

## EVALUATION OF RENAL AND CENTRAL HEMODYNAMICS IN PATIENTS WITH CHRONIC KIDNEY DISEASE WHO UNDERWENT COVID-19

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### ABSTRACT

Currently, the world community is faced with a new infectious disease, namely the COVID-19 pandemic (coronavirus disease 2019). The article aimed to study the renal and central hemodynamics in patients with chronic kidney disease who had and did not have a coronavirus infection.

The study included 45 patients with chronic renoparenchymatous diseases who had a coronavirus infection. The patients were divided into two groups: group 1—a group of patients with chronic kidney disease who did not have COVID-19; group 2 – a group of patients with chronic kidney disease who had COVID-19. All patients underwent general clinical and laboratory-instrumental examinations: general analysis of blood, urine, biochemical tests, the concentration of urea and creatinine and serum electrolytes, the lipid spectrum. The glomerular filtration rate was determined by the formula CKD-EPI (1.73 ml/min/m<sup>2</sup>).

The study results indicate a relatively high prevalence of kidney pathology in patients who underwent COVID-19, both in laboratory and instrumental indicators.

Early detection, correction of filtration and excretory function of the kidneys, including adequate hemodynamic support and restriction of nephrotoxic drugs, can improve the prognosis of recovery of a patient with COVID-19.

**Keywords:** Chronic Kidney Disease, COVID-19, Diastolic Dysfunction, Urea, Creatinine.

### I. INTRODUCTION

Around the world, for more than a year, scientists and doctors have been trying to assess the harm that COVID-19 causes to the human body, but despite more than 400 thousand deaths, millions of patients and thousands of studies, the picture has not been fully clarified.

Although the coronavirus primarily affects the lungs, the infection has also spread to the kidneys in some patients. According to a sample study conducted in China, 27 percent of the 85 patients admitted to Wuhan hospitals with coronavirus had kidney problems.

In another study, 59 percent of the nearly 200 patients hospitalized in Hubei and Sichuan provinces had a protein in their urine indicating infection, and 44 percent had blood, indicating serious kidney damage. Moreover, in patients with renal insufficiency (RI), the risk of death was five times higher than in ordinary patients with COVID-19.

Despite the achievements of modern medicine, the prognosis in patients with chronic kidney diseases remains unfavorable. According to the results of epidemiological studies, the mortality structure in patients with RI has changed significantly over the past year [2,5,16]. Currently, the main cause of death in chronic kidney disease is cardiovascular events against the background of COVID-19 [2, 15].

Cardiovascular complications are diagnosed at any stage of chronic kidney disease (CKD) in coronavirus infection and account for 47 percent of the total mortality in severe and terminal chronic kidney failure (CKF) [1,4]. The most common among them are arterial hypertension (AH) – 30-85 percent, coronary heart disease (CHD) – 35 percent, heart failure (HF) – 61 percent and cardiac arrhythmias – 27 percent [8-10]. Important factors determining the prognosis are left ventricular hypertrophy (LVH), impaired LV diastolic function (DF), and chronic heart failure (CHF). Most often (40-63 percent of cases), patients with CKD are diagnosed with concentric LVH (CGLH), which reflects the processes of adaptation of the heart muscle to hemodynamic overload with blood pressure (BP) in uncontrolled hypertension, atherosclerosis, and aortic stenosis [17].

The formation of eccentric LVH (ELVH) in patients with CKD is associated with an increase in preload due to hypernatremia, hypervolemia, anemia, and, in some cases, the functioning of the arteriovenous fistula. Diastolic dysfunction (DD) LV in patients with the initial stages of CKF is diagnosed in 60-78 percent of cases, and as the nitrogen-releasing function of the kidneys decreases, it reaches 80 percent in patients on hemodialysis [8,18]. In 30-65 percent of patients with CKF, there is a violation of the systolic function of the LV [3,7].

Thus, structural and geometric changes in the LV are combined with a violation of left ventricular diastolic function. Subsequently, as CKD progresses, they are accompanied by a decrease in the systolic function of the LV.

## II. MATERIALS AND METHODS

The study included 45 patients with chronic renoparenchymatous diseases who had a coronavirus infection. Patients were divided into two groups: group 1—a group of patients with CKD who did not have COVID 19; group 2 – a group of patients with CKD who had COVID-19. The causes of CKD were primary renoparenchymatous diseases: diabetic nephropathy – 34 (75 percent), chronic pyelonephritis – 8 (17 percent), and chronic glomerulonephritis – in 3 (0.6 percent) patients.

All patients underwent a general clinical and laboratory-instrumental examination: including general analysis of blood, urine, from biochemical analyses of the concentration of urea, creatinine and serum electrolytes, and the lipid spectrum. The glomerular filtration rate (GFR) was determined by the formula CKD-EPI(1.73 ml/min/m<sup>2</sup>) [NKF K/DOQI, 2002]. According to the results obtained, the stage of CKD was determined.

Echocardiography (EchoCG) scanning was conducted on a SONOSCAPES20 ultrasound machine (USA) with a 3.5 MHz sensor using the traditional Simson technique. It was studied the ejection fraction (EF), the interventricular septum thickness (IST), the posterior wall of the LV (PWL) in the diastole, the final diastolic size of the LV, the size of the left atrium (LA), calculated the LV myocardium mass (LVMM) and the LVMM index (LVMMI).

According to the results of echocardiography, variants of LV structural disorders were identified: concentric remodeling of LV, concentric hypertrophy of LV and eccentric hypertrophy of LV.

Dopplerography of the renal arteries was performed. The initial systolic rate (V<sub>max</sub>), final diastolic rate (V<sub>min</sub>), resistance index (RI), pulse index (PI), and systolic-diastolic index (S/D) were determined. The programs "STATISTICA 5.0" were used in the statistical processing of the results.

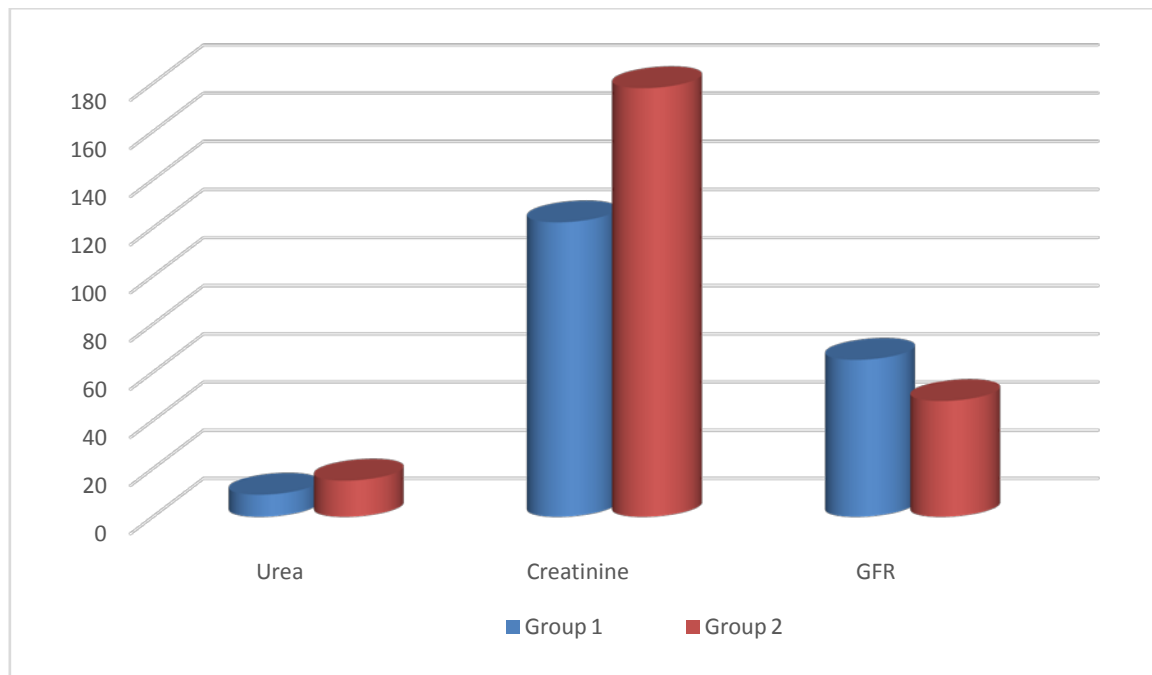
### III. RESULTS

In order to evaluate renal dysfunction, it was assessed urea, creatinine, and Glomerular filtration rate (GFR) values in the study groups. When comparing the results of the first and second groups, there was a significant decrease in renal function in patients with Covid-19, respectively, urea  $9.2 \pm 0.11$ - $15.04 \pm 0.44$ , creatinine  $122.3 \pm 2.04$ - $178 \pm 2.17$  and GFR  $65.2 \pm 3.05$ - $48.1 \pm 3.13$  ( $p < 0.05$ ). An increase of creatinine and urea in the blood was observed with a decrease in GFR. There is a positive correlation between urea and creatinine and a significant negative correlation between urea GFR and creatinine GFR.

A comparative study of the results from groups 1 and 2 showed that urea and creatinine in the blood were significantly higher in group 2 than in group 1. There was a positive correlation between them. GFR decreased significantly in group 2 compared to group 1, and the GFR score showed a significant negative correlation with blood urea and creatinine (see Figure 1).

Figure 1.

The ratio of biochemical parameters in patients (in groups)



Note: Confidence between groups \*-( $p < 0.05$ )

The analysis of the main parameters of echocardiography of LV remodeling showed that in patients with CKD, IST by 7.4 percent ( $p = 0.03$ ), LVMM by 9.8 percent ( $p = 0.04$ ) and LVMMI by 8.4 percent ( $p = 0.03$ ) more than in the group of patients with CKD who had not suffered a coronavirus infection.

Table 1

Parameters of echocardiographic examination in patients (in groups)

Echocardiography indicators	Group 1	Group 2
IST	0,92 ± 0,04	1,2 ± 0,03*
EDVLV	122,3 ± 0,11	154,4 ± 0,44**
ESVLV	42,3 ± 0,04	68 ± 0,17*
ESSLV	4,1 ± 0,03	5,2 ± 0,05*
EDSLV	3,05 ± 0,22	5,8 ± 0,92*
LVMM	212,5 ± 11,6	250,5 ± 10,67**
LVMMI	157,2 ± 10,67	174,5 ± 11,67*
LVEF	62,1 ± 0,92	54,3 ± 1,12*

Note: Confidence between groups \*-( $p < 0.05$ ), \*\*-( $p < 0.01$ ).

When comparing the structural function of the ventricle between groups one and two, the end-diastolic volume (EDV) and the end-systolic volume of the left ventricle (ESV) showed a significant difference ( $p < 0.05$ ) in group 2, compared with group 1, respectively  $154,04 \pm 0,44$ - $122,3 \pm 0,11$ ,  $68 \pm 0,17$ - $42,3 \pm 0,04$ . At the same time, there

was a significant difference ( $p<0.05$ ) in ESV, EDV, and Ejection fraction (EF) in group 2, respectively,  $5,2\pm 0,05-4,1\pm 0,03$ ,  $5,8\pm 0,92-3,05\pm 0,22$  and  $54, 3\pm 1.12-62.1\pm 0.92$ . An increase in the volume and size of the heart, i.e., EDV, ESV, and IST, created a positive ( $p<0.05$ ) correlation with LVMM and LVMMI, respectively ( $r=0.36$ ,  $r=0.34$ ). The volume and size of the LV formed a significant ( $p<0.05$ ) negative correlation with EF and GFR, respectively ( $r=0.39$ ). The expansion of the heart cavities and the decrease in EF cause stagnation of blood in the kidneys, leading to impaired renal function and CKD progression (see Table 1).

Table 2

Indications of Doppler examination of renal arteries in patients (in groups)

Dopplerography of the renal arteries	Group 1	Group 2
Rightrenalartery		
Vmax	$0,95 \pm 0,03$	$1,5 \pm 0,04$
Vmin	$0,4 \pm 0,02^*$	$0,46 \pm 0,01^*$
RI	$0,63 \pm 0,07^*$	$0,79 \pm 0,04^*$
PI	$1,30 \pm 0,05^*$	$1,58 \pm 0,03^*$
S/D	$4,23 \pm 0,9^*$	$3,21 \pm 0,02^*$
Leftrenalartery		
Vmax	$0,92 \pm 0,06^*$	$1,75 \pm 0,06^*$
Vmin	$0,32 \pm 0,07$	$0,48 \pm 0,06$
RI	$0,7 \pm 0,02$	$0,72 \pm 0,03^*$
PI	$1,62 \pm 0,03$	$1,53 \pm 0,02^*$
S/D	$4,11 \pm 0,04$	$3,54 \pm 0,06$

Note: Confidence between groups \* - ( $p<0.05$ )

In the study groups, renal dysfunction was assessed by studying GFR and renal hemodynamics. Initial systolic velocity (Vmax), final diastolic velocity (Vmin), resistance index (RI), pulse index (PI), and systolic-diastolic index (S/D) were studied. A comparative study of groups 1 and 2 showed that group 2 patients had a significant ( $p<0.05$ ) decrease in renal blood flow. The final diastolic velocity, pulse index, and systolic-diastolic index were associated with a significant negative ( $p<0.05$ ) correlation. The renal vascular resistance index (RI) and pulse index (PI) were positively correlated with the end-diastolic volume of the left ventricle (EDV) and the last diastolic measurement of the left ventricle ( $p<0.05$ ) (see Table 2).

#### IV. DISCUSSION

Although the main target of coronavirus is the lungs and the severity of their damage is the main predictor of an unfavorable outcome, the involvement of other organs and systems in the process can also have a negative impact on the prognosis. It is what largely determines the severe course of the disease in patients with concomitant pathology. According to the meta-analysis, the detection rate of CKD was significantly lower than in the general population, averaging less than 1 percent [33]. However, such a low prevalence of renal pathology may be due to insufficient patient awareness at the pre-hospital stage.

According to studies with screening determination of GFR, the prevalence of CKD reaches 11-13 percent of the population [34], which can be extrapolated to patients with coronavirus infection. The data of Cheng and co-authors also evidence the high prevalence of renal pathology: 43.9 percent of patients with COVID-19 at the time of hospitalization had proteinuria. In 13.1 percent of patients, the GFR rate was less than 60 ml/min/1.73 m<sup>2</sup>, which corresponds to CKD 3 [16]. Our data also indicate a fairly high prevalence of kidney pathology in patients who underwent COVID-19, both in the laboratory and instrumental indicators. Thus, at the time of hospitalization, blood creatinine was elevated in 25 patients (15 percent).

Patients with CKD who had a coronavirus infection, already in its early stages, are characterized by a high frequency of LV remodeling (from 40 to 90 percent) than in patients with CKD who hadn't COVID-19. In patients with CKD who had a coronavirus infection, LVH occurs in the early stages of the disease, and most cases have a concentric character. The eccentric form of hypertrophy is formed with the onset and progression of CRF.

An increase in the heart cavities, values of Impact volume (IV), and EF due to hypervolemia are characteristic of patients with moderate and severe renal insufficiency, with a significant increase in the indexed indicators of the size of the cavities in the group of patients who suffered from coronavirus infection concerning patients who did not suffer from coronavirus infection.

The main changes in renal function were associated with the resistance index (RI) and the pulse index (PI). That is, in patients of group 1, an increase in vascular resistance and a decrease in the pulse index were observed. The index of renal vascular resistance was positively correlated with the final systolic size of the left ventricle ( $p < 0.05$ ).

However, in CKD with COVID 19, there is already a significant thickening of the interventricular septum IVS ( $1.1 \pm 0.2$  cm) in the early stages. In patients of group 1, an eccentric form of myocardial remodeling is detected more often than in group 2. Unlike patients with CKD who have not had a coronavirus infection, who are more likely to have signs of diastolic dysfunction, patients with CKD who have had a coronavirus infection show signs of impaired systolic function in the later stages of the disease.

## V. CONCLUSION

Thus, kidney disease is a frequent complication of COVID-19 and a significant risk factor for fatal outcomes. Therefore, monitoring of renal function should be initiated in patients with mild respiratory symptoms of COVID-19. Early detection, correction of filtration and excretory function of the kidneys, including adequate hemodynamic support and restriction of nephrotoxic drugs, can improve the prognosis of recovery of a patient with COVID-19.

It is possible that the new algorithm for the management of patients with COVID-19 allow us to determine the current characteristics of patients, approaches to treatment and prevention for the development of a model of the risk of complications.

## CONFLICT OF INTERESTS AND CONTRIBUTION OF AUTHORS

The authors declare the absence of apparent and potential conflicts of interest related to this article's publication and report on each author's contribution.

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