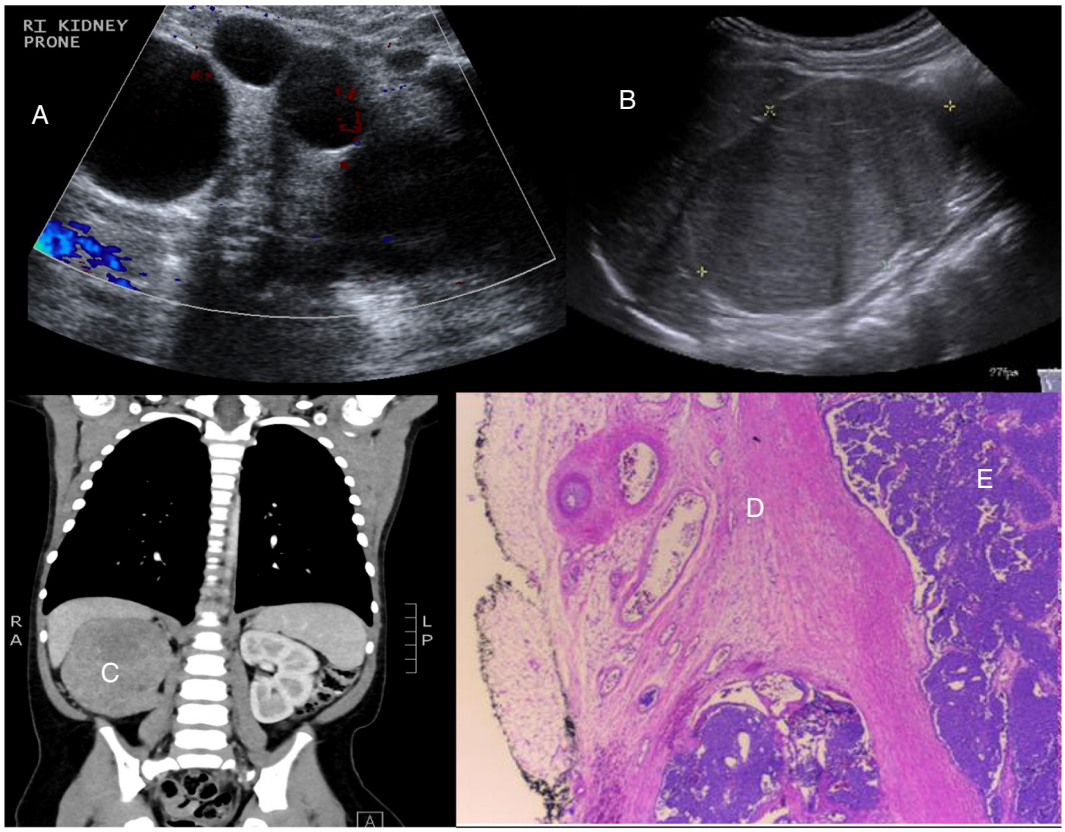


Fig. 4. Right Wilms' tumor in MCDK. A: Postnatal USS showing Right MCDK. B: USS at age 29 months showing 7 cm Right Wilms' tumor in place of MCDK C: CT showing Right Wilms' tumor. D: Histopathology - Cystic dysplastic renal tissue at tumor periphery showing fibro-connective tissue with scattered immature tubules, surrounded by collarettes of mesenchyme, and glomeruli with sclerosis. E: Histopathology - Blastematous triphasic Wilms' tumor tissue.

associated renal or bladder anomalies. These children were suspected to have an infection within the MCDK. Histopathology on the excised MCDK in these cases showed acute on chronic inflammation with cystic dysplastic renal parenchyma.

HTN was noted in four cases (3.7%) with MCDK (Table 2). Of these, two (50%) were managed satisfactorily with medication alone, but the other two were refractory to medical management and were referred for MCDK nephrectomy. One of the two had normalization of blood pressure post-surgery and required no further medication, but one remained hypertensive. The literature suggests that HTN is an uncommon but not rare association with MCDK, with a systematic review of over 3000 MCDK cases suggesting a 3.2% rate of HTN [16]. Definitions of hypertension are not standardized, making it difficult to estimate the true association. The etiology of HTN in MCDK is likely multifactorial, as a significant proportion but not all hypertension resolves after unilateral MCDK nephrectomy [1].

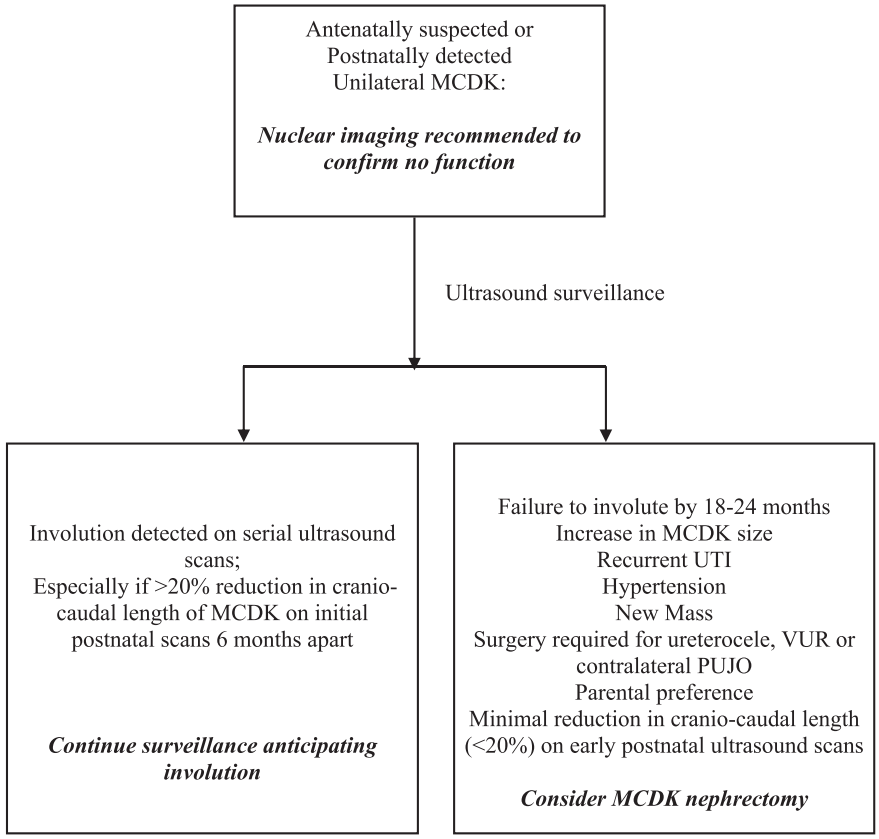
One child developed Wilms' tumor in an MCDK in our study. Although there are numerous published case reports of Wilms' in MCDK, systematic meta-analyses (which exclude case reports in their data analysis) report a rare risk of malignancy in MCDK, 0.07% in a recent paper [16]. The importance of serial USS surveillance of MCDK in picking up changes suggestive of solid tumor formation is highlighted. However, the ideal interval between USS during surveillance is unclear. One algorithm suggests performing an initial postnatal USS and one at 1 year with any further follow-up imaging guided by any abnormality of the contralateral kidney, abnormal blood pressure, or enlarging MCDK [7]. Lengthy periods between surveillance scans such as a year may miss the opportunity to detect neoplasms early. Whilst the risk of developing Wilms' in an MCDK may not be higher than in a healthy kidney; unlike the healthy kidney, the MCDK is not providing the child with a functional benefit, but poses a risk to the child. It would thus be reasonable to consider the option of early MCDK nephrectomy if families prefer it to taking the risks of morbidity during surveillance, even though these risks are low.

Management of asymptomatic MCDK, while generally conservative with USS surveillance, involves vigilance with regards to MCDK morbidity, and also the awareness that over one-third will fail to spontaneously involute [1]. In our centre, children with asymptomatic MCDK that are showing no evidence of involution on serial USS are offered elective MCDK nephrectomy by age 18–24 months. The literature suggests that early MCDK involution correlates with contralateral renal hypertrophy and better creatinine clearance in childhood [18]. There is a concern that a non-involuted MCDK may prevent contralateral renal growth through 'vascular steal', but these factors, including any association between hypertrophy and glomerular hyperfiltration in the long term, are not well understood [18].

There were no complications from MCDK nephrectomy recorded in our study and no blood transfusions required. Studies report an increasing tendency to offer minimally invasive surgery for MCDK nephrectomy, with high safety and low complication rates [19].

Conservative management of MCDK carries a significant cost and is associated with a degree of anxiety [20]. Each surveillance USS at our centre is estimated to cost 104 Australian dollars; add to this time out from families' lives and jobs to attend MCDK follow-up. Whilst the MCDK is present, in our experience, there is a tendency to focus on the abnormal kidney rather than routine surveillance of the functioning contralateral kidney. From a cost perspective, some studies recommend nephrectomy after a short period of surveillance [20]. It is important to note that medical surveillance of the health of the contralateral kidney remains recommended in the long term. At our centre, this occurs under the care of the pediatric nephrology team or the general

Table 4
Proposed MCDK management algorithm.



practitioner and usually involves an annual clinical review with urinalysis for proteinuria and blood pressure check.

The literature suggests that likelihood of MCDK involution correlates well with small initial length of MCDK [21, 22]. We assessed whether our data on early rate of involution could additionally help to reliably predict the cohort of MCDK that would eventually spontaneously involute. We assessed the cohort of 72 cases who had exactly 6 months between the initial and subsequent postnatal scans. We found that a reduction in the maximal cranio-caudal length of the MCDK >20% between the initial postnatal USS and the USS done 6 months later was highly predictive of ongoing future involution to completion (Table 3). Babies showing this degree of MCDK length reduction at 6 months can thus be serially monitored, and parents counseled that the MCDK is very likely to involute. The parents of children whose MCDK did not involute by 20% between the first postnatal scan and the scan 6 months later could be counseled accordingly and potentially offered the option of early elective MCDK nephrectomy, avoiding the cost and anxiety of MCDK surveillance, and the small risk of MCDK-associated morbidity. Increasingly, families have independent access to information about management options. Increasingly, there is an expectation of shared decision-making models of care, where families weigh up the pros and cons of available management options, for example conservative surveillance of MCDK versus early MCDK nephrectomy, before reaching an agreed treatment approach with the managing practitioner [23].

Children with morbidity such as contralateral high grade VUR with febrile UTI, contralateral PUJO requiring pyeloplasty, or ipsilateral associated ureterocele, may be offered MCDK excision at the time of ureteric reimplantation surgery, ureterocele puncture or excision, or pyeloplasty. We summarize a suggested simple algorithm for managing unilateral MCDK (Table 4).

Our study is useful as it captures the follow-up of MCDK based in a single tertiary pediatric hospital servicing the population of an entire state. The study has limitations. It is retrospective, with information collected from hospital records. There was some unavailability of antenatal data. We also acknowledge that the outcome of nephrectomy is to a degree an artificial outcome determined by parental and surgical decision making. Despite these constraints, we believe that this study provides valuable information about the outcome of MCDK.

5. Conclusion

MCDK lack of function should be objectively confirmed with early postnatal nuclear imaging to confirm antenatal suspicion. MCDK fails to involute in 30–40%; and may be associated with morbidity such as UTI, and less commonly HTN and tumor formation. We may be able to predict future involution or not based on the MCDK change in cranio-caudal length between the first postnatal scan and the next one 6 months later. If >20% reduction of maximal MCDK cranio-caudal length is noted within the first 6 months of postnatal life, involution is highly likely to occur and ongoing surveillance may be advised. Surgery for MCDK nephrectomy should be considered a safe elective option if the MCDK fails to involute; if there is associated morbidity; if families wish to avoid MCDK surveillance or the risks of morbidity; and may be offered concurrently if the child is undergoing associated urological surgery.

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