Congenital solitary functioning kidneys: which ones warrant follow-up into adult life?

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Congenital anomalies of the kidney and urinary tract (CAKUT) are the leading cause of paediatric end-stage renal failure (ESRF) [1,3]. The clinical spectrum of CAKUT includes a variety of malformations of the urinary tract. Understanding the rate of progression for the different CAKUT categories and predicting long-term outcome is critical for a correct clinical management of these patients and for the transition of care from paediatric to adult nephrology.

Among CAKUT categories, congenital solitary functioning kidney (SFK) has been the object of debate whether it constitutes a benign condition or presents a significant risk of progression to ESRF [2–14].

In the present issue of Nephrology Dialysis and Transplantation, Westland et al. report on the results of the KIMONO-study (REF ID pending). The authors analysed a large cohort of 206 children with SFK of congenital origin to identify indicators of renal injury. Among them, 116 had a primary congenital solitary functioning kidney (pSFK) and 90 had a secondary solitary functioning kidney (sSFK) after unilateral nephrectomy due to congenital anomalies of the kidney or urinary tract. Ipsilateral CAKUT was present in ~30% of children from both groups. Among the patients with pSFK (which encompasses unilateral renal agenesis and multicystic dysplastic kidney), ipsilateral anomalies were significantly more frequent in cases with renal agenesis. Similarly, high blood pressure was present in comparable proportions between pSFK and sSFK, and it was significantly higher in the subgroup with renal agenesis. About 20% of children were using renoprotective agents and ~12% had albuminuria. Overall, >30% of patients with SFK showed evidence of renal injury. These data indicate that a significant fraction of children with congenital solitary kidney show evidence of renal parenchyma damage early in life and can potentially progress to ESRF in adulthood. These numbers are consistent with our previous report on long-term outcome in CAKUT patients, in which 50% of children with solitary kidney reached ESRF by the age of 30 [11]. Westland et al. explored the rate of progression by generalized estimated...
50% but, for example, 10 to ESRF by the age of 30 in the general population is not who present with signs of renal damage and who progress proportion of patients with a congenital solitary kidney have a more aggressive course of disease. If, in fact, the ability to help identify subgroups of patients who are likely to are inflated, but on the other hand, these studies are invaluable in introduction of bias and confounding. While the list of potential causal genes for this condition is long, the genetic basis of each case remains elusive [10]. A second critical aspect is that all of the studies reported in the literature have, by necessity, an observational design since large prospective studies for rare conditions that are present at birth are very difficult to conduct and require decades of follow-up. The validity of the results is, therefore, subjected to all the limitations of the observational studies, including ascertainment and selection bias, limiting the possibility of generalizing the conclusions to the entire population. While most of the confounders can be accounted for by rigorous study design and by statistical incorporation of confounders and covariates in the models, the selection bias seems the most important because in most of these studies, the referral hospitals were tertiary medical centres. The patients served at these institutions are more likely to be the most severely affected. The result is over-sampling of children with more complex malformations and/or already renal parenchyma injury, which are consequently more likely to progress to ESRF later in life. On one hand, we have to keep in mind that the estimates of renal injury and the proportion of patients who reach ESRF are inflated, but on the other hand, these studies are invaluable to help identify subgroups of patients who are likely to have a more aggressive course of disease. If, in fact, the proportion of patients with a congenital solitary kidney who present with signs of renal damage and who progress to ESRF by the age of 30 in the general population is not 50% but, for example, 10–20%, it is in any case extremely important to (i) identify this category early in life in order to establish a close follow-up, (ii) treat the associated conditions that accelerate progression, like coexistent anomalies in the unique kidney, high blood pressure and proteinuria and (iii) plan a careful transition from paediatric to adult nephrology services.

A good outcome in patients with a congenital solitary kidney has been erroneously suggested by translating results derived from surgical SFK from donor transplant programs or long-term survivors from Wilms’ tumour diagnosed in childhood [7,11]. These categories represent completely different entities compared to congenital anomalies, in which the environmental or genetic defects affect the development of the urinary tract starting before birth and continue throughout life. The remaining kidney is, in fact, healthy in the case of living kidney donors or surgical SFK from tumours, while various anomalies are often detectable in the congenital SFK and urinary tract by imaging studies or clinical and laboratory tests. Moreover, living donors represent a highly selected population that is subjected to accurate screening for any cause of renal impairment. As a result, the rate of development of ESRF in healthy kidney donors is lower than in the general population [7,9].

Based on the data available to date, we propose an aggressive approach to patients with solitary kidney of congenital origin (Figure 1). Our approach requires that every child diagnosed with SFK undergo imaging studies for kidney size parameters (renal ultrasound and function (isotopic scan) and presence of vesicoureteral reflux (VUR) by voiding cystoureterography. When possible, a static magnetic resonance of the urinary tract should be performed to evaluate renal parenchyma on the basis of $O_2$ consumption curves. If imaging studies identify CAKUT in the unique kidney, an endoscopic or surgical approach would be considered as appropriate: high-grade VUR and

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**Fig. 1.** Clinical approach to patients with a solitary kidney of congenital origin. Labs = laboratory tests for kidney function parameters and urinary analyses; BP = blood pressure; HT = hypertension; CRF = chronic renal failure.
ureteral stenosis should be treated endoscopically and, in
the case of treatment failure, open surgery would be indi-
cated. Long-term evaluation of serum creatinine, urine
albumin and proteins and blood pressure measurements
need to be conducted at least every year. Hypertension
and proteinuria should be promptly treated pharmaco-
logically. Of course, the presence and the degree of chronic
renal failure may require more frequent monitoring. If the
imaging studies exclude the presence of overt ipsilateral
CAKUT, the management will depend on the presence of
indicators of kidney injury at diagnosis. If the patient
presents with high blood pressure, proteinuria or a reduction
in estimated glomerular filtration rate, he or she has to be
treated like a patient with ipsilateral CAKUT and closely
monitored. If the patient does not show any evidence of
kidney injury at diagnosis, the follow-up with laboratory
analyses and measurement of blood pressure should be
performed every 2 years until puberty (or age 14) and then,
if the patient remains asymptomatic, every 3–5 years. An
open question concerns the use of angiotensin-converting-
enzyme (ACE) inhibitors and/or angiotensin II receptor
blocking agents to control proteinuria and hypertension
in patients with a solitary kidney. The only randomized
study conducted on children testing the effect of ACE inhi-
bition on the progression of renal failure showed a beneficial
effect of the treatment [16]. While this study included a
group of patients with renal hypoplasia, specific trials on
CAKUT and, especially, on solitary kidney patients have
not yet been conducted.

This aggressive approach should result in the early
detection of patients who are more likely to progress to
ESRF who need to be treated for precipitating factors like
proteinuria and hypertension. This is very intuitive for
patients with complex forms of CAKUT in which the
solitary kidney presents additional malformations. These
children have a more severe phenotype at diagnosis and
require immediate surgical and/or pharmacological treat-
ment. Conversely, children with SFK and no ipsilateral
CAKUT, who tended to be considered as having a benign
condition, are more likely to be overlooked and then
present later in life already in chronic renal failure. By close
monitoring, we will be able to identify the fraction (un-
known at the present time) of patients who will develop
ESRF in adulthood and facilitate a transition of care from
paediatric to adult nephrology service.

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(See related article by Westland et al. Renal injury in children with a soli-
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References

1. Centers for Disease Control and Prevention (CDC). State-specific
acquired solitary kidney: is the difference relevant? Nephrol Dial
Transplant 2010 doi 10.1093/ndt/gfq659 [epub ahead of print]
3. Ardissino G, Dacco V, Testa S et al. Epidemiology of chronic renal
111: e382–e387
term outcomes. Arch Dis Child 2006; 91: 820–823
5. Chevalier RL. When is one kidney not enough?. Kidney Int 2009; 76:
475–477
6. Dursun H, Bayazit AK, Cengiz N et al. Long-term outcomes of
monitoring and renal functions in children with a solitary kidney. Pediatr
Nephrol 2007; 22: 559–564
8. Hegde S, Coulthard MG. Renal agenesis and unilateral nephrectomy:
what are the risks of living with a single kidney?. Pediatr Nephrol
2009; 24: 439–446
10. Sanna-Cherchi S, Caridi G, Weng PL et al. Genetic approaches to
human renal agenesis/hypoplasia and dysplasia. Pediatr Nephrol
2007; 22: 1675–1684
with congenital anomalies of the kidney and urinary tract. Kidney Int
2009; 76: 528–533
12. Seeman T, Patzer L, John U et al. Blood pressure, renal function, and
proteinuria in children with unilateral renal agenesis. Kidney Blood
13. Vu KH, Van Dyck M, Daniëls H et al. Renal outcome of children with
one functioning kidney from birth. A study of 99 patients and a review
serum cystatin C in children with congenital solitary kidney. Pediatr
Nephrol 2006; 21: 688–693
15. Westland R, Schreuder MF, Bokenkamp A et al. Renal injury in
children with a solitary functioning kidney—the KIMONO study.
Nephrol Dial Transplant 2011; 26: 1533–1541
16. Wuhl E, Trivelli A, Pieca S et al. Strict blood-pressure control and
1639–1650

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