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Solitary kidney. Study of renal morphology and function in 95 children

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SUMMARY

The aim of the study was to evaluate renal growth and function of solitary kidney in paediatric patients.

Materials and methods: *A prospective study was performed in a fifteen years period between 1988 and 2003 in paediatric patients with a solitary kidney, in a Children's Hospital. All the following parameters were evaluated every year: age, sex, ethiology, elapsed time since the concept of solitary kidney was assessed (ET), blood pressure, renal function measured by GFR, urinary excretion of solutes, concentration ability and microalbuminuria (MA). DMSA was made at the beginning and every five years and renal ultrasonography was carried out every two years. Two groups were made depending of nephrourologic malformations in the remanent kidney and/or antecedents of pyelonephritis: Group I with antecedents of pyelonephritis and/or malformations; Group II, nor antecedents of pyelonephritis neither malformations.*

Results: *Ninety five patients were evaluated, 69% (n = 66) were males and 31% (n = 29) were females, with an age at diagnosis of 3.5 yrs (ranged 0.1-17 yrs). ET was 9.2 yrs (range 1-20 yrs). The ethiology was: Nephrectomy of the contralateral kidney 39 patients (pts) (41%), renal agenesis (RA) 47 pts (49%) and nonfunctioning multicystic displastic kidney (MCDK) 9 pts (9.4%). Functional alterations were found in 18 pts (19%), such as MA in 12 pts (12.6%), decreased GRF in 5 pts (5.5%) and hypertension in 3 pts (3.2%). It was observed more significant functional alterations in the patients of the Group I (58%)* versus *Group II (9%) ($p < 0.001$).There was in Group II a significant correlation between kidney size and GFR ($p < 0.01$, $r = 0.3$), and between kidney size and ET ($P < 0.05$; $r = 0,3$).*

Conclusions: *Any alteration in the renal function was observed in the 12.6% of the children. The most frequent affected parameter of renal damage was MA, followed by GFR reduction. Arterial hypertension was not a prominent finding. Alterations have been less frequently found in RA and MCDK of the Group II, so clinical reviews should be made with a lesser frequency.*

Key words: ***Solitary kidney. Nephrectomy. Renal agenesis. Multicystic displastic kidney. Outcome.***

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VALORACIÓN DE LA MORFOLOGÍA Y FUNCIÓN RENAL EN UNA SERIE DE 95 PACIENTES PEDIÁTRICOS CON RIÑÓN ÚNICO

RESUMEN

El objetivo de nuestro trabajo es mostrar los resultados de la función así como la morfología renal en una población infantil, que tienen un solo riñón y consecuentemente a los hallazgos encontrados, tratar de racionalizar y adecuar las revisiones médicas.

Material y métodos: *Se trata de un estudio prospectivo de los pacientes monorrenos seguidos entre el año 1988 y 2003. Cada año se estudiaron los siguientes parámetros: variables demográficas (sexo, edad), clínicas (etiología, tiempo de riñón único, tensión arterial), función renal (Filtrado glomerular (FG), Excreción fraccional (EF) de iones y Microalbuminuria (MA). El estudio de morfología renal se realizó mediante ecografía renal bianual y DMSA quinquenal. Se hicieron dos grupos en función de los antecedentes de pielonefritis aguda y/o alteraciones nefrourológicas: Grupo I con antecedentes de pielonefritis Y/o alteraciones; Grupo II, sin antecedentes ni alteraciones.*

Resultados: *Del total de 95 pacientes el 69% fueron varones (n = 66) y el 31% fueron mujeres (n = 29). La edad media al diagnóstico fue de 3,5 años (0,1-17 años). El tiempo medio con riñón único fue 9,2 años (1-20 años). La etiología fue: Nefrectomía contralateral (NF) en 39 (41%), Agenesia renal (AR) en 47 (49%) y Displasia Multiquística (DM) con función renal anulada en 9 (9,4%). Se objetivó una función renal alterada (microalbuminuria elevada y/o HTA y/o Insuficiencia renal) en 18 pacientes (19%). La MA fue la alteración funcional más frecuente (n = 12, 12,6%), seguido de descenso del FG (n = 5, 5,3%) e HTA (n = 3, 3,2%). Se observó una prevalencia mayor de alteraciones funcionales en los pacientes del grupo I (58%) frente a los pacientes del grupo II (9%) (p < 0,001)*

En los pacientes del Grupo II encontramos correlación significativa entre el tamaño renal y el FG (p < 0,01, r = 0,3), así mismo entre el tamaño renal y el tiempo de RU (P < 0,05; r = 0,3).

Conclusiones: *El 12% de los pacientes mostraron alguna alteración de la función renal, siendo la más frecuente la microalbuminuria, seguida de la reducción del filtrado glomerular. La HTA fue un hallazgo escaso. Éstas alteraciones fueron menos frecuentes en los pacientes con AR o DMQ que no tenían antecedentes de pielonefritis aguda ni alteraciones nefrourológicas asociadas, por lo que las revisiones en éste grupo deben ser menos frecuentes.*

Palabras clave: ***Riñón único. Agenesia renal. Nefrectomía. Displasia multiquística. Niños. Pronóstico.***

INTRODUCTION

Renal functioning progression has in solitary kidney patients has been and still is a matter of debate. Already in the 1980s, Brenner hypothesized on long-term renal function loss as a result of a decrease in nephron numbers.[1,2,3] This theory stimulated the performance of studies in those cases with a single kidney, particularly in the pediatric population as they have a longer progression time. There are experimental studies that show that after early nephrectomies there occurs a decrease in glomerular filtration rate, which is preceded by proteinuria or arterial hypertension.[4] The time interval from nephrectomy to glomerular filtration decrease varies and depends on several factors.[5,6,7,8] There are no yet

enough number of studies with long-term progression to clarify the prognosis of solitary kidneys in childhood.[7,9]

The aim of our study was to present the data on renal function and morphology of a pediatric population with solitary kidney and, subsequently, to try to rationalize and adapt medical follow-ups.

MATERIAL AND METHODS

This is an analytical and prospective study on 95 pediatric patients (younger than 18 years) with solitary kidney, seen at the Pediatric Nephrology Department of Niño Jesús Hospital, between 1988 and 2003. All patients were studied at the outpatient clinic. The protocol included: clinical history, weight, height, blood pressure; yearly blood and urine analysis with creatinine (Cr), creatinine clearance (CrCl), ion fractional excretion (FE) and microalbuminuria (MA), bi-yearly renal ultrasound, and initial and quinquennial renal scintigraphy. The date of the last performed ultrasound was used as the reference date to determine the patient's follow-up. Vital statistics such as gender and age at the time of diagnosis were analyzed; clinical variables (etiology of solitary kidney, time of progression of solitary kidney, history of acute pyelonephritis and/or associated nephro-urologic abnormalities, presence of arterial hypertension); renal function (Cr, CrCl, ion EF, elevated microalbuminuria (MA); morphological and functional renal characteristics from the last imaging study (calculation of the z score of longitudinal size expressed as standard deviation for age,[10] renal scintigraphy (DMSA)). For further analysis, patients were categorized into two groups. Group I was defined as patients that associated a history of acute pyelonephritis and/or one or more nephro-urologic abnormalities in the solitary kidney, independently of the cause originating the solitary kidney condition, and Group II was comprised by those patients that did not have any associated nephro-urologic abnormality in the solitary kidney nor a history of acute pyelonephritis. Functional impairment was considered when there was microalbuminuria > 30 µg/min/1.73 m^2 and/or decrease of glomerular filtration rate defined as CrCl < 80 mL/min/1.73m^2 and/or arterial hypertension (> 95 Percentile for age according to the Task Force height and gender percentile tables).[11]

SPSS® software, version 11.0 from SPSS Inc., was used for the statistical analysis. Means were expressed as mean and standard deviation (SD). Student's t test was used for comparison of the means between groups and Chi-square to look for any association between qualitative variables. Pearson's correlation coefficient was used for linear association measurement between two variables. All tests used were done considering a maximal alpha error of 5% ($p < 0.05$) and bilateral contrast.

RESULTS

Of the 95 patients, 69% (n = 66) were male and 31% (n = 29) were female patients.

The etiology of solitary kidney was renal agenesia (RA) in 49% (n = 47), nephrectomy (NT) in 41% (n = 39) and, finally, multicystic renal dysplasia (MRD) with abolished renal function in 9 patients (9.4%). NT was done for renal tumor in 20 cases (21% of total), uropathy in 17 (18%), one patient undergone NT after an accident and another one following a thrombosis episode. There were no statistically significant differences between both genders. Table I shows their frequencies and gender distribution.

Mean age at diagnosis was 3.5 years (minimum: at birth; maximum: 17.9 years). MRDs had lower mean age at diagnosis: 0.04 years (minimum: at birth; maximum: 4 months) and NTs secondary to renal tumor had the highest mean age: 6.7 years (minimum: 6 months; maximum: 14.9 months). Mean age at diagnosis for RA was 2.8 years (minimum: at birth; maximum: 10.5 months).

At the time of the study, mean progression time with solitary kidney was 9.1 years (8.7 years for RA, 6.5 years for MRD, 12.5 years for uropathy-related NF, and 10.1 years for tumor-related NT). Mean follow-up time at the Pediatric Nephrology Department from the time of diagnosis was 7.9 years (7 years for RA, 6.5 y. for MRD, 11.6 y. for uropathy-related NF, and 7.7 y. for tumor-related NT).

Associated nephro-urologic abnormalities are listed in Table II. Group I was comprised by 19 patients (20%) whereas Group II included 76 patients (80%).

Patients diagnosed with MRD were those having nephro-urologic abnormalities less frequently (only 1 case). Ten out of 47 patients with RA diagnosis (21%) had associated nephro-urologic abnormalities of the remnant kidney.

Table I. Etiology of solitary kidney and gender distribution

	Boys (n)	%	Girls (n)	%	Total (n)
Renal agenesia	35	74.5	12	25.5	47
Dysplasia Multicystic Cystic	7	77.8	2	22.2	9
Nephrectomy	24	61.5	15	38.5	39

Eighteen patients had functional impairments (18.9%). A greater prevalence of functional impairments was seen among Group I patients (58%) than among group II patients (9%) ($p < 0.001$).

Microalbuminuria was the most frequently described functional impairment, with 12.6% (n = 12) of the cases, followed by decreased creatinine clearance in 5.3% (n = 5), and arterial hypertension in 3.2% (n = 3). Distribution by study groups is shown in Table III.

By etiology of solitary kidney, microalbuminuria (MA) was verified in 8.5% of RA cases and in 20.5% of NTs. No patient with MRD had MA at the time of the study.

Mean CrCl for the 95 patients was 119.6 (± 7) mL/min/1.73m^2 (SD: 33.7), median 120 mL/min/1.73m^2. Mean z score for renal size of all 95 patients was +1.6 SD. Table IV shows the mean CrCl and z scores values for the longitudinal renal size with the corresponding standard deviations (SD) by Groups I and II, and by presence or absence of associated nephro-urologic abnormalities.

Of the 5 patients presenting a significant CrCl decrease, 2 had been diagnosed with RA (4.3% of RAs) and 3 had nephrectomy (7.6% of NTs). CrCl in these patients was 49 mL/min/1.73 m^2 (SD: 26.2) (min: 8; max: 78 mL/min/1.73 m^2).

Only 3 patients had arterial hypertension at the time of the study, 2 of them with renal agenesia (4.3% of RA cases) and one with NT (2.6% of NT).

In the larger group (Group II), we found a positive correlation between z score of renal longitudinal size and CrCl ($p > 0.01$; $r = 0.3$) (Fig. 1) (with no patient in this group with CrCl < 80 mL/min/1.73m^2). In this group, we also found a positive correlation between renal size and time with solitary kidney ($p < 0.005$; $r = 0.3$) (Fig. 2). Similarly, patients with nephromegaly (renal size ≥ 2.5 SD) had higher CrCl than those without nephromegaly ($p < 0.05$) (Fig. 3). We did not find any significant difference between existence or absence of functional impairments and presence of nephromegaly, although we obtained a p value of 0.05.

Table III. Solitary kidney-associated functional impairment

	Total	Group I	Group II	p
With functional impairment	18.9%	58%	9%	> 0.001
Microalbuminuria	*12.6%*	*31.6%*	*7.9%*	*> 0.05*
Renal failure	*5.3%*	*26.3%*	*0.0%*	*> 0.001*
Arterial hypertension	*3.2%*	*10.5%*	*1.3%*	*NS*
				p = 0.052
Without functional impairment	81.1%	42%	91%	

DISCUSSION

The present study evaluates the etiology of solitary kidney, its growth and function in a group of 95 pediatric patients with solitary kidney in order to clarify the complications they may present, at what time of its course, and consequently what monitoring level these patients require throughout.

Renal agenesia has been the most frequent cause of solitary kidney in the studied sample, largely because these patients are children. It is likely that among adult patients neoplasms outweigh malformation pathologies.

The mean age at diagnosis for renal agenesia is striking (2.8 years), with a maximum at 14.9 years

Table II. Associated nephro-urologic pathology in solitary kidney patients

	RA (n = 47)	%	MCD (n = 9)	%	NT (n = 39)	%	Total (n = 95)	%
With abnormalities and/or history (Group I)	***10***	***21.3***	***1***	***11.1***	***8***	***20.5***	***19***	***20***
With nephro-urologic abnormalities								
Vesicoureteral reflux	3	6.4			2	5.1	5	5.3
Posterior urethra valves					3	7.7	3	3.2
Pyelic-ureteral stenosis	1	2.1					1	1.1
Renal dysplasia	2	4.3					2	2.1
Urethral dilation	1	2.1			1	2.6	2	2.1
Renal ectopia	2	4.3					2	2.1
Urinary bladder diverticuli			1	11.1			1	1.1
Post-radiation nephritis					1	2.6	1	1.1
History of acute pyelonephritis								
Acute pyelonephritis	1	2.1			1	2.6	2	2.1
No abnorlities	**37**	**78.7**	**8**	**88.9**	**31**	**87.2**	**76**	**80**

RA: renal agenesia; MCD: multicystic dysplasia; NT: nephrectomy.

Table IV. Mean CrCl and z score for renal longitudinal size and standard deviations (SD)

	Functional impairments		p	Nephro-urologic malformation		p	
	NO	YES		NO	YES		Total
Z score	1.8 (DT: 1.6)	1.3 (DT: 1.9)	NS	1.7 (DT: 1.5)	1 (DT: 2.2)	NS	1.6 (DT: 1.6)
CrCl	126.6 (DT: 29.7)	92.2 (DT: 37.3)	< 0.001	122.7 (DT: 25.9)	107.9 (DT: 53.6)	NS	119.6 (DT: 34.1)

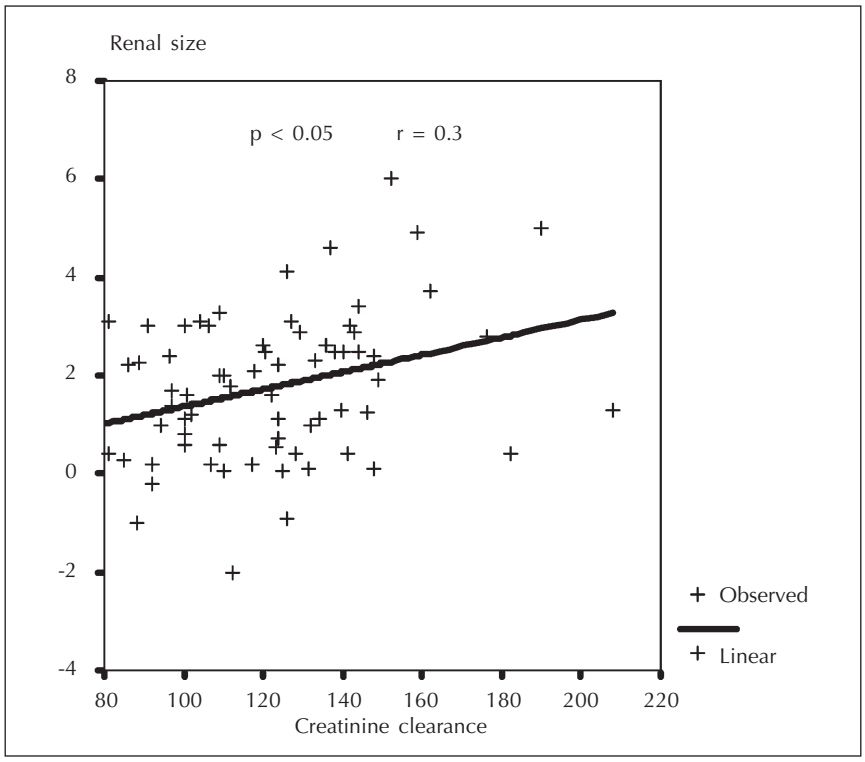

Fig. 1.—Creatinine clearance and z score for renal longitudinal size in Group II.

likely because many of these patients were borne before the current intra-uterus follow-up. Most of the cases represent an incidental finding at some abdominal imaging test. It is important since its diagnosis may infer an attitude change concerning management of urinary tract infections. In the 14 cases of unilateral renal agenesia reviewed by Reng-Ru *et al.* in 1996[8], symptoms and signs referred by patients at their first visit were flank pain (50%), dysuria (36%), associated genitourinary abnormalities (21%), and others non-urinary tract related (36%). In the 157 patients with renal agenesia and normal solitary kidney reported by Argueso *et al.,* mean age at diagnosis was 37 years (1-78 years), which highlights how unrecognized these impairments may be.

Kaneyama y cols.[12] have recently reviewed the prevalence and nature of associated contralateral nephro-urologic abnormalities in 57 cases of solitary kidney for renal agenesia, non-cystic renal dysplasia, and muticystic renal dysplasia. Of these 57 patients, 40% (23) associated some contralateral urological impairment. The most frequently associated urological impairment was vesicoureteral reflux, present in 28% of the cases, followed by frequency by stenosis of the vesicoureteral (VU) junction and of the pyelic-ureteral (PU) junction. In our patients, the presence of nephro-urologic abnormalities was observed in 20% of the cases, vesicoureteral reflux being the most frequent one, although in our clinical follow-up protocol CJNs is not routinely included as in other centers. Similarly to our series, these occur significantly less frequently in the cases with muticystic renal dysplasia.

Caslo y cols., also agreed that the nephro-urologic abnormality most frequently associated to renal agenesia was vesicoureteral reflux. The same as Song

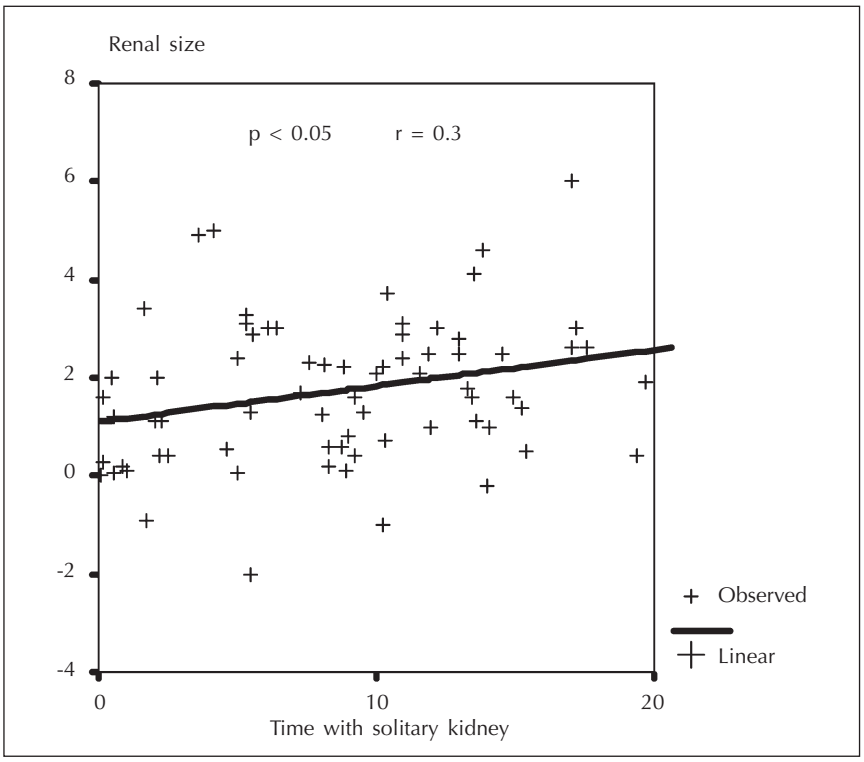

Fig. 2.—Time with solitary kidney and z score for renal longitudinal size in Group II.

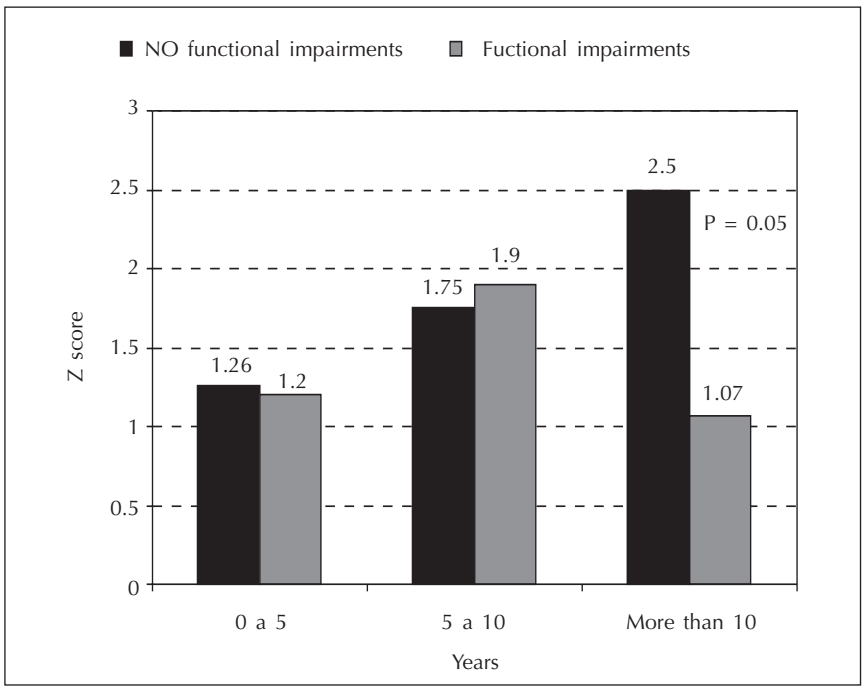

Fig. 3.—Presence of functional impairments in relation to time with solitary kidney and z score for renal longitudinal size in Group II.

et al. that found 34% of vesicoureteral reflux cases in a sample of 51 patients with renal agenesia.

In order to establish its possible influence on patients evolution, we established two study groups, according to they presented or not any of these nephro-urologic abnormalities (table II). We verified that more than half of the patients that associated any of these abnormalities had functional impair-

ment, whereas the latter was present in only 9% of the patients associating no nephro-urologic abnormality, a percentage that is still remarkable. It is noticeable that none of the patients with muticystic dysplasia had functional impairment at the time of the study. It is likely that the small number of patients with this condition included in the sample would have had an influence.

In our study, after a mean time with solitary kidney of 9.1 years, the most frequently reported renal impairment was microalbuminuria (12%), followed by creatinine clearance decrease. Only 3.2% of the patients had arterial hypertension at the time of the study, likely because it is a complication that appears later in life. Goldfarb *et al.* analyzed renal function, blood pressure, and protein excretion in a sample of 70 renal donor patients after 25 years of mean follow-up, and they observed that 19% of the patients had proteinuria (> 150 mg/24 h); blood pressure and serum creatinine values were similar to those in the general population. However, the study by Argueso[6] points to blood pressure as the most frequent functional impairment in patients with renal agenesia, affecting 4% of the 47 patients of his study group, with a mean age of 63 years (38-83 years).

In the 22 patients studied by Rugiu *et al.*[9] (9 with solitary kidney for renal agenesia and 13 with nephrectomy), the frequency of arterial hypertension was significantly higher in the group of patients with renal agenesia than in the nephrectomy group. In our patients, both microalbuminuria and CrCl decrease appeared more frequently in patients with single kidney due to nephrectomy. Taking into account that most of nephrectomies correspond to neoplasm cases, it is likely that these findings may be influenced, at leas in part, by chemotherapy and other baseline disease-associated complications, which would have been interesting to take into account in the present study.

Rugiu *et al.* considered the 10-year progression time as the critical time from which the likelihood of renal function impairment significantly increases, with occurrence of proteinuria and creatinine clearance impairment.

The work by Baudoin[7] is very illustrative as regards to renal function progression in nephrectomized patients, since the follow-up interval is wide, between 7.1 and 52.9 years. They stratified patients by gender, age, at nephrectomy > or < 4.5 years, and post-nephrectomy interval > or < 25 years, and they compared them according to glomerular filtration rate, effective plasma renal flow, creatinine clearance, SBP, DBP, proteinuria and albuminuria. They did not find any significant difference by age at nephrectomy, but they did find significant differences by post-nephrectomy interval in all studied parameters.

As for renal size, we found that in the group without associated renal malformations, there is a significant correlation between renal size and progression time with solitary kidney condition. Zerin *et al.*[16] studied remnant kidney growth post-nephrectomy in 134 patients with Wilms tumor, verifying by ultrasound a greater growth than in the control group in 50% of the patients, with no apparent relationship with the age at which nephrectomy was performed, laterality, tumor stage, or previous chemo- or radiotherapy. According to Wikstad y cols.,[17] compensatory hypertrophy of the remnant kidney after a nephrectomy for Wilms tumor is delayed for the first two years after nephrectomy.

In our patients that did not associated urological malformations, we demonstrate a direct correlation between renal size and progression time of the solitary kidney condition. Indeed, John at al. and White *et al.* already pointed out that hypertrophy of the non-involved kidney starts as early as in intra-uterus life, and that it remains during childhood, growing at an approximate rate of 0.89 cm/year, according to White.

We found a trend (NS, p = 0.05) that suggests a higher prevalence of functional impairments in Group II patients, with smaller kidneys, especially after a long period with solitary kidney. In his 1987 work, Brenbridge[20] also concluded that renal hypertrophy does not reflect the renal function impairment severity of renal disease, although it does indicate its presence.

In summary, we consider 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. It is likely that in the future mean age at diagnosis will decrease since currently most of diagnoses are done in-uterus.

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