ORIGINAL ARTICLE

# Which Factors Influence Prognosis in Congenital Solitary Functioning Kidney?

Inês Ganhão[1], Catarina M. Lacerda[1], Tânia Carvalho[2], Telma Francisco[3], Raquel Santos[3], Gisela Neto[3], Ana Paula Serrão[3], Margarida Abranches[3]

Port J Pediatr 2020;51:25-32
DOI: https://doi.org/10.25754/pjp.2020.16420

## Abstract

**Introduction:** Premature, low birthweight, and small for gestational age newborns may have low nephron endowment at birth. When associated with solitary functioning kidney, especially if other congenital anomalies of kidney and urinary tract or urinary tract infections are present, it can negatively influence the prognosis. This study aims to identify factors that can influence renal outcome in children with congenital solitary functioning kidney.

**Methods:** Retrospective analysis including children with congenital solitary functioning kidney presented in a pediatric nephrology unit of a tertiary Portuguese center from 2012 to 2017. Renal injury defined as hypertension, albuminuria, moderately impaired glomerular filtration rate, and/or use of renoprotective medication.

**Results:** We identified 147 children with congenital solitary functioning kidney (62.7% with multicystic dysplasia), three quarters had prenatal diagnosis. Prematurity, low birthweight, small for gestational age, and other congenital anomalies of the remaining kidney/ipsilateral urinary tract were present in 14.3%, 13.6%, 19%, and 14.3%, respectively. Approximately half met the criteria for renal injury. A significant association was established between urinary tract infection and severely impaired estimated glomerular filtration rate ($p$ = 0.007) as well as between other congenital anomalies of kidney and urinary tract and hypertension ($p$ = 0.01), moderately impaired estimated glomerular filtration rate ($p$ = 0.01) and albuminuria ($p$ = 0.001). The only independent factor for renal injury was the presence of congenital anomalies in the remaining kidney/ipsilateral urinary tract (odds ratio 16.7, $p$ = 0.007). No significant association was found between perinatal factors and signs of renal injury.

**Discussion:** Congenital solitary functioning kidney is not a harmless condition, as described in recent decades, and early and lifelong follow-up is needed. Urinary tract infection and coexistence of other anomalies of the remaining kidney and/or ipsilateral urinary tract are related to worse outcome.

**Keywords:** Adolescent; Child; Kidney/abnormalities; Portugal; Prognosis; Solitary Kidney/congenital; Solitary Kidney/complications

## Introduction

Congenital anomalies of the kidney and urinary tract (CAKUT) represent up to 20%-30% of all major birth defects and are a main cause of morbidity and chronic kidney disease (CKD) in children and young adults.[1,2] One important condition in the spectrum of CAKUT is the congenital solitary functioning kidney (CSFK). Routine ultrasound screening of pregnant women has led to an increase in its detection before birth and it has a global prevalence of 1:1,300 live births.[3,4] Observational studies report male as well as left-side predominance. However, the reasons for this are not fully understood.[3,4] Congenital solitary functioning kidney may result from unilateral renal agenesis (URA) or multicystic dysplastic kidney (MCDK). Unilateral renal agenesis is defined as the congenital absence of renal parenchymal tissue and results from a major disruption of metanephric development at an early stage. It occurs in 1:2,000 to 1:3,000 live births.[4-6] Multiple factors are thought to be implicated in the pathogenesis of unilateral renal agenesis including mutations in important genes for the renal development, namely paired box (*PAX*) 2, formin and glial cell line-derived neurotrophic factor (*GDNF*) genes, and teratogenic and environmental agents, such as cocaine exposure.[1,6-8] In addition, some

1. Pediatrics Department, Barreiro-Montijo Hospital Center, Barreiro, Portugal
2. Pediatrics Department, Vila Franca de Xira Hospital, Vila Franca de Xira, Portugal
3. Pediatric Nephrology Unit, Dona Estefânia Hospital, Central Lisbon Hospital Center, Lisbon, Portugal
**Corresponding Author**
Inês Ganhão
https://orcid.org/0000-0002-4113-6604
inesieganhao@gmail.com
Centro Hospitalar Barreiro-Montijo, Avenida Movimento das Forças Armadas, 2834-003 Barreiro
Received: 09/01/2019 | Accepted: 03/09/2019 | Published: 02/01/2020

maternal factors, such as black race and preexisting diabetes mellitus, have been shown to be associated with unilateral renal agenesis.[9] Multicystic dysplastic kidney consists of numerous noncommunicating cysts separated by dysplastic tissue. There is typically no identifiable renal tissue. However, in some cases, some minimal functional renal tissue may exist. The cause of multicystic dysplastic kidney is unclear but there may be an underlying genetic predisposition, as demonstrated in some studies. A large cohort of children with CAKUT reported association of multicystic dysplastic kidney with mutations in the chromodomain-helicase-DNA-binding protein 1-like (*CHD1L*), roundabout guidance receptor 2 (*ROBO2*), hepatocyte nuclear factor 1β (*HNF1B*) and spalt like transcription factor 1 (*SALL1*) genes.[10] The incidence of multicystic dysplastic kidney ranges from 1:3,600 to 1:4,300 live births.[4,11,12] Most cases are unilateral, with the left kidney being more often affected. The exact mechanisms leading to this lateralization remain to be determined but may involve vascular development, differential gene expression, or susceptibility to environmental factors such as hypoxia.[13] In most cases, the involution of the multicystic dysplastic kidney can be demonstrated by serial renal ultrasounds.[14,15]

Although some authors, in recent decades, considered CSFK to be a harmless condition, in 2009 it was demonstrated that up to 50% of patients born with one kidney required dialysis by the age of 30 years old.[2,3,16] In patients with CSFK, the low nephron endowment will lead to compensation in the residual nephrons, resulting in hypertrophy and hyperfiltration. However, this adaptation may have adverse effects according to the hyperfiltration theory.[17,18] By reabsorbing more sodium and raising glomerular pressure, systemic blood pressure rises, and albuminuria may develop. This results in sclerosis of glomeruli, which may progress to end-stage renal disease.[19]

Moreover, other predisposing factors can compete for reduced nephron number and worsen the prognosis in the CSFK. Renal development is influenced by any insult disturbing the fine balance in the interactions that form the kidney. The most important factors influencing fetal development are malnutrition and uteroplacental insufficiency. This may result in intrauterine growth restriction that leads to a lower number of nephrons. Premature births and low birthweight (BW) can also disturb nephrogenesis and conduct to a nephron deficit as nephrogenesis ceases around 36$^{th}$ week of gestation.[19,20] The existence of ipsilateral CAKUT and history of urinary tract infection (UTI) in patients with CSFK may further influence clinical outcome.[21]

The purpose of this study is to assess which factors influence the renal outcome in pediatric patients with CSKF presented in a nephrology unit of a tertiary center between 2012 and 2017.

## Methods

### Study population, period, and design

Retrospective evaluation of medical records from all patients aged 0-18 years with CSFK followed at a tertiary nephrology center (Dona Estefânia Hospital, Central Lisbon University Hospital Center, Lisbon, Portugal), from January 1, 2012 to December 31, 2017. The minimum period of follow-up was one year.

Congenital solitary functioning kidney was defined as the unilateral absence of a functioning kidney due to agenesis or multicystic dysplasia, diagnosed by ultrasound and confirmed by dimercaptosuccinic acid (DMSA) renal scintigraphy.

### Variables and definitions

Data concerning gestational and birth history, etiology of CSFK, presence of other CAKUT (such as pelviureteric junction obstruction or vesicoureteral reflux), malformation of another organs, comorbidities, and renal function were collected.

Blood pressure was measured in the right arm with automated oscillometer devices using an appropriately sized cuff and the average of three measurements was made. Hypertension was defined as the average clinical measured systolic and/or diastolic blood pressure ≥ 95$^{th}$ percentile (based on age, sex, and height percentiles).[22]

Albuminuria was defined using the KDIGO terminology as albuminuria/creatinine in urine ratio > 30 µg/mg confirmed in three samples of the first morning void.

Estimated glomerular filtration rate (eGFR) was calculated using the bedside Schwartz equation revised in 2009[23]:

eGFR = 0.413 x height (cm)/serum creatinine (mg/dL)

For children over 2 years old, eGFR was[23]:

- Moderately impaired eGFR: eGFR 60-89 mL/min/1.73 m$^2$ (CKD stage 2);
- Significantly impaired eGFR: eGFR < 60 mL/min/1.73 m$^2$ (CKD stage 3).

If under 2 years old, eGFR was[24]:

- Moderately impaired eGFR: > 1 standard deviation (SD) and < 2 SD below the mean for age;
- Significantly impaired eGFR: > 2 SD below the mean for age.

Renoprotective medication was defined as the use of antihypertensive or antiproteinuric medication.

Renal injury was defined as persistent presence of any

of the following hypertension and/or albuminuria and/or at least moderately impaired eGFR and/or use of renoprotective medication.

Ipsilateral CAKUT was defined as an anomaly of the remaining kidney or the ipsilateral urinary tract, such as vesicoureteral reflux or ureteropelvic junction obstruction. To study the possible differences on outcome, we divided the population into subgroups according to etiology, BW, presence of other ipsilateral CAKUT, and history of urinary tract infections.

### Statistical analysis

The demographic and clinical data were assessed. The values were expressed as mean and SD for quantitative variables and percentages for qualitative variables. For the comparative study, continuous variables were grouped in classes. We assumed that the missing values are completely at random (MCAR) and, therefore, they are not expected to bias the obtained results.

The data collected were analyzed using student's t-test (quantitative variables), chi-square, and V Cramer tests (categorical variables) with IBM SPSS version 22.0® software. Logistic regression analysis was used to identify predictors of renal injury and to control the confounding variables. Clinical and demographic characteristics were included in the model. The level of significance considered was $p < 0.05$.

## Results

### Population characteristics

The sample included 147 children with CSFK followed in the pediatric nephrology unit in the study period, with male predominance and mean age 7.7 years (± 4.8 years) at the last follow-up visit (Table 1). Minimum and maximum period of follow-up was one and 18 years, respectively. Twenty (13.6%) were discharged from hospital follow-up to primary health care.

Three-quarters of CSFK were prenatally identified. Left-sided CSFK was predominant. The most frequent etiology was multicystic dysplastic kidney. Ipsilateral CAKUT was found in 21 patients (14.3%) and vesicoureteral reflux represented 11 (52.4%) of the CAKUT. Malformation of another organ was present in 33 (22.4%). Twenty-nine patients (19.7%) of the study population had already had at least one urinary tract infection, being that, among these, seven had ipsilateral CAKUT. Sample characteristics are shown in Table 1.

### Renal injury

Eighty patients (54.4%) met the criteria for renal injury. There was no statistical difference in the mean age between patients with and without renal injury (7.6 *vs* 7.8 years old, respectively, $p = 0.786$, 95% confidence interval (CI)). Table 2 shows the details.

The incidence of renal injury was higher in the subgroup with other CAKUT in the remaining kidney/ipsilateral urinary tract (90.1% *vs.* 48.4%, $p < 0.001$). Except for eGFR severely impaired, all types of renal injury were significantly greater in this subgroup (Table 3).

Furthermore, previous urinary tract infections (19.7%) only had a positive correlation with severely impaired eGFR (Table 4).

No significant relationship was shown in the occurrence of renal injury between subgroups according to BW and gestational age (Table 5). There was also no difference between median age at the last follow up between subgroups: BW < 2500 g and > 2500 g (6.4 *vs* 7.4 years old, $p = 0.365$); small for gestational age (SGA) *versus* appropriate for gestational age (AGA) and large for gestational age (LGA) (6.3 *vs.* 7.5 years old, $p = 0.217$; and preterm *versus* term birth (8.2 *vs.* 7.2 years old, $p = 0.404$). Moreover, etiology of CFSK did not significantly influence the percentage of renal injury ($p = 0.508$) (Table 6).

**Table 1. Clinical characteristics of study population**

| Characteristics | n (%) |
|---|---|
| Sex | |
| Male | 90 (61.2) |
| Female | 57 (38.7) |
| CSFK side | |
| Left | 77 (52.4) |
| Right | 70 (47.6) |
| Etiology | |
| MCDK | 92 (62.7) |
| URA | 55 (37.4 |
| Gestational age | |
| Term | 116 (78.9) |
| Preterm | 21 (14.3) |
| Missing value | 10 (6.8) |
| Birthweight | |
| > 2500 g | 115 (78.2) |
| LBW (1500-2500 g) | 19 (12.9) |
| VLBW (< 1500 g) | 1 (0.7) |
| Missing value | 12 (8.2) |
| Weight appropriated to GA | |
| AGA | 99 (67.3) |
| SGA | 28 (19.0) |
| LGA | 6 (4.1) |
| Missing value | 14 (9.5) |

AGA - appropriate for gestational age; CSFK - congenital solitary functional kidney; GA - gestational age; LBW - low birth weight; LGA - large for gestational age; MCDK - multicystic dysplastic kidney; SGA - small for gestational age; URA - unilateral renal agenesis; VLBW - very low birth weight.

The only independent factor identified as significant predictor of renal injury was the presence of CAKUT in the remaining kidney/ipsilateral urinary tract (OR 16.7, *p* = 0.007). Age, low BW, SGA, preterm birth, and previous urinary tract infections were not significant predictors for renal injury (Table 7).

**Table 2. Renal injury in congenital solitary functional kidney**

| | n (%) |
|---|---|
| Renal injury | 80 (54.4) |
| Hypertension | 3 (2.0) |
| Albuminuria | 9 (6.1) |
| eGFR moderately impaired | 65 (44.2) |
| eGFR severely impaired | 11 (7.5) |
| Renoprotective medication | 11 (7.5) |

eGFR - estimated glomerular filtration rate.

There was no one with end stage CKD or renal replacement therapy.

## Discussion

### Population characteristics

This study is a pioneer in Portugal. Although it embraces a single center, it has a significant sample (147 patients) as we are one of the five reference centers of pediatric nephrology and it includes a wide range of ages (0-18 years). Prenatal diagnosis contributed to an earlier identification and, consequently, follow-up. Consistently like in other reports, there is a male and left side solitary functioning kidney predominance and other CAKUT of the CSFK is present in 14.3%.[16]

**Table 3. Renal injury in the absence/presence of other congenital anomalies of the kidney and urinary tract**

| | With CAKUT | Without CAKUT | *p* |
|---|---|---|---|
| Total, n | 21 | 126 | - |
| Renal injury, n (%) | 19 (90.1) | 61 (48.4) | **0.001** |
| Hypertension, n (%) | 2 (9.5) | 1 (0.1) | **0.009** |
| Albuminuria, n (%) | 5 (23.8) | 4 (3.2) | **0.001** |
| eGFR moderately impaired, n (%) | 17 (80.1) | 48 (38.1) | **0.001** |
| eGFR severely impaired, n (%) | 2 (9.5) | 9 (7.1) | 0.817 |
| Renoprotective medication, n (%) | 5 (23.8) | 7 (4.8) | **0.002** |

CAKUT - congenital anomalies of the kidney and urinary tract; eGFR - estimated glomerular filtration rate.

**Table 4. Renal injury in subgroups with and without previous urinary tract infections**

| | UTI | No UTI | *p* |
|---|---|---|---|
| Total, n | 29 | 118 | - |
| Renal injury, n (%) | 17 (58.6) | 63 (53.4) | 0.612 |
| Hypertension, n (%) | 0 | 3 (2.5) | 0.386 |
| Albuminuria, n (%) | 3 (10.3) | 6 (5.1) | 0.413 |
| eGFR moderately impaired, n (%) | 12 (41.4) | 53 (44.9) | 0.731 |
| eGFR severely impaired, n (%) | 5 (17.2) | 6 (5.1) | **0.032** |
| Renoprotective medication, n (%) | 3 (10.3) | 8 (6.8) | 0.513 |

eGFR - estimated glomerular filtration rate; UTI - urinary tract infection.

**Table 5. Renal injury in the subgroups according to birth weight and gestational age**

| | BW < 2500 g | BW > 2500 g | *p* |
|---|---|---|---|
| Total, n | 20 | 115 | - |
| Renal injury, n (%) | 13 (65.0) | 61 (53.0) | 0.321 |
| | **SGA** | **AGA and LGA** | ***p*** |
| Total, n | 28 | 105 | - |
| Renal injury, n (%) | 18 (64.3) | 55 (52.4) | 0.261 |
| | **Preterm birth** | **Term birth** | ***p*** |
| Total, n | 21 | 116 | - |
| Renal injury, n (%) | 12 (57.1) | 63 (54.3) | 0.810 |

AGA - appropriate for gestational age; BW - birthweight; LGA - large for gestational age; SGA - small for gestational age.

**Table 6. Renal injury in the congenital solitary functioning kidney of different etiology**

| | URA | MCDK | *p* |
|---|---|---|---|
| Total, n | 55 | 92 | - |
| Renal injury, n (%) | 28 (50.9) | 52 (56.5) | 0.508 |
| Hypertension, n (%) | 0 | 3 (3.2) | 0.176 |
| Albuminuria, n (%) | 5 (9.1) | 4 (4.3) | 0.246 |
| eGFR moderately impaired, n (%) | 23 (41.8) | 42 (45.6) | 0.651 |
| eGFR severely impaired, n (%) | 3 (5.4) | 8 (8.7) | 0.420 |
| Renoprotective medication, n (%) | 5 (9.1) | 6 (6.5) | 0.567 |

eGFR - estimated glomerular filtration rate; MCDK - multicystic dysplastic kidney; URA - unilateral renal agenesis.

**Table 7. Results of final multivariate logistic regression model, including six candidate predictive factors for renal injury**

| Characteristics | OR | 95% CI | *p* |
|---|---|---|---|
| Age | 0.98 | 0.91-1.07 | 0.693 |
| BW < 2500 g | 1.13 | 0.33-3.90 | 0.850 |
| SGA | 1.58 | 0.55-4.59 | 0.399 |
| UTI | 1.18 | 0.46-3.03 | 0.730 |
| Preterm birth | 1.00 | 0.34-2.96 | 0.996 |
| CAKUT | **16.70** | **2.13-130.79** | **0.007** |

BW - birth weight; CAKUT - congenital anomalies of the kidney and urinary tract; CI - confidence interval; OR - odds ratio; SGA - small for gestational age; UTI - urinary tract infection

## Renal outcome

Our study demonstrates the occurrence of renal injury in a very important proportion of children with CSFK (54.4%) and a significant percentage (7.5%) of severe eGFR impairment. Our findings are in line with most recent studies. The KIMONO study, a prospective study including over 400 children from the Netherlands, showed that nearly one in three children with SFK had signs of renal injury at a mean age of 10 years.[23] Similarly, in another prospective study, at a tertiary nephrology center in Slovakia, renal injury was described in 38.1% at a median age of 11 years.[26] However, a direct comparison with our study is not possible because of the sampling and study design. Both studies also included acquired SFK and their definitions of renal injury included eGFR < 60 mL/min/1.73 $m^2$ and not < 90 mL/min/1.73 $m^2$ as ours. In opposition, a rather more optimistic view of the outcomes was given by other authors[16] which cohort had 306 patients with CSFK diagnosed prenatally and renal injury was only 3.9% after a median follow-up of 7.2 years. Nevertheless, that optimistic view could not be extended to adolescence and early adulthood as the study did not fully encompass those periods.

Furthermore, there was no difference in the patients' age between groups with and without renal injury, which led to the suspicion that there were other factors early in life that might contribute to a worse prognosis. In our sample, the most common etiology of CSFK was MCKD, in opposition to other reviews,[16,25] yet it did not seem to influence the prognosis. Renal injury development was independent of CSFK etiology, but was significantly correlated with the presence of an additional ipsilateral CAKUT (90.1% of patients with other CAKUT had a renal injury, $p < 0.001$), as shown in the international literature.[4,16,21] In our study, children with ipsilateral CAKUT had 16.7 times more renal injury than those without it, independently of other factors such as age or a previous urinary tract infection. Studies demonstrate also a higher percentage of end stage CKD in patients with ipsilateral CAKUT.[26] Even though our cohort had a significant percentage of SFK with ipsilateral CAKUT (14.3%), no patients required renal replacement therapy during the follow-up period. Prematurity, low BW, and SGA were not associated with poorer prognosis in this cohort, which was not expected from the literature review.[19,21] It might be justified by the small number of children with those characteristics in our sample. Authors had explored another possible reason - median age at the last follow-up between groups with and without those characteristics - but it was not statistically different. Despite these results, those variables must be considered. Concerning post-natal factors, urinary tract infection is a well-recognized factor that worsens the prognosis.[4,21] In our study, 20% of the children with a previous urinary tract infection had eGFR severely impaired ($p = 0.007$), but it was not proven to be an independent predictive factor.

## Implications

Routine fetal ultrasound has modified natural history of this condition, by allowing an earlier diagnosis and, therefore, a precocious assessment of other risk factors. Since renal injury may develop from infancy, clinical follow-up of every child with CSFK should start at birth in order to delay the progression toward renal injury.[4] It should include blood pressure monitorization and proteinuria assessment. For patients with ipsilateral CAKUT, clinical follow-up should be more frequent. Urinary tract infection must be prevented and, if it occurs, early diagnosis and treatment is mandatory. In addition, it is noteworthy that eGFR impairment may not be preceded by hypertension or proteinuria. Therefore, eGFR must be determined.

To date, there are no follow-up guidelines for children with CSFK, just recommendations, which emphasize the need for more research into this topic.[4]

## Strengths and limitations

Our study is one of the first published studies characterizing a CSFK Portuguese pediatric population and has a large sample. This study also emphasizes the importance of the identification of risk factors (such as other CAKUT and urinary tract infection) and the need for follow-up early in life, before the occurrence of any potential renal damage.

The limitations of our study are[21,23,26,27]:

- The retrospective design did not allow us to access to some information, like the age at which children developed renal injury;
- It might implicate a selection bias, since our sample is followed in a tertiary center;
- It is important to take into consideration that the data used for statistical analysis is only from the last appointment.
- Other factors associated to renal and cardiovascular diseases, like diet (namely protein and salt intake), body mass index, and sports contact performance, were not evaluated in this study.

To summarize, our research corroborates the most recent studies, as it draws attention to the poor renal outcome in a high percentage of cases, showing that CSFK is not a harmless clinical condition as described in the past decades.[4,16,23] The results highlight the relevance of early and lifelong need for follow-up.

**WHAT THIS STUDY ADDS**

- More than a half of children with congenital solitary functioning kidney progresses toward renal injury during childhood.
- Congenital solitary functioning kidney is not a harmless clinical condition as described in recent decades.
- The presence of ipsilateral congenital anomalies of the kidney and urinary tract is an independent risk factor for the development of renal injury.
- This study reinforces the importance of early clinical follow-up in patients with congenital solitary functioning kidney.

## Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

## Funding Sources

There were no external funding sources for the realization of this paper.

## Protection of human and animal subjects

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

## Confidentiality of data

The authors declare that they have followed the protocols of their work center on the publication of patient data.

## Provenance and peer review

Not commissioned; externally peer reviewed

## Awards and presentations

This study was presented at 19th National Congress of Pediatrics, 2018, Estoril, Portugal.

This study was awarded with the Prémio Investigação e Formação Avançada Pfizer Vaccines - SPP (Programa Crescemos Consigo).

## References


1. Rosenblum S, Pal A, Reidy K. Renal development in the fetus and premature infant. Semin Fetal Neonatal Med 2017;22:58-66. doi: 10.1016/j.siny.2017.01.001.
2. Sanna-Cherchi S, Ravani P, Corbani V, Parodi S, Haupt R, Piaggio G, et al. Renal outcome in patients with congenital anomalies of the kidney and urinary tract. Kidney Int 2009;76:528-33. doi: 10.1038/ki.2009.220.
3. Taranta-Janusz K, Zalewska-Szajda B, Gościk E, Chojnowska S, Dmochowska M, Pszczółkowska M, et al. New tubular injury markers in children with a solitary functioning kidney. Pediatr Nephrol 2014;29:1599-605. doi: 10.1007/s00467-014-2802-y.
4. Westland R, Schreuder MF, van Goudoever JB, Sanna-Cherchi S, van Wijk JA. Clinical implications of the solitary functioning kidney. Clin J Am Soc Nephrol 2014;9:978-86. doi: 10.2215/CJN.08900813.
5. Delmas LH, Kohler M, Doray B, Lémery D, Francannet C, Quistrebert J, et al. Congenital unilateral renal agenesis: Prevalence, prenatal diagnosis, associated anomalies. Data from two birth-defect registries. Birth Defects Res 2017;109:1204-11. doi: 10.1002/bdr2.1065.
6. Parikh CR, McCall D, Engelman C, Schrier RW. Congenital renal agenesis: Case-control analysis of birth characteristics. Am J Kidney Dis 2002;39:689-94. doi: 10.1053/ajkd.2002.31982.
7. Piscione TD, Rosenblum ND. The malformed kidney: Disruption of glomerular and tubular development. Clin Genet 1999:13:341-56. doi: 10.1034/j.1399-0004.1999.560502.x.
8. Chávez GF, Mulinare J, Cordero JF. Maternal cocaine use during early pregnancy as a risk factor for congenital urogenital anomalies. JAMA 1989;262:795-8. doi: 10.1001/jama.1989.03430060091031.
9. Correa A, Gilboa SM, Besser LM, Botto LD, Moore CA, Hobbs CA, et al. Diabetes mellitus and birth defects. Am J Obstet Gynecol 2008;199:237.e1-9. doi: 10.1016/j.ajog.2008.06.028.
10. Hwang DY, Dworschak GC, Kohl S, Saisawat P, Vivante A, Hilger AC, et al. Mutations in 12 known dominant disease-causing genes clarify many congenital anomalies of the kidney and urinary tract. Kidney Int 2014;85:1429-33. doi: 10.1038/ki.2013.508.
11. Gordon AC, Thomas DF, Arthur RJ, Irving HC. Multicystic dysplastic kidney: Is nephrectomy still appropriate? J Urol 1988;140:1231-4. doi: 10.1016/s0022-5347(17)42009-x.
12. 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;24:1810. doi: 10.1093/ndt/gfn777.
13. Schreuder MF. Unilateral anomalies of kidney development: Why is left not right? Kidney Int 2011;80:740-5. doi: 10.1038/ki.2011.204.
14. Hayes WN, Watson AR. Unilateral multicystic dysplastic kidney: Does initial size matter? Pediatr Nephrol 2012;27:1335-40. doi: 10.1007/s00467-012-2141-9.
15. Rabelo EA, Oliveira EA, Diniz JS, Silva JM, Filgueiras MT, Pezzuti IL, et al. Natural history of multicystic kidney conservatively managed: A prospective study. Pediatr Nephrol 2004;19:1102-7. doi: 10.1007/s00467-004-1549-2.
16. Marzuillo P, Guarino S, Grandone A, Di Somma A, Della Vecchia N, Esposito T. et al. Outcomes of a cohort of prenatally diagnosed and early-enrolled patients with congenital solitary functioning kidney. J Urol 2017;198:1153-8. doi: 10.1016/j.juro.2017.05.076.
17. Hostetter TH, Olson JL, Rennke HG, Venkatachalam MA, Brenner BM. Hyperfiltration in remnant nephrons: A potentially adverse response to renal ablation. J Am Soc Nephrol 2001;12:1315-25.
18. Brenner BM, Lawler EV, Mackenzie HS. The hyperfiltration theory: A paradigm shift in nephrology. Kidney Int 1996;49:1774-77.
19. Schreuder MF, Delemarre-van de Waal H.A, van Wijk A. Consequences of intrauterine growth restriction for the kidney. Kidney Blood Press Res 2006;29:108-25. doi: 10.1159/000094538.
20. Schreuder MF. Life with one kidney. Pediatr Nephrol 2018;33:595-604. doi: 10.1007/s00467-017-3686-4.
21. Westland R, Kurvers R, van Wijk J, Schreuder MF. Risk factors for renal injury in children with a solitary functioning kidney. Pediatrics 2013;131:e478-85. doi: 10.1542/peds.2012-2088.
22. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics 2017;140:e20171904.
23. Westland R, Abraham Y, Bokenkamp A, Stoffel-Wagner B, Schreuder MF, van Wijk JA. Precision of estimating equations for gfr in children with a solitary functioning kidney: The KIMONO study. Clin J Am Soc Nephrol 2013;8:764-72. doi: 10.2215/CJN.07870812.
24. International Society of Nephrology. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int 2013;3:1-150.
25. Kolvek G, Podracka L, Rosenberger J, Stewart RE, van Dijk JP, Reijneveld SA. Solitary functioning kidney in children. A follow-up study. Kidney Blood Press Res 2014;39:272-8. doi: 10.1159/000355804.
26. Committee on Sports Medicine and Fitness. American Academy of Pediatrics: Medical conditions affecting sports participation. Pediatrics 2001;107:1205-9. doi: 10.1542/peds.107.5.1205.
27. Radhakrishna V, Govindarajan K, Sambandan K, Jindal B, Naredi B. Solitary functioning kidney in children: clinical implications. Braz J Nephrol 2018;40:261-5. doi: 10.1590/1678-4685-JBN-3942.

**Que Fatores Influenciam o Prognóstico no Rim Solitário Funcional Congénito?**

**Introdução:** A prematuridade, baixo peso ao nascer e recém-nascidos leves para a idade gestacional condicionam um menor número de nefrónios ao nascimento. Quando associados a rim único funcionante, sobretudo na presença de outras anomalias congénitas do rim e trato urinário, podem influenciar negativamente o prognóstico. O objetivo deste estudo é identificar fatores que influenciam o *outcome* renal em doentes com rim único funcionante congénito.
**Métodos:** Análise retrospetiva de doentes com rim único funcionante congénito acompanhados em consulta de nefrologia pediátrica de um hospital terciário português entre 2012 e 2017. Lesão renal definida como hipertensão arterial, albuminúria, diminuição moderada da taxa de filtração glomerular e/ou uso de terapêutica renoprotetora.
**Resultados:** Foram identificadas 147 crianças com rim único funcionante congénito (62,7% com displasia multiquística), três quartos tinham diagnóstico pré-natal. Prematuridade, baixo peso ao nascer, leve para a idade gestacional e outra anomalia congénita do rim e trato urinário ipsilateral estavam presentes em, respetivamente, 14,3%, 13,6%, 19% e 14,3%. Aproximadamente metade cumpria critérios de lesão renal. Foi estabelecida uma associação significativa entre infeção do trato urinário e diminuição grave da taxa de filtração glomerular ($p$ = 0,007) e, também, entre anomalias congénitas do rim e trato urinário e hipertensão ($p$ = 0,001), diminuição moderada de taxa de filtração glomerular ($p$ = 0,01) e albuminúria ($p$ = 0,001). O único fator independente para lesão renal foi a presença de anomalias congénitas do rim remanescente / trato urinário ipsilateral (*odds ratio* 16,7, $p$ = 0,007). Não foi identificada uma associação significativa entre fatores perinatais e sinais de lesão renal.
**Discussão:** O rim único funcionante congénito não é uma patologia inocente, como descrito nas últimas décadas, e é necessário um acompanhamento precoce e ao longo da vida. A infeção do trato urinário e a coexistência de outra anomalia congénita do rim e/ou trato urinário ipsilateral estão relacionadas com um pior prognóstico.

**Palavras-Chave:** Adolescente; Criança; Portugal; Prognóstico; Rim/anomalias congénitas; Rim Único/congénito; Rim Único/complicações