

Features of the indices of the resistance index of vasorenal vessels in monitoring the progression of chronic kidney disease

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Abstract Objective of the study. Analysis of the relationship between the resistance indices (IR) of the main and intrarenal renal arteries, measured by ultrasound Doppler ultrasound (DUS), and clinical and laboratory data, as well as the identification of their prognosis in assessing the progression of chronic kidney disease (CKD).

Materials and methods. The study included 106 patients with CKD, divided into groups with glomerular or interstitial diseases. At the first hospitalization, the glomerular filtration rate (GFR) calculated using the CKD-EPI formula, the degree of proteinuria (PU), the size of the kidneys, the thickness of the renal parenchyma and the parenchymopielic index, IR of the main and intrarenal vessels were determined. The average duration of observation of patients was 12 ± 2.64 months. Upon readmission, the rate of GFR decline was analyzed.

Results. IR of the main and intraparenchymal vessels depends on the patient's age and pulse pressure. In the group of patients with glomerular diseases, IRs are associated with GFR and PU, while in the group of interstitial diseases, with the size and structure of the kidneys. IR of interlobar arteries (MA) is the most sensitive predictor of deterioration of renal function with a cut-off value of 0.65, comparable to the predictive value of PU.

Conclusion. Indicators of the resistance index of vasorenal vessels in the main and intraparenchymal vessels can be considered as a predictor of the progression of renal function.

Keywords: Duplex scanning, Doppler sonography, resistance index, chronic kidney disease.

The high standardized mortality rate in patients with chronic kidney disease - CKD (70 per 1000 patients) necessitates continuous improvement of approaches to identifying signs of kidney damage in its early stages [1]. Modern diagnostics of CKD includes the following parameters: glomerular filtration rate (GFR), albuminuria / proteinuria, changes in urine sediment and electrolyte balance due to tubular damage, nephro biopsy data, a history of transplantation, as well as features of changes in the structure and size of the kidneys according to ultrasound) [2-4]. At the same time, in the initial diagnosis of CKD, these data do not allow for a sufficiently accurate characterization of the severity of kidney damage and the degree of nephrosclerosis, especially since a kidney biopsy for this purpose is not always possible. In this regard, the search for clinical and laboratory factors of an

unfavorable prognosis of CKD is justified. According to a number of studies, these include the patient's age, the severity of proteinuria (PU), a decrease in GFR, and the presence of arterial hypertension (AH) [4-6]. In addition, impairment of intrarenal hemodynamics contributes greatly to the progression of CKD. One of the methods of visual assessment, which makes it possible to characterize the features of intrarenal blood flow, is Doppler ultrasound (USDG) of the renal vessels, which makes it possible to determine the calculated indices, in particular the resistance index (IR), which reflects the resistance of the muscle layer of the vessel wall. In order to clarify the diagnostic value of USDG in determining the rate of progression of CKD, we compared the clinical and laboratory parameters with the IR values of the main and intrarenal arteries.

Materials and methods

The retrospective study included 106 patients with signs of CKD who were under observation at the Department of Nephrology, Bukhara Regional Multidisciplinary Medical Center from February 2020 to November 2021. Among them, 50 (47.2%) were women and 56 (52.8 %) men; the average age was 45.4 ± 14.6 years. All patients were divided into two groups of comparable size: 52 with a predominance of glomerular pathology (chronic glomerulonephritis - CGN) and 54 with tubulointerstitial injuries, in particular, 18 patients suffered from tubulointerstitial nephritis (TIN), 8 - chronic pyelonephritis, 12 - associated kidney damage disease, 10 - with antiphospholipid syndrome, the remaining - polycystic kidney disease. At the first hospitalization, the clinical, instrumental and laboratory data of the patients were analyzed: age, daily PU, GFR (calculated using the CKD-EPI formula), systolic and diastolic blood pressure, pulse pressure (PP), IR according to USDG data. To determine the rate of progression of renal failure over time, GFR was assessed. A decrease in GFR by $10 \text{ ml} / \text{min} / 1.73 \text{ m}^2$ was regarded as a decrease in renal function. The observation period of patients was 14 ± 2.64 months. Standard ultrasound and USG were performed on all 106 patients using an expert class ultrasound machine Sonoline Antares (Siemens Medical Solutions) using a transducer with a frequency of 1-5 MHz. The length and transverse size of the kidneys, the thickness of the renal parenchyma were measured with subsequent calculation of the average values. The parenchymopielic index (PIP) was calculated as the ratio of the size of the parenchyma to the size of the central echo complex, which includes the calyx-pelvic system with adipose tissue, blood and lymphatic vessels [7]. IR is the ratio of the difference between the maximum systolic velocity and the end diastolic velocity to the maximum systolic velocity, determined for the renal artery (PA), interlobar arteries (MA), and renal arc arteries. For comparative analysis of the correlation in independent samples between quantitative data, Pearson's test was used (where $p < 0.05$ was assessed as a statistically significant result). When calculating the correlation coefficients, the average value of the IR of the renal arteries was taken on the basis that this indicator varies slightly between organs [8].

To assess the prognostic significance of IR of PA, segmental arteries (SA) and MA, their sensitivity and specificity, ROC analysis was used with the construction of curves of the same name.

To determine the factors influencing intrarenal hemodynamics, a stepwise multivariate regression analysis was used.

Results

When analyzing the relationship of IR with clinical and laboratory parameters in all patients, it was revealed that IR of renal vessels is in direct proportion to the age of patients and PD (Table 1). IR of the PA orifice and intrarenal arteries are inversely related to GFR (see Table 1), no statistically significant relationship with the severity of PU was found.

Due to the fact that corticomedullary differentiation of the kidney structure is impaired in polycystic disease, patients with cystic changes in the kidneys were excluded from the sample to correctly assess the relationship between IR and kidney size. It turned out that the IR of the mouth of the PA ($r = 0.370$; $p = 0.006$) and CA ($r = 0.377$; $p = 0.007$) is in direct relationship with the length of the kidney, while MA is inversely ($r = -0.564$; $p = 0.0001$). The lateral size of the kidney directly positively correlated with the IR of the PA ($r = 0.357$; $p = 0.009$), CA ($r = 0.521$; $p = 0.0001$) and MA ($r = 0.377$; $p = 0.005$). For the analysis of structural changes, the thickness of the renal parenchyma and PPI were assessed. In feedback with the index of the thickness of the renal parenchyma and the values of PPI, there were IR PA ($r = -0.440$; $p = 0.004$; $r = -0.392$; $p = 0.011$), CA ($r = -0.361$; $p = 0.024$; $r = -0.334$; $p = 0.038$), MA ($r = -0.310$; $p = 0.033$; $r = -0.345$; $p = 0.025$).

For a more detailed analysis of the relationship between clinical and laboratory parameters of IR, the sample, which is characterized by heterogeneity of diseases with fundamentally different pathogenesis, were divided into 2 groups: patients with glomerular diseases and patients with interstitial diseases (hypertension, pyelonephritis and TIN). This ratio was 49.05 and 35.83%.

In the group of patients with glomerular diseases, a positive correlation was found between IR and the severity of PU and a negative correlation with GFR (Table 2). At the same time, in the group of glomerular diseases, the size of the kidney and indicators reflecting its structure, in particular, the thickness of the parenchyma and PPI, did not depend on IR.

Parameter	IR of the mouth of the PA	IR SA	IR MA
Age	$r=0,323$ ($p=0,015$)	$r=0,478$ ($p=0,016$)	$r=0,486$ ($p=0,001$)
AP	$r=0,328$ ($p=0,025$)	$r=0,335$ ($p=0,016$)	$r=0,271$ ($p=0,034$)
CKD-EPI	$r=-0,365$ ($p=0,006$)	$r=-0,438$ ($p=0,001$)	$r=-0,394$ ($p=0,003$)

Table 1. Relationship between patient's age, PD and GFR determined by the CKD-EPI formula, and IR in the PA ostium and intrarenal arteries GFR by the formula

Table 2. Relationship between PU and IR of the mouth of the PA and parenchymal renal arteries in patients with glomerular diseases

Parameter	Glomerular diseases			Interstitial diseases		
	IR of the mouth of the PA	IR SA	IR MA	IR the mouth of the PA	IR SA	IR MA
PU	r=0,464 (p=0,015)	r=0,471 (p=0,011)	r=0,405 (p=0,036)	r=-0,129 (p=0,548)	r=-0,256 (p=0,250)	r=-0,301 (p=0,153)
GFR according to the CKD-EPI formula	r=-0,498 (p=0,006)	r=-0,535 (p=0,002)	r=-0,495 (p=0,005)	r=-0,371 (p=0,052)	r=-0,218 (p=0,284)	r=-0,204 (p=0,297)
Kidney length	r=0,040 (p=0,842)	r=-0,026 (p=0,897)	r=0,070 (p=0,724)	r=0,356 (p=0,019)	r=0,567 (p=0,004)	r=0,793 (p=0,001)
Transverse dimension	r=0,039 (p=0,846)	r=-0,043 (p=0,829)	r=0,072 (p=0,716)	r=0,433 (p=0,027)	r=0,770 (p=0,001)	r=0,523 (p=0,006)
Parenchyma thickness	r=-0,254 (p=0,176)	r=-0,304 (p=0,096)	r=0,142 (p=0,455)	r=-0,397 (p=0,030)	r=-0,247 (p=0,041)	r=-0,218 (p=0,047)
PPI	r=-0,155 (p=0,412)	r=-0,229 (p=0,216)	r=-0,296 (p=0,112)	r=-0,490 (p=0,006)	r=-0,409 (p=0,031)	r=-0,393 (p=0,032)

Almost the opposite situation was observed in the group of patients with interstitial kidney lesions.

Thus, the indices of vascular resistance did not correlate with the values of PU and GFR (determined by calculation formulas), but correlated with the size of the kidney (see Table 2). The RI value of the PA mouth as a prognostic sign of deterioration of renal function had an area under the ROC-curve of 0.668 ($p = 0.038$), which characterizes its quality as good. The inflection point of the curve, i.e. the threshold value at which deterioration of renal function was observed was 0.715, with sensitivity reaching 56% and specificity 71%. Under the ROC-curve for IR CA was greater than for the PA mouth 0.749 ($p = 0.002$), with an inflection point of 0.67, in

which the sensitivity is 62.5%, and specificity - 78%. The largest area under the ROC-curve was determined for IR MA - 0.781 ($p < 0.001$), where the inflection point of the curve was 0.655 with a sensitivity of 71% and a specificity of 72%. Thus, this study demonstrates that IR MA has the greatest predictive value for assessing the rate of progression of CKD. In addition, we compared the sensitivity and specificity of IR of PA and intrarenal vessels with a reliable prognostic sign of deterioration in renal function - PU. The predictive value of IR is comparable to that of PU (AUC = 0.749; $p = 0.002$).

To assess the influence of factors that determine intrarenal hemodynamics, a step-by-step multivariate regression analysis was used, which included the patient's age, BMI, PD, proteinuria value, GFR (calculated by CKD-EPI and determined by the Reberg-Tareev formula), creatinine and uric acid concentrations in blood. It turned out that among the studied parameters, IR was statistically significantly influenced by the patient's age ($\beta = 0.522$; $p = 0.0001$) and plasma creatinine concentration ($\beta = 0.482$; $p = 0.001$; $r^2 = 0.5$; $p < 0.001$).

Discussion

The results of this work make it possible to consider the measurement of IR in patients with CKD as reasonable due to a number of reasons. Thus, the value of IR directly depends on the patient's age and PD. This result indicates that IR is a reflection of the degree of damage to renal vessels, which largely depends on pathological processes such as hypertension and atherosclerosis. The direct relationship between the values of RI of the mouth of the PA and PD indicates that this index reflects disorders of systemic hemodynamics; the same is shown in other works. It is important to note that an increase in MA IR is a risk factor for the development of cardiovascular diseases in elderly patients, and is also associated with a high risk according to the Framingham scale. In our work, it was shown that USG with the calculation of the IR of renal vessels of different caliber makes it possible to determine the signs and severity of impaired renal function and structure: a decrease in GFR, renal parenchyma thickness, and changes in PPI.

In glomerular diseases, IR of renal vessels is associated with the severity of PU and a decrease in GFR, probably due to fibrosis of the renal parenchyma, while in interstitial diseases, it is a violation of the size of the kidney and its structure. Whether IR of renal vessels reflects the severity of glomerulosclerosis is a moot point. The absence of correlations between IR values and the severity of histological changes. The same conclusions were reached by N. Bige et al., and according to their results, isolated glomerular damage was not even associated with a change in IR. Moreover, in one of the latest studies on a fairly large sample ($n = 202$) of patients with glomerulonephritis and lesions of interstitial tissue, it was shown that IR of the renal vessels correlates with the severity of glomerular sclerosis. The relationship between sclerosis of the glomeruli, interstitial tissue and the growth of IR has also been previously shown. However, given the generally contradictory results of the work, the absence of large randomized trials, it is difficult to say, reflected the change

in the IR value, the degree of damage to the glomerular apparatus. It is likely that an increase in the IR of the renal vessels of a smaller caliber reflects damage to the glomerular apparatus. In addition, both mentioned works are characterized by the fact that the sample includes patients with different groups of nephropathies. In our work, we compared the data of patients with a predominantly primary glomerular and predominantly interstitial mechanism of nephropathy. Due to this, for the first time, a correlation was noted between IR and PU.

The increased IR values obtained in the study of patients with predominantly interstitial kidney damage coincide with the data of other authors. The main mechanisms that lead to such a relationship are an increase in vascular resistance and intravascular pressure due to atherosclerosis of the branches of the renal arteries and fibrosis of the renal parenchyma. In addition to the connection with clinical and laboratory parameters and the severity of histological changes, the importance of measuring the IR value is dictated by the fact that its increased and high values are associated with deterioration of renal function.

One of the first works, which showed the predictive value of IR in relation to the severity of the course of nephropathy, conducted on a sample of patients with lupus nephritis. Much later, showed the predictive value of IR in a sample of 311 people with CKD with a follow-up period of 2 years. At the same time, in both studies, a different threshold value of IR was shown, which is associated with the study of vessels of different calibers, as well as the degree of GFR decrease - with IR 0.70, the degree of decrease over 2 years was 10 ml / min 1.73 m² / year, and with IR 0.65 - 5 ml / min 1.73 m² / year. Considering this difference, we examined vessels of different calibers. According to our data, MA IR is the most accurate parameter for determining the degree of progression of CKD, while an IR of more than 0.65 is prognostically unfavorable. The predictive value of this value coincides with that of PU, a proven risk factor for the progression of CKD. It is important to emphasize that IR 0.65 is within the reference values; nevertheless, it is associated with deterioration of renal function, which necessitates adequate therapy.

Another conclusion of our work is that the most significant factors influencing the IR of MA are the patient's age and the serum creatinine concentration.

Conclusion

Thus, USDG data of renal vessels, in particular IR, make it possible to clarify the degree of renal fibrosis and can be used as an additional prognostic factor to predict the rate of progression of CKD.

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