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ABSOLUTE AND RELATIVE RENAL LENGTH IN CHRONIC KIDNEY DISEASES

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The aim of the paper is to evaluate the significance of absolute and relative renal length in the diagnoses of several chronic kidney diseases (CKDs) in which kidney size changes in different manners during the disease course.

The study included 181 patients: 35 with Balkan endemic nephropathy (BEN), 31 with diabetic nephropathy (DN), 30 with primary glomerular diseases (GN), 30 with autosomal recessive polycystic kidney disease (ADPKD), and 58 healthy controls (C). Absolute renal length was the distance between two most distant points on their poles and it was measured ultrasonographically, and relative length was obtained as the ratio of renal length and body height (kidney/body ratio, KBR). In the statistical analysis, One Way ANOVA test was used to establish the differences in absolute lengths and KBR between the studied groups; χ^2 test was used to establish the differences in the number of examinees of male and female gender; correlation and linear regression analysis were used to assess the association between age of the examinees and absolute and relative parameters of kidney size.

The obtained results demonstrated that the average lengths of the right and left kidney were highest in ADPKD and lowest in BEN group. The average values of KBR of the right and left kidney showed a trend similar to that of average absolute lengths in all groups, except in GN and DN groups, in which absolute parameters of kidney size differed significantly from relative parameters. The correlation analysis showed that a significant negative correlation between age and absolute i.e. relative parameters of kidney size existed only in BEN group, but even in this case the differences between correlation coefficients of absolute and relative length of both kidneys were not statistically significant.

Based on the obtained results, we could not establish the advantage of absolute over relative kidney length and vice versa in the studied CKDs. Further studies of larger patient samples with better gender and age distribution are therefore warranted. *Acta Medica Medianae 2015;54(2):17-23.*

Key words: *absolute length, relative length, chronic kidney disease, ultrasonography*

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Introduction

Kidney size is a significant parameter in the diagnosis and follow-up of renal diseases (1). It is most commonly reported as renal length, kidney volume, cortical thickness or volume. The most precise among the above parameters is kidney volume, since the shape of this organ commonly varies (2,3). However, the most commonly used parameter is renal length due to simple measurement and easy reproducibility (2). The most common method for kidney size measurement is ultrasonography (4).

Since kidney size physiologically also depends on body size, age and gender, these variables have to be accounted for in the assessment of the size of a diseased kidney (5,6).

In spite of a considerable interest in the topic, generally accepted nomograms for the assessment of size of a healthy and diseased kidney have not yet been devised.

So far, investigations have dealt mostly with the correlation between kidney length and body height, weight and surface area (5,6).

A number of authors have established that the kidney length/body height ratio (KBR; relative kidney length) better reflects kidney size than its absolute length. It has to be mentioned, though, that these studies enrolled populations without any

signs of kidney disease (7-9). Similar studies of patients with kidney diseases have not been published so far.

In this paper, we shall try to assess ultrasonographically the significance of absolute and relative renal length in the diagnosis of several chronic renal diseases in which kidney size changes differently during the disease course.

Examinees and methods

Our prospective ultrasonographical evaluation of absolute and relative renal length was performed at the Clinic of Nephrology, Clinical Center Niš, in the period from January to July 2014. The study included 126 patients with different chronic kidney diseases (CKD) as follows: 35 with Balkan endemic nephropathy (BEN), 31 with diabetic nephropathy (DN), 30 with primary glomerular diseases (GN), and 30 with autosomal dominant polycystic kidney disease (ADPKD). The control group (C) was composed of 55 individuals without kidney disease, hypertension and diabetes. A part of the control group was composed of the employees of the Clinic, and the rest were the patients visiting the Clinic for nonrenal abdominal complaints. The average age of the examinees was 66 years for BEN patients; 66 years for DN patients; 52 years for GN patients and 56 years for ADPKD patients. The average age of the control group subjects was 44 years.

The study was performed at the Clinic of Nephrology of the Clinical Center Niš, during the routine clinical and laboratory evaluation of the analyzed cases, and did not involve any invasive procedures.

The most important demographic and anthropometric parameters, such as age, gender, weight and height, were recorded for all the examinees. Kidney function, expressed by glomerular filtration rate was assessed by endogenous creatinine clearance values obtained using the MDRD GFR equation; the function was considered to be reduced if below 60ml/min/1.73m^2 (10).

Both kidneys were ultrasonographically examined by the same examiner using the Acuson x300 ultrasound system by Siemens, with 3.5MHz convex probe. Prior to examination, the patients had been fasting and their bladders had been emptied in order to prevent hydration-induced renal length increase.

Absolute renal length is the distance between two most distant points on their poles measured in four positions (supination, pronation, and left and right decubitus) and taken as the mean value for the purpose of the study. Relative renal length (KBR index) is the quotient of absolute renal length (in mm) and body height (in cm).

The data were presented as mean values and standard deviations and as a median with range.

The One Way ANOVA test was used to establish the differences in absolute lengths and KBR between the observed groups; the Chi square (χ^2) test was used to establish the differences related to the number of examinees of male and female gender; correlation and linear regression analysis were used to examine the association of age of the studied cases and their absolute and relative kidney size parameters.

The results are presented in tables and graphs.

Results

The descriptive statistics of absolute and relative kidney size parameters in the studied groups is presented in Table 1.

Based on χ^2 testing of the results, it was established that there were no statistically significant differences in the studied groups regarding gender prevalence of the patients (χ^2=8.52; n=18; df=4; p=0.074).

The results of One Way ANOVA test demonstrated that the average age of the studied groups was statistically significantly different (F(4.175)-=20.98; p<0.001). Using the Student-Newman-Keuls post hoc test, it was found that the average age of BEN and DN groups was statistically significantly higher (p<0.05) compared to other groups, while the average age of GN and ADPKD groups did not show statistically significant difference (p>0.05). The average age of the control group was significantly lower (p<0.05) than those in other studied groups.

The results of creatinine clearance test as a parameter of renal function status showed that its average value (Figure 1) was, as expected, significantly different across the studied groups (F(4.176)=37.18; p<0.001). The values of this parameter in controls were significantly higher (p<0.05) than those in ADPKD, GN, DN and BEN groups. The values in GN group were lower than those in controls, but significantly higher (p<0.05) than those in ADPKD, DN and BEN groups. Finally, the average values in ADPKD, DN and BEN groups were significantly lower (p<0.05) than those in controls and in GN group, but they did not show statistically significant differences among themselves (p>0.05).

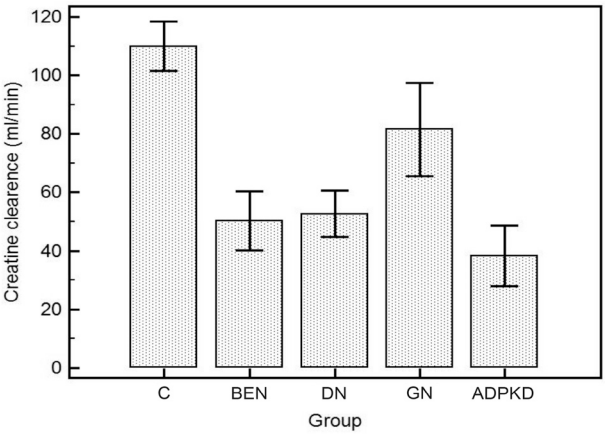

Figure 1. Mean creatine clearance of the analyzed age groups

Table 1. Descriptive statistics of the absolute and relative kidney's size parameters in evaluated groups

Parameter	N	Mean	SD	Median	Minimum	Maximum
Control (n=55)						
Age	55	44.38	15.68	44	20	77
Creatine clearence (ml/min)	55	109.98	31.07	105.40	50.10	200.00
Left kidney length (mm)	55	111.94	7.45	112.00	91.00	125.00
Right kidney length (mm)	55	110.74	8.47	110.00	91.00	135.00
KBR left	55	0.066	0.004	0.066	0.057	0.077
KBR right	55	0.066	0.005	0.067	0.055	0.076
BEN (n=35)						
Age	35	65.54	8.38	66	48	84
Creatine clearence (ml/min)	35	50.26	29.39	43.70	10.20	139.18
Left kidney length (mm)	35	97.63	11.29	100.00	70.00	116.00
Right kidney length (mm)	35	94.74	12.42	93.00	76.00	130.00
KBR left	32	0.061	0.008	0.062	0.043	0.075
KBR right	32	0.058	0.008	0.058	0.046	0.082
DN (n=31)						
Age	31	66.29	7.53	66.00	38.00	77.00
Creatine clearence (ml/min)	31	52.73	21.47	49.60	18.80	119.30
Left kidney length (mm)	31	116.77	12.17	120.00	85.00	140.00
Right kidney length (mm)	30	115.10	10.54	115.00	95.00	135.00
KBR left	31	0.069	0.008	0.069	0.054	0.093
KBR right	30	0.068	0.006	0.068	0.052	0.084
GN (n=30)						
Age	30	52.07	15.57	53.00	26.00	83.00
Creatine clearence (ml/min)	30	81.63	42.68	83.75	19.50	183.90
Left kidney length (mm)	30	126.14	11.62	124.00	104.00	159.00
Right kidney length (mm)	30	124.52	11.16	122.50	107.00	146.00
KBR left	30	0.072	0.005	0.071	0.064	0.084
KBR right	30	0.071	0.006	0.071	0.060	0.083
ADPKD (n=30)						
Age	30	55.97	13.89	59.00	23.00	73.00
Creatine clearence (ml/min)	30	38.31	27.88	33.20	5.00	95.00
Left kidney length (mm)	30	172.60	31.76	170.00	125.00	260.00
Right kidney length (mm)	30	168.77	40.84	160.00	120.00	300.00
KBR left	30	0.101	0.017	0.101	0.071	0.141
KBR right	30	0.099	0.022	0.095	0.068	0.162

The average length of the left kidney differed significantly between the studied groups ($F(4.176)=102.30$; $p<0.001$) (Figure 2A). It was significantly higher ($p<0.05$) in patients with ADPKD than in other groups, while in BEN group it was significantly lower ($p<0.05$) compared to other groups. Control group had significantly lower values ($p<0.05$) of renal length compared to ADPKD and GN groups, but significantly higher ($p<0.05$) than BEN group. The same holds for the average length of the right kidney (Figure 2A).

The average value of KBR of the left kidney (Figure 2B) showed a tendency similar to that for the average length of the left kidney ($F(4.173)=98.76$; $p<0.001$). It was statistically significantly higher ($p<0.05$) in ADPKD group than in other groups. The average value in GN group was significantly higher ($p<0.05$) compared to those in control and BEN groups. In DN group, the average KBR value was significantly higher ($p<0.05$) only when compared to BEN group.

The average KBR of the right kidney (Figure 2B) showed some statistically significant differences between the observed groups ($F(4.172)=66.34$; $p<0.001$). It was statistically significantly higher ($p<0.05$) in ADPKD group than in other groups. The values of KBR in GN, DN and control groups were significantly higher ($p<0.05$) than in BEN group.

The results of One Way ANOVA analysis of the absolute and relative parameters of kidney size could indirectly lead us to the conclusion that the studied groups differed to a more significant degree one from another in absolute kidney length than in KBR. This especially holds true for the cases in GN and DN groups.

Correlation analysis was performed to assess the significance of association between age and absolute and relative morphometric kidney

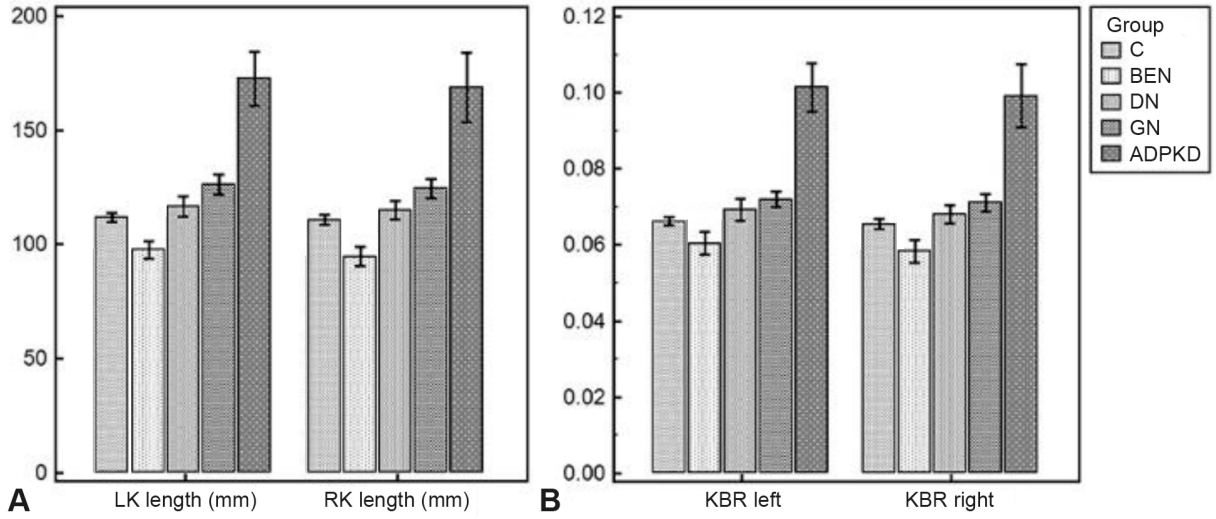

Figure 2. **A –** Absolute parameters of the right and left kidney's length; **B** – relative parameters of the right and left kidney's length

parameters, as well as their association with creatinine clearance as a parameter of renal function.

In control, DN and GN groups, a negative correlation was observed between the values of morphometric kidney parameters and age, even though without statistical significance ($p>0.05$). In ADPKD group, there was a positive correlation between the above variables, again without statistical significance. In the above groups, there was a significant negative correlation between age and creatinine clearance.

The correlations between absolute and relative parameters of kidney size and age were significantly negative in BEN group (Table 2). Linear correlation coefficient for the left kidney length was $R=-0.58$ ($n=35$; $p=0.0002$), and $R=-0.58$ ($n=35$; $p=0.0003$) for the right kidney length. Its value was slightly lower for the left ($R=-0.48$; $n=32$; $p=0.006$) and right KBR ($R=-0.51$; $n=32$; $p=0.003$). The comparison of coefficients of correlation of left kidney length and left KBR with age did not reveal any statistically significant differences ($z=0.60$; $p>0.05$), which was established as well for coefficients of correlation of right kidney length and right KBR with age ($z=0.41$; $p>0.05$). In this group, a significant negative correlation was found between age and creatinine clearance ($R=-0.63$; $n=35$; $p=0.0001$). The abso-lute and relative parameters of kidney size in this group correlated significantly with creatinine clearance.

Linear regression analysis was performed in order to estimate the impact of age on the values of absolute and relative parameters of kidney size in patients with BEN.

Age has a significant impact on the length of left and right kidney in patients with BEN. It is also a significant predictor of relative parameters of kidney size in BEN patients. However, the variance of left (23%) and right (26%) KBR as explained by the model during the process of aging is lower than that for absolute parameters of the left (34%) and right (34%) kidneys.

Discussion

Chronic renal diseases in their natural course induce changes in kidney size in different manners (11,12). Many of them (glomerulopathies, tubulo-interstitial diseases, etc.) are associated with permanent reduction of kidney size (13,14). DN is characterized by initial nephromegaly, followed by a continual discrete reduction of kidney size (11-13). ADPKD, from its earliest stages, is characterized by kidney enlargement; in final stages, kidneys can be very large (15-17). The chronic course of amyloidosis and human immunodeficiency virus-associated nephropathy is also characterized by kidney enlargement (11,13).

In view of the fact that kidney size also physiologically depends on body size, gender and age (5,6), these factors have to be taken into account in the assessment of size of an affected kidney. In addition to its size, the quality of the parenchyma and vascularization status have to be analyzed as well (12).

Most commonly used and sometimes the only available imaging method for the evaluation of a diseased kidney is ultrasonography. Ultrasonography is a simple, noninvasive, and cost-effective method that does not involve ionizing radiation exposure, special preparation procedures, use of medication or contrast media, with wide availability and easy reproducibility (4).

Renal length and renal volume are the most important parameters in the diagnosis and surveillance of a renal disease. However, renal length is the most commonly used parameter due to easy measurement and reproducibility (2). Since it usually cannot be directly related to most important anthropometric parameters (height, weight, body surface), nor to age or gender, its

significance is rather questionable. Numerous studies have shown that renal length correlates positively with the above anthropometric parameters (5,6), being markedly greater in men compared to women and diminishing with advancing age, especially after 60 years of age (7,8). According to the literature data, the use of KBR index may eliminate the differences related to height and gender, and its wider use in clinical practice is therefore recommended (7,8). That was the reason why in this paper we simultaneously tested the significance of two parameters of renal length, absolute and relative length, in our evaluation of four chronic kidney diseases.

Gender distribution in the studied groups was relatively balanced, and average age was statistically significantly unbalanced. The average value of creatinine clearance varied significantly across the studied groups as well, being reduced in all groups except the control group.

The results of investigation of absolute and relative renal length in this paper (Figure 2) demonstrated a similar trend of significance of differences in these parameters between the studied groups. The only more significant differences were those in absolute length between GN and DN groups related to relative length of the same groups. Such trends in examined morphometric parameters between the studied groups were the consequence of nature of these diseases, i.e. their morphological substratum and functional status, as well as the average age. Other authors have also reported the impact of nature of the disease on kidney size (11,12). It has also been shown that renal length is reduced with diminished creatinine clearance, most intensely between 70 and 30 ml/min (18). Renal length is reduced with ageing as well (5,7,8). The explanation of the phenomenon may be sought in the fact that the number of nephrons is progressively reduced with the progression of CKDs and advancing age (19,20). Such a type of changes would correspond to BEN (21). The group with DN had a somewhat higher value of length compared to BEN and controls, which corresponded to initial nephromegaly in the course of this disease, as described by other authors as well (11,16). Compared to DN group, slightly higher values of renal length were encountered in GN group, which was the consequence of a better functional status of the kidneys and lower average age of the group. ADPKD group had highest values of renal length, which was not surprising in view of the nature of this hereditary renal disease and lowest functional reserve in this group. Similar findings have been reported by other authors as well (15-17). Opposite to the absolute, kidney's relative length parameters did not detect the differences between GN and DN groups and this might confirm their reduced diagnostic sensitivity.

Since the average values of age in the examined groups were significantly different, and age (particularly after 60 years) had a considerable impact on renal length (5,7), in this paper we made use of the correlation and linear regression analysis to evaluate the significance of correlation between age of the examinees in the studied groups and absolute and relative renal lengths, as well as their association with creatinine clearance as an indicator of renal function. The observed negative correlation of morphometric parameters in control, DN and GN groups with advancing age, although without statistical significance, was in concord with other authors' findings (5,7,13). In case of BEN, the analyzed morphometric parameters were in a significant negative correlation with age and creatinine clearance, which could be possibly explained by the highest average age in this group (Table 1 and 2). However, it was interesting that the correlation coefficients of absolute parameters did not differ statistically significantly from the corresponding coefficients of relative parameters in this group. The correlation of examined morphometric parameters in ADPKD group was positive with age, in contrast to other groups, although without statistical significance.

Using linear regression analysis to establish the influence of age on the studied morphometric parameters in patients with BEN, it was found that the variances of left and right KBRs explainable by aging were lower than the corresponding values for absolute parameters which may additionally confirm their lesser diagnostic sensitivity.

Conclusion

Based on the results of this study, the following conclusions can be drawn: One Way ANOVA testing revealed markedly higher values of absolute and relative parameters of size of the left and right kidney in ADPKD, while these values were lowest in BEN group. The values of these parameters in GN, DN and control group were lower compared to ADPKD cases and higher than those in BEN group. Moreover, a similar tendency of significance of the differences was observed across the studied groups concerning absolute and relative parameters of kidney size. The absolute parameters of kidney size were significantly different from relative parameters solely in GN and DN groups.

Since the average age of the studied groups varied significantly across the groups, correlation analysis was utilized to assess its association with absolute and relative parameters of kidney size. A significant negative correlation between age and absolute, as well as relative, parameters of kidney size, was observed only in BEN group. Additionally, the difference in correlation coefficients of absolute and relative length of the right, and left kidney as well, was not statistically significant. By way of linear regression, a slightly greater influence of age on absolute parameters of kidney size was found in this group.

Based on the above facts, any advantage of absolute versus relative renal length (and vice versa) could not be established in the studied groups. Therefore, a valid evaluation of the size of

a diseased kidney has to involve, in addition to its functional status, the most relevant anthropometric parameters (height, weight and body surface), gender and age of the patient. It is therefore necessary to undertake further studies on larger patient samples and with more appropriate gender and age structure.

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APSOLUTNA I RELATIVNA DUŽINA BUBREGA KOD HRONIČNIH BUBREŽNIH BOLESTI

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Cilj rada bio je da se ispita značaj apsolutne i relativne dužine bubrega u dijagnostici nekoliko hroničnih bubrežnih bolesti (HBB) kod kojih se veličina bubrega menja na različit način tokom njihove evolucije.

Istraživanjim je obuhvaćen 181 slučaj i to 35 sa balkanskom endemskom nefropatijom (BEN), 31 sa dijabetesnom nefropatijom (DN), 30 sa primarnim glomerulskim bolestima (GN), 30 sa autozomno dominantnom policističnom bolešću bubrega (ADPKD) i 58 zdravih kontrolnih slučajeva (K). Apsolutna dužina bubrega je predstavljala distancu između dve najudaljenije tačke na njihovim polovima i određivana je ultrazvučnom metodom, a relativna dužina je dobijena kao odnos dužine bubrega i visine tela (kidney/body ratio, KBR). U statističkoj analizi korišćeni su One Way Anova test za utvrđivanje razlika u apsolutnim dužinama i KBR između posmatranih grupa, χ^2 test za utvrđivanje razlika između broja ispitanika muškog i ženskog pola, a korelaciona i linearna regresiona analiza u cilju ispitivanja veze između starosti ispitanika i apsolutnih i relativnih parametara veličine bubrega.

Dobijeni rezultati pokazuju da su prosečne apsolutne dužine desnog i levog bubrega bile najviše kod ADPKD, a najniže kod BEN grupe. Prosečne vrednosti KBR desnog i levog bubrega ispoljavale su sličan trend kao i prosečne apsolutne dužine u slučajevima svih ispitivanih grupa, izuzev kod GN i DN grupe, kod kojih su se apsolutni parametri veličine bubrega značajnije razlikovali u odnosu na relativne parametre. Korelaciona analiza je pokazala da značajna negativna korelacija između starosti i apsolutnih, odnosno relativnih parametara veličine bubrega, postoji samo u BEN grupi, ali da ni u tom slučaju, razlike između koeficijenata korelacije apsolutne i relativne dužine oba bubrega nisu bile statistički značajne.

Na osnovu dobijenih rezultata kod ispitivanih HBB nije se mogla ustanoviti prednost primene apsolutne u odnosu na relativnu dužinu bubrega i obratno. Stoga su neophodna dalja ispitivanja na većem uzorku ispitanika i sa boljom polnom i starosnom strukturom.
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Ključne reči: *apsolutna dužina, relativna dužina, hronična bubrežna bolest, ultrazvuk*