

Relationship between ultrasonographically determined kidney volume and progression of chronic kidney disease

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ABSTRACT

Aim To investigate a correlation between calculated creatinine clearance as a measure of kidney's functional abilities and ultrasonographically determined kidney volume, which represents actual size of the kidney, in fact residual renal mass in chronic kidney disease, in order to determine possibilities of ultrasound as a diagnostic method in diagnosing and follow up of chronic renal disease.

Methods Prospective study included 150 patients with registered demographic and anthropometric data, and also with relevant laboratory tests of renal function. Longitudinal diameter, thickness and width of the kidney and renal volume calculated according to the Dinkel's formula were measured by ultrasound. A correlation between the measured volume of the kidneys and calculated creatinine clearance was done by the Spearman method, with statistical significance of $p < 0.05$.

Results Statistically significant correlation between the estimated creatinine clearance values and the average of the calculated values of kidney volume was found ($p < 0.01$). Average value of the kidneys' volume showed a linear decrease with the progression of chronic kidney disease: the kidney volume in the control healthy group was 171.7 ± 32.6 mL (95.22- 229.59 mL), and in the subjects classified in stage IV it was 74.7 ± 24.6 mL (43.22-165.65 mL).

Conclusion Calculated volume of kidney well correlated with creatinine clearance as a measure of functional ability of the kidneys and with the stage of chronic renal disease. It can be used in clinical practice for monitoring of chronic kidney disease in conjunction with other clinical and laboratory parameters.

Key words: ultrasound, kidneys, CKD

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INTRODUCTION

Chronic kidney disease is a major public health problem due to the increasing incidence and prevalence, resulting number of undesirable outcomes of this disease worldwide (1,2). This disease is characterized by the destruction of renal mass with irreversible sclerosis and loss of nephrons, which results in the progressive decline in renal function which reflecting glomerular filtration rate (3,4). The most accurate parameter for determining the functional status of the kidneys is to calculate nephrons' number, which represents the total number of nephrons in the kidneys (5-8). Studies have shown that there is a significant correlation between renal masses and nephrons' number, in fact renal mass is directly proportional to this number (8). In other words, the above studies have shown that there is a direct correlation between the size of the kidneys and number of nephrons (9), and that there is a direct correlation between the size of the kidney and its functions (10). Measurement of renal mass and nephrons' number can only be done *ex vivo* (8). On the other hand, the renal volume is proportional to renal masses and as such can be used as an *in vivo* surrogate for nephron number as in the healthy population and in the population of patients diagnosed with chronic kidney disease (11). Ninan et al. have shown that the size of the kidney measured by ultrasound, in comparison with other radiological methods, best corresponded to the size of the kidney measured during the surgical procedure (12), which is considered to be the gold standard for measuring the size of the kidney (13).

Numerous authors have proven that in normal population the actual size of the kidney best correlated with volume of the kidney measured by ultrasound, kidney volume is the most accurate measure of the actual size of the kidney (13,14). Studies on the relationship between the kidney volume measured by ultrasound, as a parameter of remained functional renal mass in patients suffering from chronic kidney disease and the size of creatinine clearance, as the parameter of renal function, could contribute significantly to the understanding of the relationship that exists between changes in morphological characteristics and functional status of the kidneys within chronic renal disease (14).

Given the great availability of ultrasound dia-

gnostics in routine clinical practice and a large number of patients with chronic kidney disease, we decided to examine the usefulness of ultrasonographically determined kidney volume in the evaluation of chronic kidney disease.

The aim of this study was to assess the possibility of using ultrasonographically determined kidney volume as an indicator for diagnosing and monitoring stages of progression of chronic kidney disease.

The results of this study should be of benefit primarily to clinicians - nephrologists for diagnosing and monitoring the progression of chronic kidney disease. The numerical expression of residual renal mass and of kidneys volume reduction during the progression of kidney disease should stimulate patients to adopt healthier lifestyles and follow up the guidelines for patients suffering from chronic kidney disease.

PATIENTS AND METHODS

Patients and study design

One-year prospective study (January 2011– January 2012) included 150 patients admitted to the Nephrology Clinic of University Clinical Center Sarajevo (UCCS), Sarajevo, Bosnia and Herzegovina, or visited in the Nephrology Outpatient Department of this Clinic. Patients were divided into 5 groups, with 30 patients in each group. Patients diagnosed with chronic kidney disease by a referring nephrologist were classified in the groups 1-4 according to the chronic kidney disease stage based on the value of estimated creatinine clearance according to the criteria of Kidney Disease Outcomes Quality Initiative (K/DOQI) (1). The group 5 consisted of healthy individuals (control group) with demonstrated absence of chronic kidney disease according to the results of complete laboratory analysis performed as routine control of renal function at the Nephrology Outpatient Department. Patients in the terminal stage of chronic kidney disease (dialysis population), kidney transplant, unstable renal function, patients diagnosed with diabetic nephropathy and polycystic kidney disease (diseases that lead to nephromegaly with simultaneous reduction in the functional ability of the kidneys), patients with hydronephrosis, anomalies of the number of kidneys, kidney tumors, decompensated concomitant disease (liver, heart, etc.), extremely obese

patients (body mass index, BMI \geq 40 kg / m²) were excluded from the study.

Methods

Serum creatinine concentration was determined by using a modification of the kinetic Jaffe reaction (15) on laser Nephelometer BN II machine (Siemens AG, Erlangen, Germany).

Assessment of creatinine clearance was calculated with Cockcroft-Goult formula (16).

After detailed laboratory and clinical management of patients and their classification in the different stages of chronic kidney disease (CKD) according to the criteria of Kidney Disease Outcomes Quality Initiative (K/DOQI) (1), ultrasound examination was performed.

All patients were examined with ultrasound machine GE Voluson 730 PRO (GE medical Systems, Zipf, Austria) at the Radiology Clinic, University Clinical Center Sarajevo, with convex probe of 3.5 MHz in the grey scale and real – time. The examinations were done in patients’ supine and lateral position. Ultrasound measurements were registered on the scans depicting the maximum orthogonal, longitudinal and transverse cross-section of the kidney. All the examinations were made by the same radiologist. Volume of the kidney was calculated using the formula by Dinkel et al.: $0,523 \times L \times W \times (D1 + D2) / 2$ (17). Because the kidneys are paired organs, which together contribute to the clearance of creatinine, after calculating the volume (V) of each kidney of each patient according to the Dinkel’s formula, their median value was calculated by the formula: $V = (V1 + V2) / 2$.

Statistical analysis

The test results were analyzed using descriptive statistics, which comprises determining the mean value (\bar{X}), standard deviation (SD) and standard error (SEM). Comparisons of mean values between the groups were performed using Student t-test for variables with normal distribution, or the Mann-Whitney test (U) for variables that do not have a normal distribution. Statistical significance of differences in mean values between the samples was determined using the Student t-test (t) and ANOVA (F) methods for variables with normal distribution, and Mann-Whitney test

for variables that do not have a normal distribution. For categorical variables χ^2 test was used. To estimate the correlation between the measured volume of the kidneys and the calculated creatinine clearance Spearman’s nonparametric bivariate correlation was used. Accepted statistical significance was $p < 0.05$.

RESULTS

Of the total 150 patients, 71 (47%) were males and 79 (53%) females. The average age of the patients was 55.43 years.

Analysis of the average value of the kidneys volume showed a linear decrease of the kidneys volume with the progression of CKD: the subjects in the control group had a maximum value of 171.7 ± 32.6 mL (95.22- 229.59 mL), and the patients classified in stage IV had at least 74.7 ± 24.6 mL (43.22-165.65 mL), ($p=0.0001$) (Table 1).

An analysis of correlation coefficients showed that there was a statistically significant correlation ($p < 0.01$) between the calculated values of creatinine clearance and the measured volume of the kidney: patients classified into a higher stage of chronic kidney disease had lower estimated creatinine clearance and a smaller volume of the kidney. In the control group the average creatinine clearance was 127.767 (mL/min) and the average kidney volume was 171.72 mL. In the stage 1 group the average creatinine clearance was 118.076 (mL/min) and the average kidney volume was 138.86 mL, in the stage 2 group 70.958 (mL/min) and 113.63 mL, in the stage 3 group 49.010 (mL/min) and 91.69 mL, and in the stage 4 group 23.075 (mL/min) and 74.68 mL, respectively (Table 1).

Table 1. Average size of the kidney volume, creatinine and creatinine clearance in different stages of chronic kidney disease (CKD)

Group (No) of patients	Kidney volume (minimum/maximum) (mL) $p < 0.01$	Creatinine (minimum/maximum) (μ mol) $p < 0.01$	Creatinine clearance (mL/min) $p < 0.01$
Control (30)	171.7163 (95.22/229.59)	73.47 (49/95)	127.767 (91.4/195.3)
Stage I (30)	138.8557 (105.61/167.55)	72.30 (40/140)	118.076 (90.5/177.9)
Stage II (30)	113.6253 (73.13/154.03)	103.87 (54/162)	70.958 (60.6/88.2)
Stage III (30)	91.6907 (64.15/128.72)	142.33 (81/269)	49.010 (32.9/58.5)
Stage IV (30)	74.6783 (43.22/165.65)	321.70 (162/610)	23.075 (14.3/29.7)
Total (150)	118.1133 (43.22/229.59)	142.73 (40/610)	77.777 (14.3/195.3)

DISCUSSION

The average value of kidney volume in subjects classified in the control (healthy) group was 171.7 ± 32.6 mL, and this value can be considered as a reference value for the volume of kidneys in healthy population (18). Statistical analysis of average values of the kidney volume showed a linear decrease in volume of the kidney with chronic kidney disease progresses, so the patients who were in the stage 1 of CKD had the highest, while the patients classified into the CKD stage 4 had a smallest kidney volume. The obtained data are consistent with data from the literature reporting kidney volume as a predictor of renal mass and the number of nephrons which are not destroyed during the course of chronic kidney disease (9-11,13). It is therefore considered that the volume of kidney reflects remaining functional ability of the kidneys measured by estimated creatinine clearance values (14).

In Bosnia and Herzegovina the exact number of patients with all stages of chronic kidney disease is unknown. The only precise data are related to the number of patients with end stage renal disease (ESRD). According to the Renal Registry of Bosnia and Herzegovina, the number of ESRD prevalent patients in Bosnia and Herzegovina was increased 66.2% in the 2002-2012 period (1.531 and 2.544 prevalent ESRD patients) (19). The incidence of ESRD patients in Bosnia and Herzegovina is in line with the European average, and the increment of number of prevalent ESRD patients in Bosnia and Herzegovina is to be expected.

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According to K/DOQI criteria, CKD stage 1 is characterized by preserved renal function, i.e. measuring only creatinine clearance does not allow the diagnosis and for this purpose we use other indicators of kidney damage, such as pathologic findings of urine and imaging examination. Ultrasonographically established kidney volume reduction can therefore be used as one of the criteria for the diagnosis of CKD stage 1 (1).

Since the ultrasound is one of the most commonly used screening methods, the pathologic kidney volume values should indicate the need for the evaluation of renal function in terms of creatinine clearance measurements in asymptomatic patients, given the fact that kidney disease is silent for long time and does not give symptoms. Our findings confirmed that a measured volume of kidney by ultrasound correlates well with the stage and progression of chronic kidney disease, suggesting this method can be reliably used in clinical practice for the diagnosis, evaluation and monitoring of chronic renal disease. All patients with diagnosed CKD regardless of the stage should have renal ultrasound including the measurement of kidney volume performed as a part of normal follow-up every 6 months.

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Conflict of interest: None to declare.

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Odnos ultrazvučno određenog volumena bubrega i progresije hronične bubrežne bolesti

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SAŽETAK

Cilj Ispitati korelaciju između izračunatog kreatinin klirensa kao mjere funkcionalne sposobnosti bubrega i ultrazvučno određenog volumena bubrega koji predstavlja stvarnu veličinu bubrega, tj. ostatnu renalnu masu u sklopu hronične bubrežne bolesti, kako bi se utvrdile mogućnosti ultrazvuka kao dijagnostičke metode za dijagnosticiranje i praćenje hronične bubrežne bolesti.

Metode Prospektivna studija obuhvatila je 150 pacijenata kojima su registrirani demografski i antropometrijski podaci, te rezultati laboratorijskih ispitivanja bubrežne funkcije. Ultrazvučno su izmjereni longitudinalni dijametar, debljina i širina bubrega, te izračunat volumen bubrega koristeći Dinkelovu formulu. Korelacija između izmjerenog volumena bubrega i izračunatog kreatinin klirensa ispitana je korištenjem Spearmanove metode uz statističku značajnost $p < 0.05$.

Rezultati Uočena je statistički značajna korelacija između izračunatog kreatinin klirensa i prosječnih izračunatih vrijednosti volumena bubrega ($p < 0.01$). Prosječne vrijednosti volumena bubrega pokazivale su linearno smanjenje s progresijom hronične bubrežne bolesti: volumen bubrega u kontrolnoj skupini zdravih ispitanika je iznosio $171,7 \pm 32,6$ mL ($95,22 - 229,59$ mL), dok je u skupini ispitanika klasificiranih u stadij IV iznosio $74,7 \pm 24,6$ mL ($43,22 - 165,65$ mL).

Zaključak Izmjereni volumen bubrega dobro korelira s kreatinin klirensom kao mjerom funkcionalne sposobnosti bubrega, tj. sa stadijem hronične bubrežne bolesti. Zajedno s drugim kliničkim i laboratorijskim parametrima može se koristiti u kliničkoj praksi za praćenje hronične bubrežne bolesti.

Ključne riječi: ultrazvuk, bubrezi, CKD