

### Evaluation of the Morphofunctional State of the Transplant in the Period after Kidney Transplantation

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#### ABSTRACT

*The article highlights the transplantation in patients who have CKD before dialysis, who are taking planned hemodialysis, and patients who did not start planned hemodialysis, as they underwent kidney allotransplantation. By employing dopplerography examination of the renal arteries in these patients, the functional condition of the kidneys was investigated. Doppler sonography is also thought to play a significant part in transplant rejection syndrome.*

#### Introduction

Doppler sonography was historically first used to measure renal hemodynamics when it was used to detect transplant or post-transplant nephropathy. The best method for dynamically monitoring the condition of a transplanted kidney is a Doppler examination of the renal vessels [9, 16, 17]. In the event of three-component immunosuppression, the rejection crisis, according to V.V. Zakharov [11], is characterized by an increase in the volume of the kidney  $>270 \text{ cm}^3$  and a rise in the resistance index (RI) of the renal artery up to  $>0.87$  [8, 9]. With mild to moderate rejection, RI may stay within the normal range or possibly drop. This is due to hyperstagnation of the blood. Therefore, the relevance of this indicator is minimal [2, 5, 15]. An increase in the renal artery resistance index may indicate postoperative transient ischemia, acute tubular necrosis, and obstructive uropathy [6, 11]. In acute tubular necrosis, RI does not exceed 0.82, and the size of the kidney increases slightly [9, 14]. In 47% of patients with chronic graft rejection, as determined by clinical and laboratory techniques, nephroscintigraphy, and biopsy an increase in RI of the intrarenal arteries by 0.75 was observed and in 6% of patients it was observed with normal graft function [7, 9]. An increase in the resistance index of more than 0.8 is a reliable criterion, even though the parameters that were examined did not allow for the identification of the precise reason of graft malfunction [8, 15]. Therefore, we considered it necessary to conduct scientific research on the analysis of spectral Doppler data in assessing the functional state of a kidney transplant in recipient patients who underwent kidney allotransplantation (KAT).

## Aim of the Study

To conduct comparative analysis of spectral Doppler data in assessing the functional state of a kidney graft in study groups consisting of patients who underwent KAT without the start of scheduled hemodialysis sessions, as well as in the pre-dialysis period of chronic kidney disease (CKD) and Doppler ultrasound of the renal vessels.

**Methodology (Materials and Methods)** The first group for the study was made up of 35 patients in the pre-dialysis period of CKD, who were treated in the nephrology department of the TMA multidisciplinary clinic. Additionally, 35 recipients were chosen for the second group, who were under observation at the Surkhandarya Regional Medical Center (at the Surkhandarya regional branch of the Republican Specialized Scientific and Practical Medical Center for Nephrology and Kidney transplantation), who received scheduled hemodialysis treatments for a predetermined amount of time before undergoing KAT in this institution. The third group consisted of patients who underwent KAT before beginning their regularly scheduled hemodialysis sessions. The age of patients ranges from 19 to 55 years, the average age of patients in the first group is  $41.7 \pm 1.69$ ; in the 2nd group  $37.4 \pm 1.47$  and in the 3rd group  $38.6 \pm 1.43$  years. The duration of planned hemodialysis in patients of the 2nd group on average is  $3.9 \pm 1.5$  years.

With purpose of determining the resistance of the renal arteries and the blood flow velocity in the veins, all patients underwent a dopplerography examination of the renal vessels. This examination was carried out using the diagnostic device "Sonoscape S20 Color Doppler" in the functional diagnostics department of the Surkhandarya clinic (of the OMMC) and in the admissions department of the TMA multi-profile clinic.

During this research, we studied the blood flow velocity and vascular resistance in the main, segmental and intersegmental vessels of the kidney by the method of spectral analysis. The study of intrarenal hemodynamics was studied by spectral analysis of intrarenal hemodynamics using Doppler ultrasound. At the access point, the right and left renal arteries are evaluated as follows:

- ✓ Maximum systolic velocity of arterial blood flow ( $V_s$  max).
- ✓ End-diastolic velocity ( $V_d$ ).

In the Intrarenal Arteries

- ✓ Segmental -  $V$  max,  $V_d$ .
- ✓ Intersegmental -  $V$  max,  $V_d$ .

The resistance index (RI) and the pulse index (PI) are used to describe renal vascular resistance. Statistical data processing used the average of the results obtained in the study of the vessels of the right and left kidneys.

## Results and Discussion

The renal vessels were examined using Doppler during our study, and the findings are as follows. Here,  $V_{smax}$  in the main renal vessels was  $57.6 \pm 0.58$  in the first group, consisting of CKD patients in the predialysis period;  $61.3 \pm 1.43$  in the 2nd group, consisting of patients who underwent sessions of planned hemodialysis, and then KAT. In the 3rd group of patients who underwent KAT before scheduled hemodialysis sessions, it was  $64.5 \pm 1.35$  cm/s. The results revealed significant values ( $p < 0.001$ ) in all our groups compared to the control group, while  $V_s$  max changed less significantly ( $p < 0.05$ ) in the 2nd group compared to the first and significant values ( $p < 0.001$ ) in the 3rd group was confirmed on the basis of statistical analysis.  $V_d$  in the first group was  $19.7 \pm 0.51$ ;  $22.4$  in patients of the 2nd group; and in the 3rd group it was  $24.8 \pm 0.56$  cm/s. When compared to the control group, all groups showed significant indicators ( $p < 0.001$ ), however  $V_d$  revealed less significant indicators ( $p < 0.01$ ) in people from the second

and third groups than from the first group ( $p < 0.001$ ).

The maximum velocity in segmental renal vessels was  $42.2 \pm 0.43$  cm/s in the first group,  $45.2 \pm 1.09$  cm/s in the second group of recipients, and  $50.4 \pm 1.19$  cm/s in the third group of recipients. It was highlighted that the results were significant ( $p < 0.001$ ) in all groups compared to the control group, while  $V_s$  max in segmental arteries was less significant ( $p < 0.05$ ) in the 2nd group than in the first and a significant increase was confirmed by statistical analysis in the 3rd group of recipients ( $p < 0.001$ ) (Table 1).

**Table 1. Parameters of blood circulation in the main and intrarenal arteries**

Blood circulation indicators	Control group n = 20	Group 1 n = 35	Group 2 n = 35	Group 3 n = 35
<i>Main renal artery</i>				
$V_s$ max, cm/s	$87,98 \pm 0,91$	$57,6 \pm 0,58$ ***	$61,3 \pm 1,43$ *** ^	$64,5 \pm 1,35$ *** ^^^
Vd, cm/s	$28,98 \pm 0,64$	$19,7 \pm 0,51$ ***	$22,4 \pm 0,62$ *** ^^	$24,8 \pm 0,56$ *** ^^^
<i>Segmental artery</i>				
$V_s$ max, cm/s	$58,38 \pm 0,82$	$42,2 \pm 0,43$ ***	$45,2 \pm 1,09$ *** ^	$50,4 \pm 1,19$ *** ^^^
Vd, cm/s	$23,11 \pm 0,32$	$16,9 \pm 0,21$ ***	$18,4 \pm 0,52$ *** ^	$20,3 \pm 0,49$ *** ^^^
<i>Interlobular artery</i>				
$V_s$ max, cm/s	$37,74 \pm 0,88$	$26,5 \pm 0,31$ ***	$27,7 \pm 0,45$ *** ^	$30,8 \pm 0,75$ *** ^^^
Vd, cm/s	$15,41 \pm 0,60$	$11,1 \pm 0,15$ ***	$12,1 \pm 0,35$ *** ^	$13,5 \pm 0,38$ ** ^^^

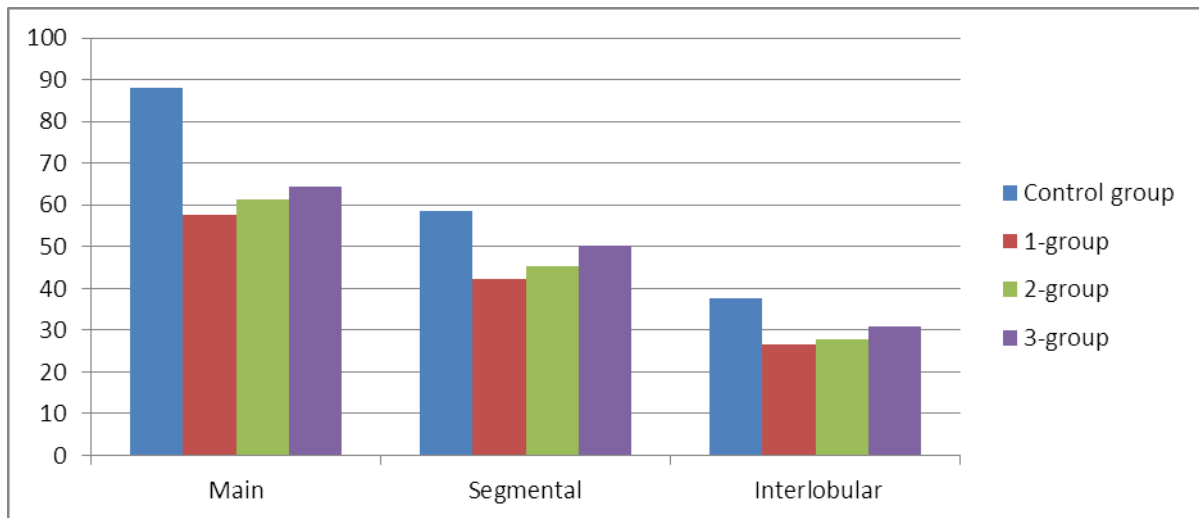
Note: \* - the differences are significant in comparison with the indicators of the control group ( $p < 0,05$ , \*\* -  $p < 0,01$ , \*\*\* -  $p < 0,001$ ); ^ - differences are significant in comparison with the indicators of the first group (^ -  $p < 0,05$ , ^^ -  $p < 0,01$ , ^^ -  $p < 0,001$ ).

Vd in the segmental renal arteries in our patients of the first group is  $16.9 \pm 0.21$ ;  $18.4 \pm 0.52$  in group 2 recipients; and in the 3rd group it was  $20.3 \pm 0.49$  cm/s. While Vd was less significant ( $p < 0.01$ ) in group 2 compared to group 1 and in recipients 3 groups ( $p < 0.001$ ), Vd in segmental arteries were all significantly different ( $p < 0.001$ ) from the control group. The statistical analyses (Table 1) reveal that it demonstrated reliable indicators:

$V_s$  max blood flow in the interlobular renal arteries in patients of the first group is  $26.5 \pm 0.31$ ;  $27.7 \pm 0.45$  in the 2nd group, and in the 3rd group of patients it is  $30.8 \pm 0.75$  cm/s. When compared to the control group in all study groups,  $V_s$  max in the interlobular renal arteries was statistically significant ( $p < 0.001$ ); however, it was less significant ( $p < 0.05$ ) in these arteries compared to the first group in the second study group. In the 3rd group, the values of  $V_s$  max ( $p < 0.001$ ) were significantly increased. Vd in the interlobular renal arteries in patients of the first group is  $11.1 \pm 0.15$ ;  $12.1 \pm 0.35$  in the 2nd group; in group 3 group it increased to  $13.5 \pm 0.38$  cm/s. In comparison to the control group, Vd in all groups significantly changed in these arteries ( $p < 0.001$ ). Vd in the second group was less significant ( $p < 0.01$ ) than it was in the first group. Based on statistical analysis, a substantial increase ( $p < 0.001$ ) was found in the 3rd group recipients (Table 1).

When comparing our research groups by assessing the results and exhibiting them on the basis of diagrams, the  $V_s$  max values in the main and intrarenal arteries revealed the following situation. Looking at the chart, it can be seen that  $V_s$  max significantly ( $p < 0.001$ ) changed in all vessels

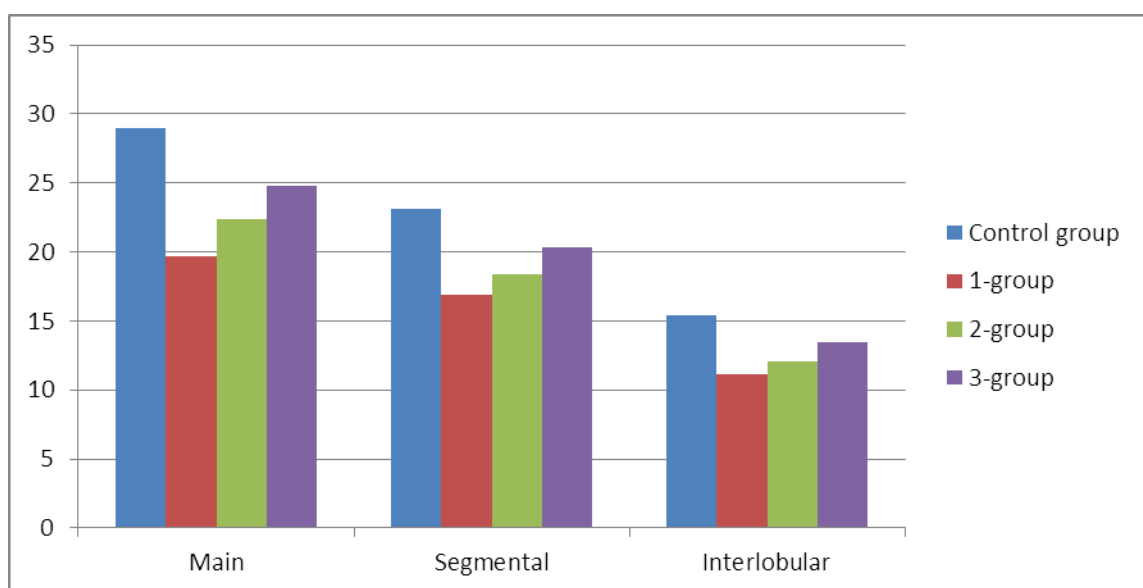
compared to the control group. The cause is that glomerular aggression (attack of immune complexes, hypercoagulability, and hemodynamic abnormalities) still exists in kidney transplant recipients as well as pre-dialysis CKD patients. As a result, during statistical analysis, it was discovered that all study groups were more reliable than the control group ( $p < 0.001$ ) (Fig. 1).



**Figure 1. Comparison of indicators of maximum systolic velocity in the main and intrarenal arteries**

When comparing the results with the first group by statistical analysis, in the second group, which comprises of recipient patients who had AP after elective hemodialysis sessions, the values of  $V_s$  max altered less considerably ( $p < 0.05$ ). In the 3rd group of recipient patients who underwent kidney transplantation without scheduled hemodialysis sessions, a significant change ( $p < 0.001$ ) was observed in all vessels.

The following figure was obtained when compared studies of  $V_d$  in the main and intrarenal arteries. The illustration in the diagram show that  $V_d$  in all main, segmental, intersegmental vessels changed significantly ( $p < 0.001$ ) compared to the control group. The reason is that, as we mentioned above, the pathological processes are still to a certain extent based on pathological conditions in the kidneys. Because of this, it was discovered through statistical analysis that all research groups except the control group had more reliable indicators than the control group ( $p < 0.001$ ) (Fig. 2).



**Figure 2. Comparison of end diastolic velocities in the main and intrarenal arteries**

In this regard, when compared the results with the statistical analysis of the first group, there is a less significant ( $p < 0.05$ ) change in group 2, which consists of recipient patients who underwent elective hemodialysis sessions, and then KAT. In the 3rd group, which consisted of recipient patients who underwent kidney transplantation without scheduled hemodialysis sessions, a significant change ( $p < 0.001$ ) was observed in all vessels. According to statistical analysis, the reliability of the values of  $V_s$  max and  $V_d$  in the vessels of the main and intrarenal arteries in patients with chronic kidney disease who underwent kidney transplantation without planned extracorporeal therapy, compared with dialysis patients, is explained by severe hemodynamic disturbances due to the negative effect of planned hemodialysis measures on the cardiovascular vascular system of the whole organism [6, 7]. In our research, the estimated **resistance index** (RI) and **pulse index** (PI), which determine the **level of resistance of the kidney vessels**, revealed the following picture:

Based on the results, the resistance index in the main renal artery in the first group, consisting of predialysis patients, was  $0.71 \pm 0.01$  and in the 2nd group it was  $0.69 \pm 0.01$ , consisting of renal transplant recipients after scheduled hemodialysis sessions. In the 3rd group it was  $0.67 \pm 0.01$ , in which recipients underwent KAT without planned hemodialysis. Statistical analyzes showed that the results were significant ( $p < 0.001$ ) in groups 1 and 2 compared with the control group and less significant ( $p < 0.05$ ) in group 3. The results are based on a statistical analysis of the fact that, compared with the first group, RI changed less significantly in the recipients of the 2nd group ( $p < 0.05$ ) and in the 3rd group ( $p < 0.001$ ) to significant values. PI in the first group is  $1.2 \pm 0.02$ ; in the 2nd group  $1.16 \pm 0.02$ ; and in the 3rd group -  $1.13 \pm 0.02$ . The results showed significant values in the first and 2nd groups ( $p < 0.001$  and  $p < 0.01$ ) compared with the control group, while PI was less significant in patients of the 2nd group ( $p < 0.05$ ) and 3 -th group ( $p < 0.01$ ) compared with the first group and was confirmed on the basis of statistical analysis in reliable values (Table 2).

**Table 2. Vascular resistance in the main and intrarenal arteries indicators  $M \pm m$**

Indicators of vascular resistance	Control group n = 20	Group 1 n= 35	Group 2 n= 35	Group 3 n= 35
<i>Main renal artery</i>				
RI	$0,65 \pm 0,01$	$0,71 \pm 0,01$ ***	$0,69 \pm 0,01$ *** ^	$0,67 \pm 0,01$ * ^^^
PI	$1,10 \pm 0,03$	$1,2 \pm 0,02$ ***	$1,16 \pm 0,02$ **^	$1,13 \pm 0,02$ *^^
<i>Segmental artery</i>				
RI	$0,63 \pm 0,02$	$0,72 \pm 0,01$ ***	$0,70 \pm 0,01$ ***^	$0,66 \pm 0,01$ * ^^^
PI	$1,02 \pm 0,02$	$1,2 \pm 0,02$ ***	$1,13 \pm 0,02$ ***^	$1,07 \pm 0,02$ *^^
<i>Interlobular artery</i>				
RI	$0,59 \pm 0,01$	$0,62 \pm 0,01$ **	$0,61 \pm 0,01$ *	$0,60 \pm 0,01$ ^
PI	$0,98 \pm 0,01$	$1,1 \pm 0,01$ ***	$1,08 \pm 0,01$ *** ^	$1,02 \pm 0,01$ **^^

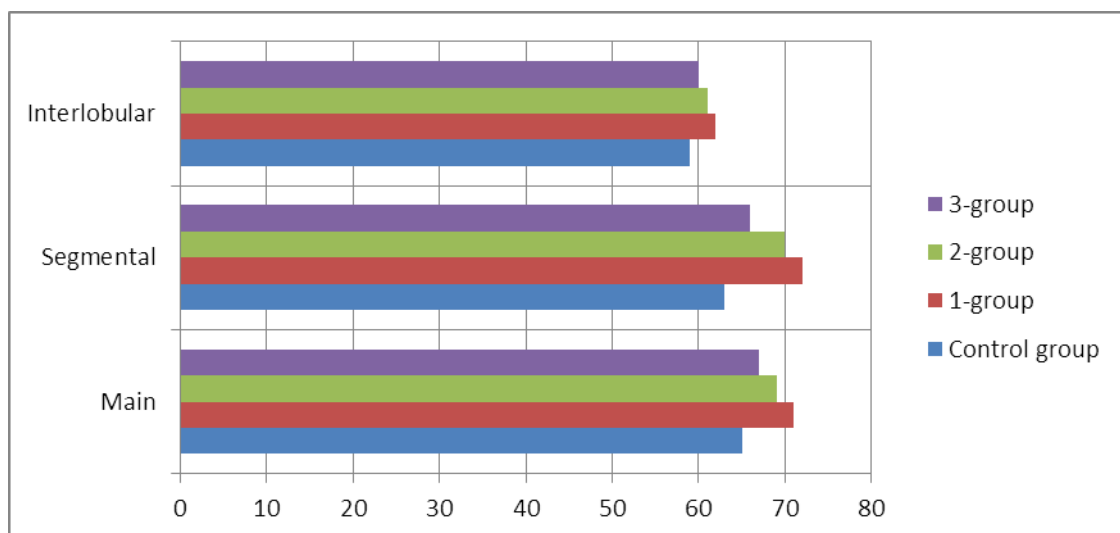
Note: \* - differences are significant in comparison with the indicators of the control group ( $p < 0,05$ , \*\* -  $p < 0,01$ , \*\*\* -  $p < 0,001$ ); ^ - differences are significant in comparison with the indicators of the first group (^ -  $p < 0,05$ , ^^ -  $p < 0,01$ , ^^^ -  $p < 0,001$ ).

With regard to segmental renal arteries, RI was  $0.72 \pm 0.01$  in predialysis patients of the 1st group and  $0.70 \pm 0.01$  in the 2nd group, consisting of recipients who underwent elective hemodialysis sessions followed by kidney transplantation. It was  $0.66 \pm 0.01$  in the third group, which consisted of individuals who underwent kidney allotransplantation without planned hemodialysis. According to statistical analyses, the first and second groups' results were significantly different from the control group ( $p < 0.001$ ), and the third group's results were marginally different ( $p < 0.05$ ). In the statistical analysis of the results compared with the first group, it was noticed that RI changed in less significant values in the 2nd group ( $p < 0.05$ ) and in the 3rd group there was a

change in significant values ( $p < 0.001$ ). PI was  $1.2 \pm 0.02$  in the first group; in the 2nd group -  $1.13 \pm 0.02$ ; and in the 3rd group -  $1.07 \pm 0.02$ . As a result, the first and second groups' results were reliable ( $p < 0.001$ ) when compared to the control group, whereas the third group's results were less significant ( $p < 0.05$ ). This indicator was less significant in the second group compared to the first ( $p < 0.05$ ), and statistical analysis revealed a shift in significant values in the subjects of the third group ( $p < 0.001$ ) (Table 2).

In the interlobular renal arteries, patients in the first group had a RI of  $0.62 \pm 0.01$  in the interlobular renal arteries, while those in the second group, who underwent elective hemodialysis sessions followed by KAT, had a RI of  $0.61 \pm 0.01$ . In the 3rd group it was  $0.60 \pm 0.01$ , in which persons underwent KAT before switching to extracorporeal therapy. When compared to the control group, statistical analysis revealed that the indicators were significant in the first group ( $p < 0.01$ ), less significant in the second group ( $p < 0.05$ ), and unreliably changing in the third group. Statistical analysis of the results in comparison with the first group showed that RI changed in non-significant values in the 2nd group and in less significant ( $p < 0.05$ ) values in the 3rd group. Certainly, as the diameter of the vessel decreases, the accuracy of the results and the level of confidence relative to each other will also decrease. PI on the interlobular renal arteries in the 1st group was  $1.1 \pm 0.01$ ;  $1.08 \pm 0.01$  in the 2nd group; and in the 3rd group it was  $1.02 \pm 0.01$ . With the help of statistical analyzes, it was confirmed that the results in all groups compared with the control group showed a significant value ( $p < 0.001$  and  $p < 0.01$ ), but this indicator was less significant in the 2nd group compared to the 1st ( $p < 0.05$ ) and in persons of the 3rd group ( $p < 0.001$ ). (Table 2).

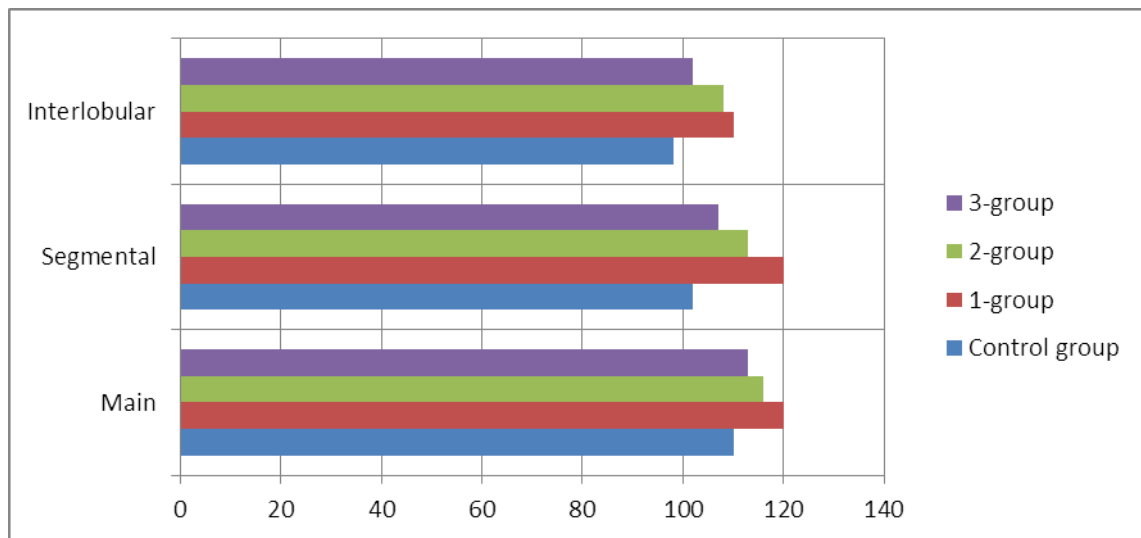
When these results are analyzed using diagrams, it is clear that the first and second groups' calculated resistance and pulse indices, which determine the level of resistance of the renal vessels, changed significantly ( $p < 0.001$ ) compared with the control group. This is explained by the fact that aggression towards balls (attack of immunocomplexes, hypercoagulability, hemodynamic disturbances) persists at any stage in patients with CKD [1, 3]. In contrast, the values in the interlobular arteries are moderate ( $p < 0.01$ ) and less significant ( $p < 0.05$ ), which is explained by a decline in significance with a reduction in the size of the vessels. Another crucial finding of our study is that, in comparison to the control group, the following 3 groups that had KAT without the initiation of planned hemodialysis activities had less significant ( $P < 0.05$ ) or unreliable values for these RI and PI indicators (Fig. 3).



**Figure 3. Comparison of indices of vascular resistance index in the main and intrarenal arteries**

However, when statistical analysis was used to compare the results with the first group, the RI and PI indicators in the second group of kidney transplant recipients after the beginning of

elective hemodialysis sessions, and even unreliable changes in the interlobular arteries, were less significant ( $p < 0.05$ ). These indicators significantly ( $p < 0.001$ ) changed in the large arteries with planned hemodialysis in the third group of recipients who underwent kidney allotransplantation without attending sessions, which is explained by the pronounced side effects of extracorporeal therapy on the cardiovascular system in the body for many years. (Fig. 4).



**Figure 4. Comparison of indicators of the pulse index of vascular resistance in the main and intracranial arteries**

Clinically adequate diuresis, a drop in serum creatinine, and no requirement for hemodialysis sessions are all signs that the transplanted kidney is functioning normally. A decrease in blood flow velocity and an increase in the resistance index by 0.8 was regarded as a decrease in the clinical and functional state of the transplanted kidney, which is also manifested by a slow increase in serum creatinine or its steady increase. The functional state of the transplanted kidney is considered unsatisfactory if the resistance index is higher than 0.8. This is characterized by an increase in serum creatinine, a decrease in diuresis, and the need for hemodialysis sessions. The restoration of kidney function is also indicated by a decline in renal graft arterial resistance and a normalization of spectral blood flow, which were discovered during dynamic monitoring. Thus, rheology, blood volume (amount), hemodynamic disturbances in the cardiovascular system, and a series of neuroendocrine control mechanisms, such as the renin-angiotensin system, are related to  $V_s$  max and  $V_d$ , which indicate blood flow in the kidneys' vessels, and RI and PI, which determine the degree of resistance. Depending on the pathogenic processes, this complicated chain creates a range of imbalances at nearly all stages of CKD. It is known that there are a number of indisputable factors that negatively affect blood rheology, cause disturbances in hemostasis and hemodynamic systems, and ultimately lead to the formation of thrombosis during planned hemodialysis procedures. The key factors that trigger pathological processes are, in particular, the interaction of vessels with arteriovenous fistulas and catheters as well as treatments that alter the dynamics of blood flow inside the vessel [12, 13]. Therefore, these findings are of great importance when choosing renal replacement therapy in CKD. Therefore, the main goal of our research is to recommend CKD patients to the practice of kidney transplantation, without involving them in elective hemodialysis activities.

## Conclusion

Indicators of maximum systolic velocity and end-diastolic velocity changed negatively in patients who underwent kidney allotransplantation after elective hemodialysis sessions, compared with patients who underwent kidney allotransplantation without elective hemodialysis sessions.

1. Compared to patients who receive KAT without elective hemodialysis sessions, patients who get KAT after elective hemodialysis sessions have higher resistance and pulse index.
2. In kidney transplant recipients, a pathological process on the side of transplant rejection is viewed as the slowing of  $V_s$  max and  $V_d$  and an increase in RI and PI.
3. It is advisable to recommend kidney transplantation to CKD patients without involving them in planned hemodialysis activities.

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