

Clinical Complications of Solitary Kidney

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Abstract: Objectives: To present causes, diagnosis and clinical complications of solitary kidney. **Data Sources:** Medline databases (PubMed, Medscape, and ScienceDirect. EMF-Portal) and all materials available in the Internet from 2006 to 2016. **Study Selection:** The initial search presented 170 articles of which 44 met the inclusion criteria. **Data Extraction:** If the studies did not fulfill the inclusion criteria, they were excluded. Study quality assessment included whether ethical approval was gained, eligibility criteria specified, appropriate controls, adequate information and defined assessment measures. **Data Synthesis:** Comparisons were made by structured review with the results tabulated. **Findings:** It seems that still there are major gaps in our knowledge regarding the most effective way to manage pain in neonates. The kidneys form a paired organ system located in the retroperitoneal space. Congenital anomalies of the kidney and urinary tract (CAKUT) are the predominant cause of ESRD in childhood. The congenital SK would present about 75% of the nephrons of a person with 2 functional kidneys. It undergoes compensatory enlargement starting with the 20th week of gestation. It has a higher number of nephrons, being hyperplastic not hypertrophic. It is accepted that the SK presents a lower number of nephrons (75%) than that of 2 functional kidneys. The congenital SK is generally well tolerated, being frequently diagnosed accidentally. The long-term outcome of individuals with a solitary functioning kidney from childhood has been a topic of extensive debate fueled by the conflicting results of observational studies. Caring for kidney transplant recipients (KTRs) requires specialized knowledge in areas as varied as nephrology, immunology, pharmacology, endocrinology, infectious disease and cardiology. **Conclusion:** Recommendations are limited because of the lack of consensus for long-term follow up and the fact that longitudinal data on the clinical outcomes of individuals with a solitary functioning kidney are absent. Efforts to keep attention on early diagnosis and evaluation of high-risk patients with CAKUT, small renal size, low birth weight, prematurity, and history of urinary tract infection. [El-Metwally L. El-Shahawy; Mohammed E. Salem; Hassan G. Abdel Salam; Ashraf T. Mahmoud and Amina A. Abdel Rahman. **Clinical Complications of Solitary Kidney.** *Nat Sci* 2016;14(6):110-117]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). <http://www.sciencepub.net/nature>. 15. doi:[10.7537/marsnsj14061615](https://doi.org/10.7537/marsnsj14061615).

Key words: kidney, solitary functioning kidney.

1. Introduction

Congenital Anomalies of the Kidney and Urinary Tract (CAKUT) are the predominant cause of ESRD in childhood. One important condition in the spectrum of CAKUT is the solitary functioning kidney, which can be congenital or acquired after unilateral nephrectomy in childhood. Although both types of solitary functioning kidney are associated with CKD and ESRD, early differentiation between patients with and without an increased risk for CKD is challenging⁽¹⁾.

Causes of the solitary functioning kidney are renal development and ipsilateral CAKUT. Normal kidney and urinary tract development requires a temporally and spatially coordinated interaction between the UB and the MM. Any insult (genetic or environmental) that disrupts this reciprocal induction can lead to different forms of CAKUT. Environmental factors that disturb renal development include medications administered during pregnancy, intrauterine growth restriction, and maternal diseases, such as diabetes mellitus⁽²⁾.

The clinical importance of a reduced nephron number has been described in the hyperfiltration hypothesis by **Brenner *et al.***⁽³⁾. **Sanna-Cherchi *et al.***⁽⁴⁾ showed that 20-50% of solitary functioning kidney patients were on renal replacement therapy at the age of 30 years. Compared with a reference group, the risk for an impaired renal outcome was even higher when VUR was present.

The congenital Solitary Kidney (unilateral renal agenesis) represents a genetic abnormality resulting in the non-existence of a kidney. The SK is usually enlarged in compensation. Diagnosis is sometimes suggested by this very fact. It affects 1/1000 persons⁽⁵⁾.

The SK occurring after nephrectomy is defined as acquired solitary kidney. The SK can be due to a disease requiring nephrectomy or to prelevation of a kidney for transplantation⁽⁶⁾.

Important differences in renal outcome may exist between congenital and acquired solitary functioning kidneys; the congenital type still has the potential to form new nephrons, whereas with the acquired type,

nephrogenesis has ceased at the time of the nephrectomy. This finding may imply a higher susceptibility for pronounced glomerular hyperfiltration in acquired solitary functioning kidney patients. The outcome of patients with a solitary functioning kidney is often derived from the excellent prognosis described in adult uninephric kidney donors⁽⁷⁾.

A differentiation between patients with and without a high risk for CKD should be made at diagnosis. This evaluation should focus on identified risk factors, such as ipsilateral CAKUT, small renal size, low birth weight, prematurity, and history of urinary tract infection⁽⁸⁾.

Although not yet widely necessary and requires a multidisciplinary approach. It is important to differentiate between patients with and without a high risk for CKD⁽⁹⁾.

The aim of this work is to present causes, diagnosis and clinical complications of solitary kidney.

2. Materials and Methods

Search Strategy:

We reviewed papers on the solitary kidney from Medline databases which are (Pub Med, Medscape, ScienceDirect) and also materials available in the Internet. We used kidney and solitary functioning kidney as searching terms. In addition, we examined references from the specialist databases EMF-Portal (<http://www.emf-portal.de>), reference lists in relevant publications and published reports. The search was performed in the electronic databases from 2005 to 2015.

Study Selection:

All the studies were independently assessed for inclusion. They were included if they fulfilled the following criteria:

Inclusion criteria of the published studies:

-Published in English language.

-Published in peer-reviewed journals.

-If a study had several publications on certain aspects we used the latest publication giving the most relevant data.

Data Extraction:

If the studies did not fulfill the above criteria, they were excluded such as, Studies on pain in neonates, reports without peer-review, not within national research programme, letters/comments/editorials/news and studies not focused on solitary functioning kidney.

Quality Assessment:

The quality of all the studies was assessed. Important factors included, study design, attainment of ethical approval, evidence of a power calculation, specified eligibility criteria, appropriate controls,

adequate information and specified assessment measures. It was expected that confounding factors would be reported and controlled for and appropriate data analysis made in addition to an explanation of missing data.

Data Synthesis:

A structured systematic review was performed with the results tabulated.

3. Results

A glomerulus consists of an afferent and an efferent arteriole, and interveining tuft of capillaries lined by endothelial cells and covered by epithelial cells that form a continuous layer with those of Bowman's capsule and the renal tubule. The space between capillaries is called the mesangium. The mesangium is an extension of the glomerular basement membrane but is less dense and contains two distinct cell types: intrinsic glomerular cells and tissue macrophage. Both cell types contribute to the development of immune-mediated glomerular disease (Figure 1)⁽¹⁰⁾.

The complex organization of the glomerulus is crucial not only for renal function but also for explaining the differences observed in glomerular disease. The renal tubule itself has a number of different structural regions: the proximal convoluted tubule from which approximately 80% of the electrolytes and water are reclaimed, the loop of Henle, distal convoluted tubule and the collecting duct where urine is concentrated and additional electrolyte and water changes are made in response to hormonal control (Figure 2)⁽¹⁰⁾.

After filtration at the glomerulus most of the Na ions and under normal conditions almost all of the K ions and glucose are actively resorbed from the tubular fluid in the proximal tubule, water is resorbed osmotically. In addition to absorption, a number of substances are secreted into the tubular fluid through the action of transporters along the renal tubule (Figure 3)⁽¹¹⁾.

Glomerular hyperfiltration may lead to glomerulosclerosis and sets a vicious cycle of additional reduction in nephron number (Figure 4). As a consequence, the nephrectomized animals showed high incidences of hypertension and proteinuria in the early stages and an ongoing decline in GFR in the long run⁽⁹⁾.

Caring for kidney transplant recipients (KTRs) requires specialized knowledge in areas as varied as nephrology, immunology, pharmacology, endocrinology, infectious disease and cardiology. In this context of increasing complexity coupled with an exponential growth in the medical literature, clinical practice guidelines (CPGs) aim at helping clinicians and other caregivers to deliver evidence-based

medicine and thereby, to improve patient outcomes (Figure 5)⁽¹²⁾.

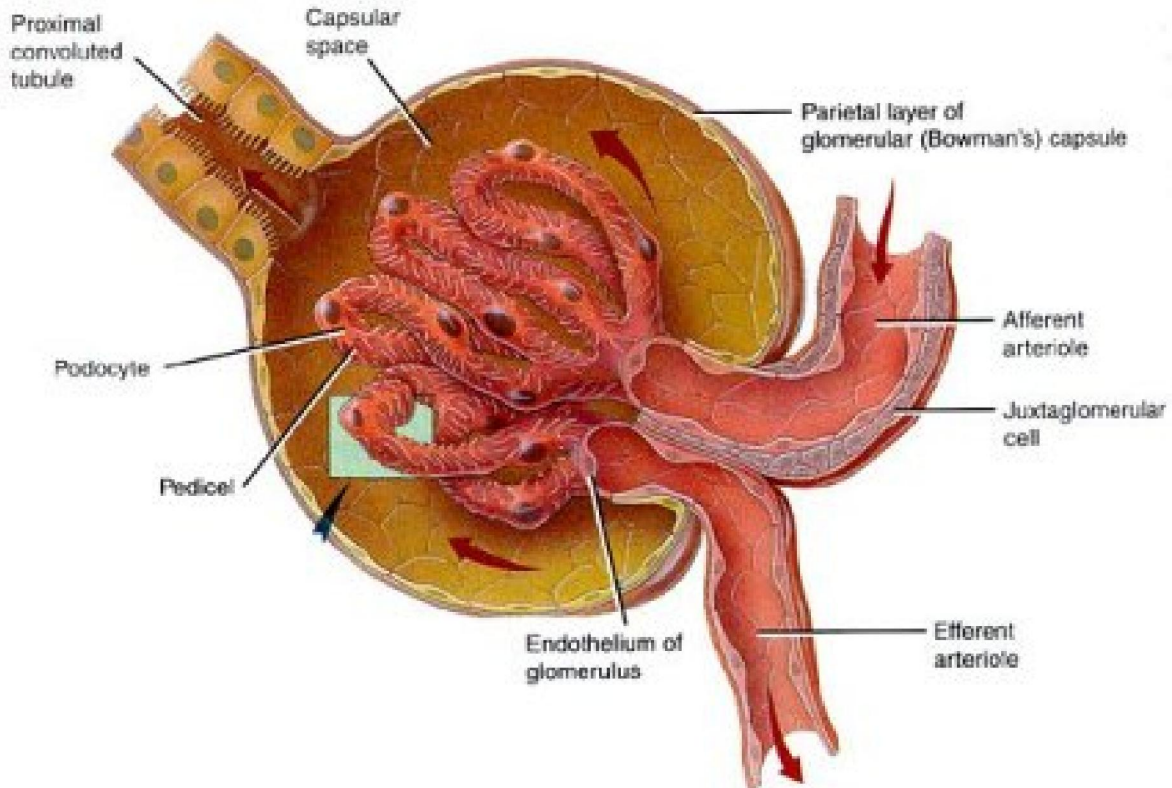


Figure (1): Anatomy of kidney glomerulus (Goodman *et al.*, 2004)

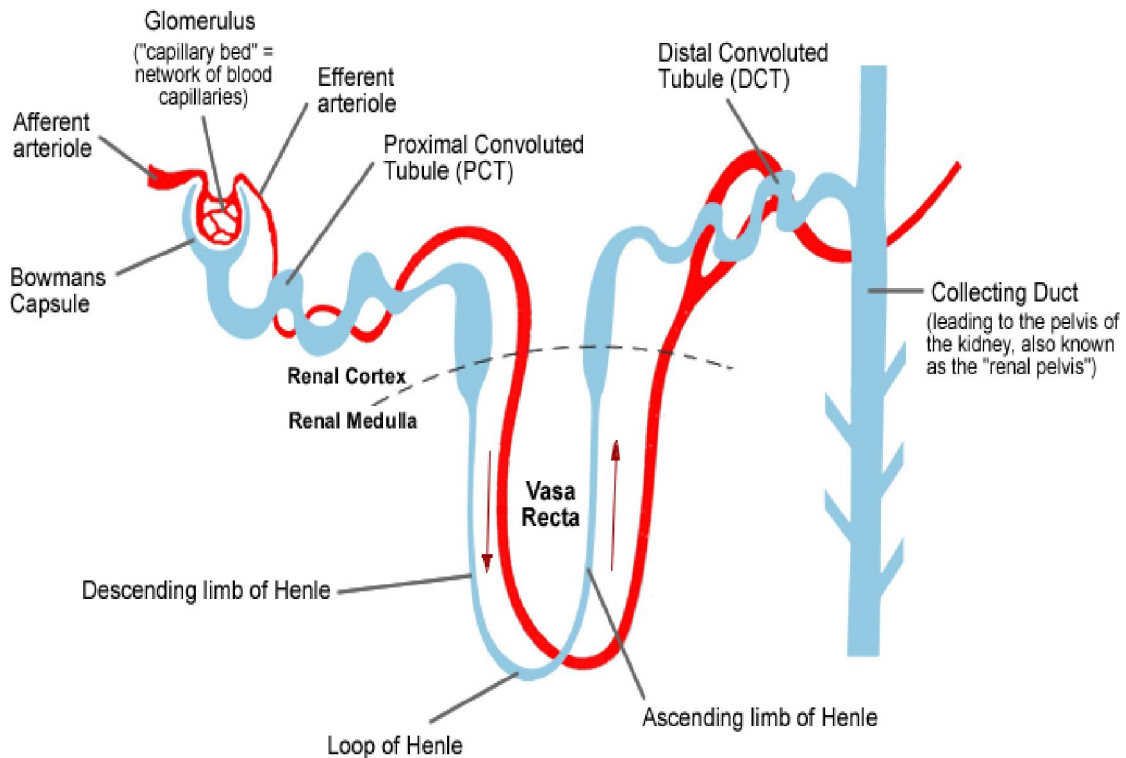


Figure (2): Anatomy of the nephron (Goodman *et al.*, 2004)

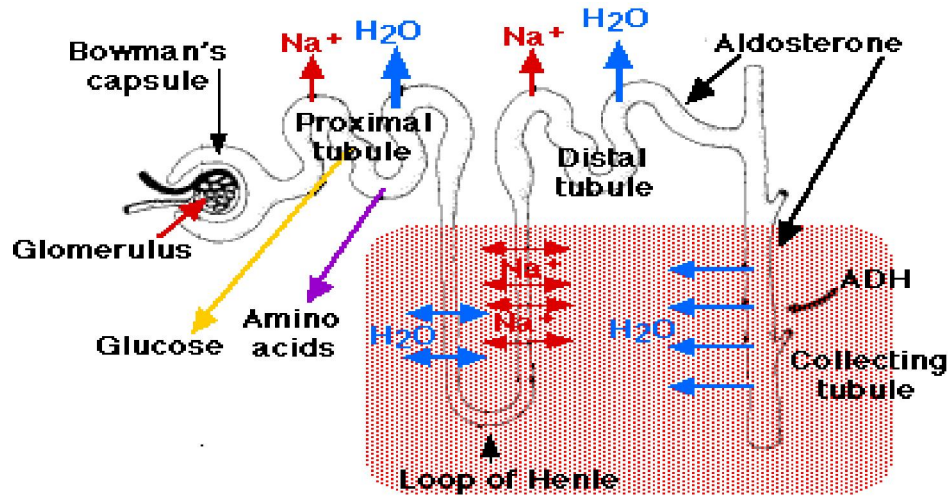


Figure (3): Physiology of the nephron (Lamp *et al.*, 2003)

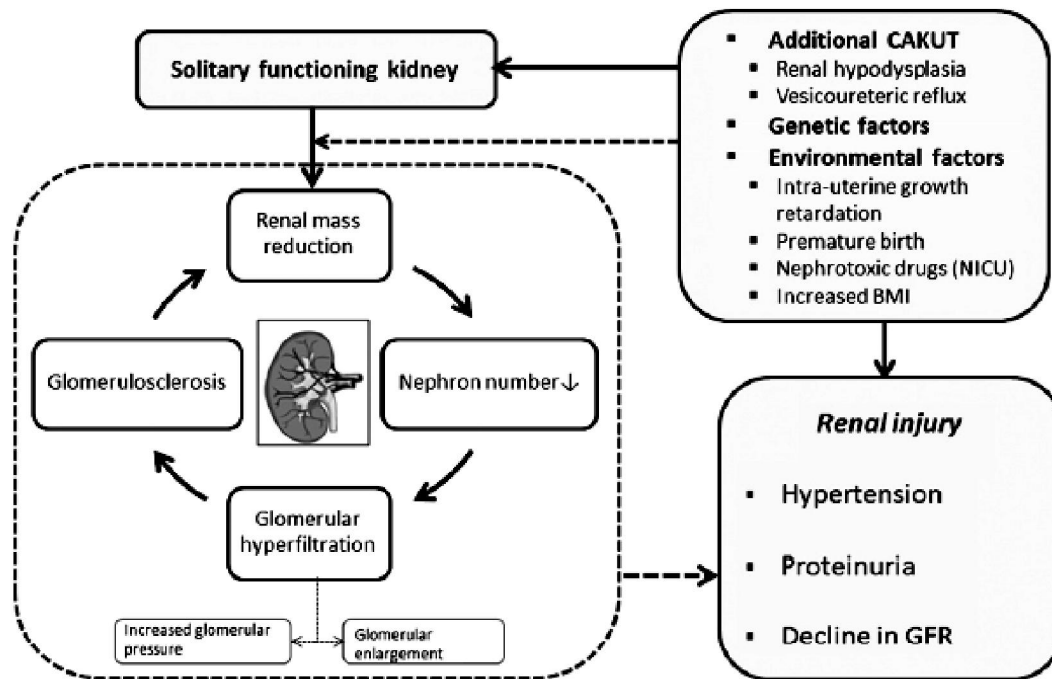


Figure (4): Possible mechanisms leading to renal injury in patients with a solitary functioning kidney. Glomerular hyperfiltration caused by insufficient nephron number could be one explanation for this impaired outcome. Nephron number could also be affected by associated congenital anomalies of the kidney and urinary tract as well as genetic and environmental factors. BMI, body mass index; CAKUT, congenital anomalies of the kidney and urinary tract; NICU, neonatal intensive care unit (Westland *et al.*, 2014).

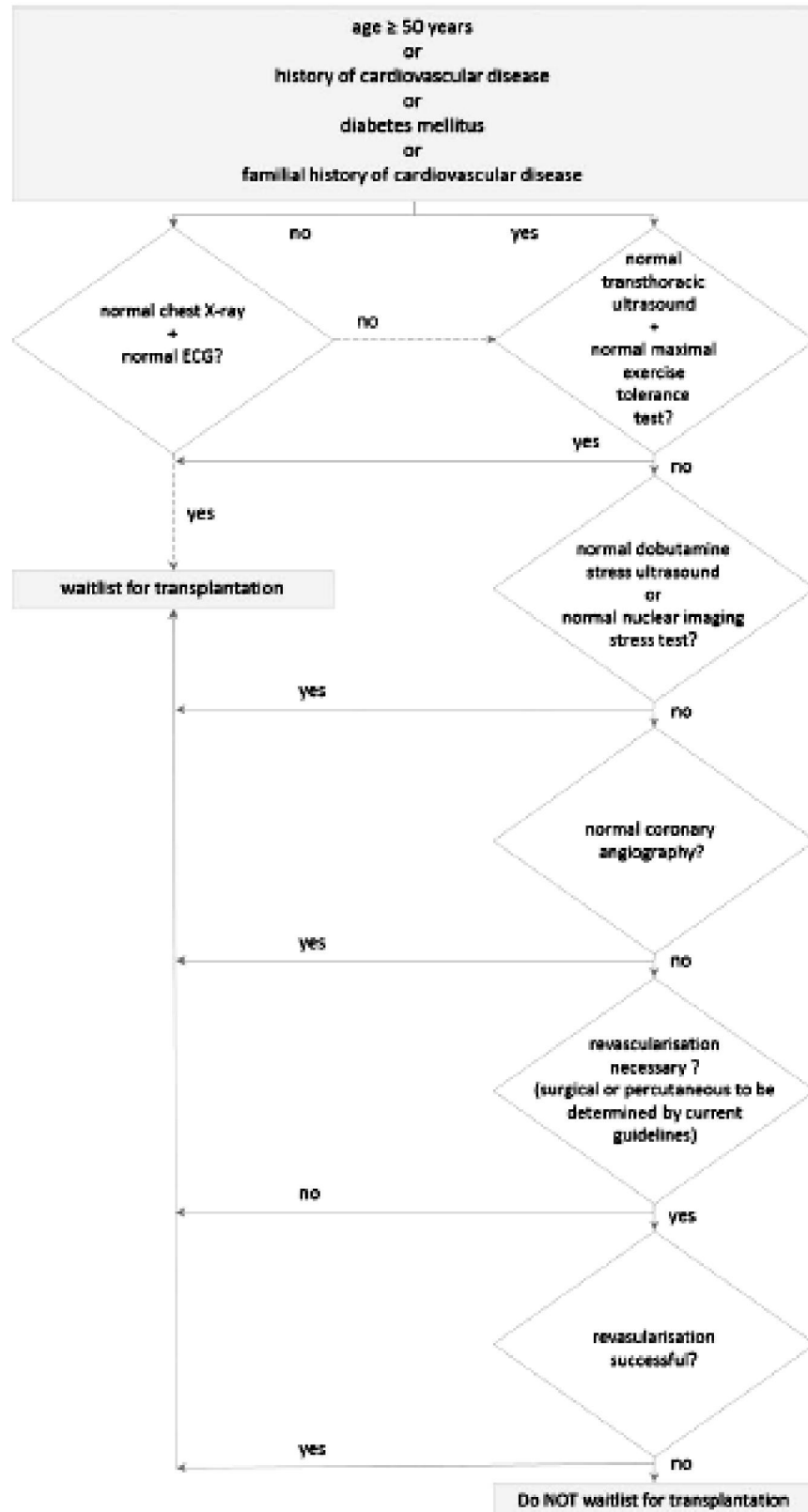


Figure (5): Decision tree pre-transplant cardiovascular screening

4. Discussion

Gonzalez *et al.*⁽¹³⁾ showed that obesity is associated with an increase in serum creatinine and the development of proteinuria in adults with a solitary functioning kidney. However, individuals with a solitary functioning kidney and preserved renal function have traditionally not been followed into adulthood, and, therefore, the availability of long-term data on the clinical outcome in these patients is limited. In this regard, there is a cardinal need for long-term studies of individuals with a solitary functioning kidney with a prenatal diagnosis, because they represent the most unbiased group of patients. When available, these data will strongly assist nephrologists in differentiating patients at risk for CKD from those patients who are not at risk for CKD. **de Lucas *et al.***⁽¹⁴⁾ presented the data on renal function and morphology of a pediatric population with solitary kidney and, subsequently, tried to rationalize and adapt medical follow-ups. They considered that control and follow up of pediatric patients with solitary kidney should be adapted to solitary kidney condition-associated nephro-urologic pathologies, which condition renal prognosis.

According to **Seeman *et al.***⁽¹⁵⁾, the renal injury expressed by AH, proteinuria and diminished GFR is more frequent in persons with SK who present associated renal abnormalities than in people without such abnormalities. The presence in persons with a SK of two associated urological abnormalities increases the risk of progression towards chronic renal failure.

As far as the evolution of the acquired SK is concerned this rarely develops into renal failure. In fact it is not known at present why some patients with congenital or acquired SK develop renal insufficiency and proteinuria, the clinical significance of mild grade proteinuria and AH is not known either⁽¹⁶⁾. It is to be mentioned that according to **Chevalier**⁽¹⁷⁾ age at time of nephrectomy does not represent an increased risk of developing renal insufficiency.

Sanna-Cherchi *et al.*⁽⁴⁾ showed that 20%–50% of solitary functioning kidney patients were on renal replacement therapy at the age of 30 years. Compared with a reference group, the risk for an impaired renal outcome was even higher when VUR was present. **Schreuder *et al.***⁽¹⁸⁾ noted in persons born prematurely that they have a significantly smaller kidney and lower GFR as compared to children with normal weight.

Rees *et al.*⁽¹⁹⁾ have modified their requirements for donor acceptance based on medical (e.g. donors with obesity or single drug hypertension) or psychosocial (e.g. nondirected donors who have no prior direct relationship with the recipient) criteria.

Bridgewater and Rosenblum⁽²⁰⁾ found gene mutations that could be responsible for absence of a kidney. Mutations of several genes were involved,

among them: the gene coding the Glial cell-derived neurotrophic factor (GDNF), the gene coding GFR-alpha, a receptor of GDNF, other genes like *Eya 1*, with the role of regulating GDNF, ICAT, gremlin, TGF-beta 2.

Akl⁽²¹⁾ pointed out in a group of 30 children with functional congenital SK associations of renal and non-renal abnormalities in 77% cases, urological abnormalities being present in 47% of the children, and neurological abnormalities in 53% of them. In children with a SK associated with other abnormalities of the urinary tract, proteinuria is present in 20% and AH in 7%.

Drug administration in the prematurely born neonate with a solitary functioning kidney can have detrimental effects on nephrogenesis and GFR, especially when administered before the 28th gestational week. The most commonly used drugs that disturb nephrogenesis are aminoglycosides and nonsteroidal anti-inflammatory drugs⁽²²⁾. Finally, **Schreuder**⁽²³⁾ reported a boy predominance in solitary functioning kidney patients, as well as a left-side predominance.

Abou Jaoudé *et al.*⁽²⁴⁾ considered that the SK preserves its renal function short- and medium-term, but that on long-term, it seems to gradually decline. However, persons with congenital SK seem to manifest better functional adaptation. The congenital SK itself can present associated lesions, some of them not identified initially, abnormalities that cause a diminution of the number of nephrons and influence its evolution. AH, proteinuria or renal function impairment were present in approximately one third of the adults with congenital SK.

Steiger⁽²⁵⁾ highlighted their favorable post-nephrectomy evolution. They develop end-stage renal disease requiring dialysis only in exceptional cases. One of the frequently asked questions is why a person needs two kidneys, since man can live long after nephrectomy with only one kidney.

Corbani *et al.*⁽²⁶⁾ suggested regular clinical follow-up for hypertension, (micro)albuminuria, and GFR every 3–5 years in a patient with a solitary functioning kidney without ipsilateral CAKUT. For patients with ipsilateral CAKUT, clinical follow-up should be conducted annually, and surgical correction of CAKUT must be performed when indicated.

Antoniewicz *et al.*⁽²⁷⁾ considered that the deterioration of kidney function is related to the volume of renal parenchymatous tissue that was lost. Regarding clinical, pathological and functional evolution after nephron-sparing nephrectomy in patients with a SK, **Mues *et al.***⁽²⁸⁾ found that in most patients renal function was not impaired by surgery.

Sanna-Cherchi *et al.*⁽²⁹⁾ identified 72 different copy number disorders in 87 patients (17%), implicating

rare, submicroscopic deletions and duplications that disrupt coding elements as a major cause of renal hypodysplasia and confirming the extreme genetic heterogeneity of this disease.

Stefanowicz *et al.*⁽³⁰⁾ assessed renal function (GFR) in Wilms tumour survivors in comparison with persons with unilateral renal agenesis and they did not find differences. Similar results were reported by **Gadalean *et al.***⁽³¹⁾.

Gluhovschi *et al.*⁽⁶⁾ showed focal and segmental glomerulosclerosis. A $\frac{3}{4}$ reduction of the renal mass is necessary for post-nephrectomy glomerular impairment to occur. In contrast to the 5/6 experimental model which remains with only 16.66% nephrons, the living donor in humans is left with 50% nephrons at the level of the remnant kidney, which allows good toleration of the situation.

Cachat *et al.*⁽³²⁾ showed that urinary albumin is weakly associated with markers of hyperfiltration in solitary functioning kidney patients, indicating that factors other than glomerular hyperfiltration likely contribute to the development of CKD.

Westland *et al.*⁽⁸⁾ showed that nearly one in three patients with a solitary functioning kidney has signs of renal injury at a mean age of 10 years. Furthermore, GFR in these patients slowly declines from as early as 9 years of age, whereas (micro)albuminuria generally develops around 16 years of age. The median age to develop renal injury in children with either type of solitary functioning kidney was 15 years.

Westland *et al.*⁽⁹⁾ showed that 47% of URA patients developed hypertension, 19% of individuals had proteinuria, 13% of individuals had an impaired GFR, and 4% of individuals died of renal failure. They have suggested a follow-up based on two factors (i.e., the presence of ipsilateral CAKUT and the presence of [signs of] renal injury). Follow-up for all is proposed, with a differentiation in the frequency of follow-up. No unequivocal evidence exists for any follow-up frequency, which will always result in an arbitrary proposal. They showed that protein restriction has a protective effect on glomerular hyperfiltration in rats. Interestingly, a combination of the Brenner hypothesis and the developmental origin of health and disease hypothesis has been proposed to cause the impaired renal outcome of very low birth weight infants.

Conclusion:

(1) Recommendations are limited because of the lack of consensus for long-term follow up and the fact that longitudinal data on the clinical outcomes of individuals with a solitary functioning kidney are absent.

(2) Efforts to keep attention on early diagnosis and evaluation of high-risk patients with CAKUT,

small renal size, low birth weight, prematurity, and history of urinary tract infection.

No Funds.

No Conflict of Interests.

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