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DYNAMICS OF MICROCIRCULATORY CHANGES IN THE RETINA OF PATIENTS WITH CHRONIC KIDNEY DISEASE AFTER KIDNEY TRANSPLANTATION

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ABSTRACT

Objective: *This study aimed to assess microvascular changes in the retina over time in patients with chronic kidney disease (CKD) following kidney transplantation.*

Methods: *A total sample of 54 CKD patients (108 eyes) was prospectively observed for 2 years to evaluate the dynamics of microvascular parameters. Two study groups were formed: Group 1 comprised 36 patients (72 eyes) who underwent kidney transplantation, and Group 2 comprised 18 patients (36 eyes) receiving hemodialysis and conservative treatment. Patients were examined before the operation, within 2 months post-operation (early postoperative period), and at 12 months post-operation (late postoperative period).*

Results: *Optical coherence tomography angiography (OCTA) results demonstrated that retinal parameters, including area, perimeter, and circularity index of the foveal avascular zone (FAZ), showed recovery over the 12-month observation period after kidney transplantation, indicating a positive trend in the macular region. Similar trends were observed for overall vessel density, perfusion, and choroidal vascularity index (CVI) parameters. Statistical analysis revealed significant differences ($p<0.05$) between the groups in terms of FAZ area and CVI.*

Conclusion: *The primary microvascular changes in the retinas of patients with end-stage CKD involve reduced vessel density and perfusion volume in the superficial capillary layer.*

KEYWORDS: *chronic kidney disease; kidney transplantation; microvascular changes; optical coherence tomography angiography (OCT-A).*

INTRODUCTION

According to recent foreign and domestic literature [4,6,14,16], structural changes in the visual organ are observed in all patients with chronic kidney disease (CKD). Visual disorders are one of the main factors determining the quality of life in patients with various somatic diseases, a significant portion of which is represented by kidney pathology [10,15]. The presence of numerous pathogenetic factors in the development of retinopathy in chronic kidney diseases confirms the potential effectiveness of compensating for kidney insufficiency through methods such as hemodialysis and organ transplantation in correcting visual impairments in this patient population [4,6,7].

Developing uremia in patients can lead to various changes in the visual organ. Visual function disorders contribute significantly to the reduction in the quality of life of CKD patients [1,2,7,8]. Given the reversibility of angioretinopathy and optic neuropathy in CKD, ensuring the stability of unaffected retinal neurons and preventing their death becomes crucial for maximizing visual function preservation for the patient [9,10]. In this context, monitoring the dynamics of functional indicators of the visual organ in CKD patients undergoing hemodialysis or kidney transplantation using specific ophthalmological research methods becomes particularly relevant.

The eye is the only organ where changes in microvessels can be visualized. In a normal state, the retina has an internal mechanism for self-regulating blood flow, responding to various physiological changes to maintain homeostasis. Both retinal and kidney tissues are supplied with blood by small vessels with low resistance, sensitive to fluctuations in arterial pressure and perfusion. Similar vascularization in both organs leads to similar complications. The methods used allow for a quantitative assessment of the diameter of retinal vessels, and these measurements are characterized by accuracy and reproducibility [12,13]. In chronic kidney insufficiency, signs of capillary insufficiency are observed in the retina, manifested by an increased ratio of the vessel wall diameter to the lumen diameter and capillary rarefaction due to endothelial dysfunction and systemic inflammation. These changes become key factors in increased cardiovascular risk. Reduction in retinal and choroidal thickness and a decrease in macular volume, even in the early stages of chronic kidney insufficiency, are signs of systemic microvessel damage and a reflection of the pathological process in the kidneys [9,10,11,13,14].

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In light of the above, the aim of this study was to assess the microvascular changes in the retina over time in patients with CKD after kidney transplantation.

MATERIALS AND METHODS

Research Organization: The study was conducted at the Republican Specialized Scientific-Practical Medical Center for Microsurgery of the Eye from 2018 to 2022. The research was part of a dissertation on the topic: "Clinical Aspects of Diagnosis and Treatment of Visual Organ Changes in Chronic Kidney Disease." The study involved a comprehensive in-depth ophthalmological examination of patients with end-stage chronic kidney disease (CKD) regularly observed and undergoing hemodialysis at nephrology and urology centers or private clinics in Tashkent. Additionally, patients who underwent surgical treatment (kidney transplantation) at the Republican Specialized Scientific-Practical Medical Center of Surgery named after Academician V.V. Vakhidov were included.

Selection Criteria and Patient Characteristics

Inclusion Criteria

presence of end-stage CKD confirmed by laboratory results based on the classification proposed by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (2002) using glomerular filtration rate data;
informed consent from the patient to participate in the study;
hemodialysis or kidney transplantation as a treatment method.

Exclusion Criteria

Diabetes Mellitus;
ophthalmological conditions hindering retinal visualization and OCT examination (mature or complete cataracts, phthisis bulbi, uveitis, vitreoretinal interface pathology);
glaucoma;
unsuccessful kidney transplant outcome within a 2-year observation period after the operation;
death within a 2-year observation period in CKD patients undergoing hemodialysis;
refractive anomalies, such as myopia less than -4.0D or hypermetropia more than +3.0D.

Based on the selection criteria, a total sample of 54 CKD patients (108 eyes) was formed. The distribution of patients by gender was 30 (55.6%) males and 24 (44.4%) females. The age of patients ranged from 20 to 45 years, with an average of 27.4±6.7 years.

The development of CKD in patients was attributed to chronic glomerulonephritis in 77.8% of cases, chronic pyelonephritis in 12.9% of cases, and polycystic kidney disease and other forms of kidney developmental anomalies in 9.3% of cases. All patients had a history of receiving hemodialysis for a duration of 1 to 3 years.

Study Design: The research had a prospective nature with the observation of dynamic indicators in patients over a 2-year period. Two study groups were formed:
Group 1, consisting of 36 patients (72 eyes) who underwent kidney transplantation.
Group 2, consisting of 18 patients (36 eyes) receiving hemodialysis and conservative treatment.

Patient examination was conducted before the operation, within 2 months after the operation (early postoperative period), and at 12 months after the operation (late postoperative period).

RESEARCH METHODS

All patients underwent a standard ophthalmological examination, including visual acuity measurement, keratorefractometry, biomicroscopy, ophthalmoscopy, OCT, and OCT angiography (OCT-A). Optical coherence tomography (OCT) of the retina and OCT-A were used to assess structural and microvascular changes in the retinas of patients with end-stage CKD. The study was conducted using the DRI OCT Triton device (Topcon).

Statistical Analysis: Standard methods of variational statistics were employed for statistical processing using Microsoft Office 2018.

RESULTS

OCTA parameters evaluated included the foveal avascular zone (FAZ) perimeter and area, FAZ circularity index, overall vessel density and perfusion, and choroidal vascularity index (CVI).

Analysis of baseline indicators did not reveal statistically significant differences ($p<0.05$) in the parameters of the study groups, indicating homogeneity and representativeness of the groups with regard to the severity of structural and microvascular changes in the retina (Table 1).

Table 1
Baseline OCT-A Indicators in Patients of the Studied Groups

Indicators	Группа 1	Группа 2	Reference values
	M±m	M±m	M±m
FAZ area, mm^2	0,26±0,06	0,25±0,05	0,16±0,04
FAZ perimeter, mm	2,3±0,12	2,28±0,14	1,82±0,23
FAZ circularity index	0,64±0,06	0,65±0,05	0,81±0,06
Total vessel density VD, mm	13,68±1,64	13,73±1,53	18,2±1,4
Total perfusion density PD, %	32,4±4,6	33,5±5,4	42,1±3,2
Choroidal vascularization index CVI	64,6±3,2	65,1±2,6	70,2±3,4

**- statistically significant compared to the indicators of group 2 at p<0.05*

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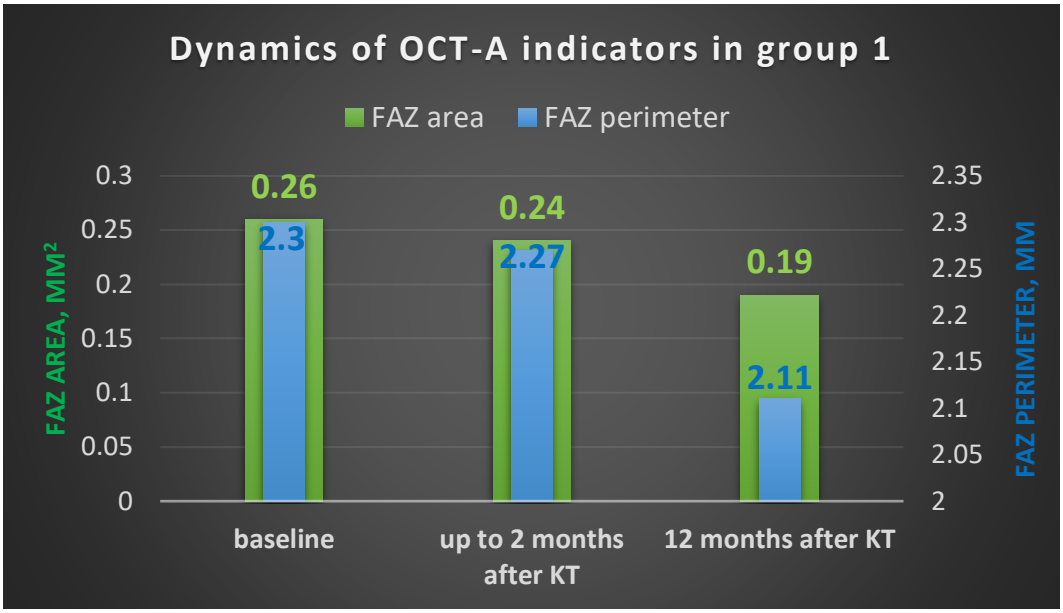

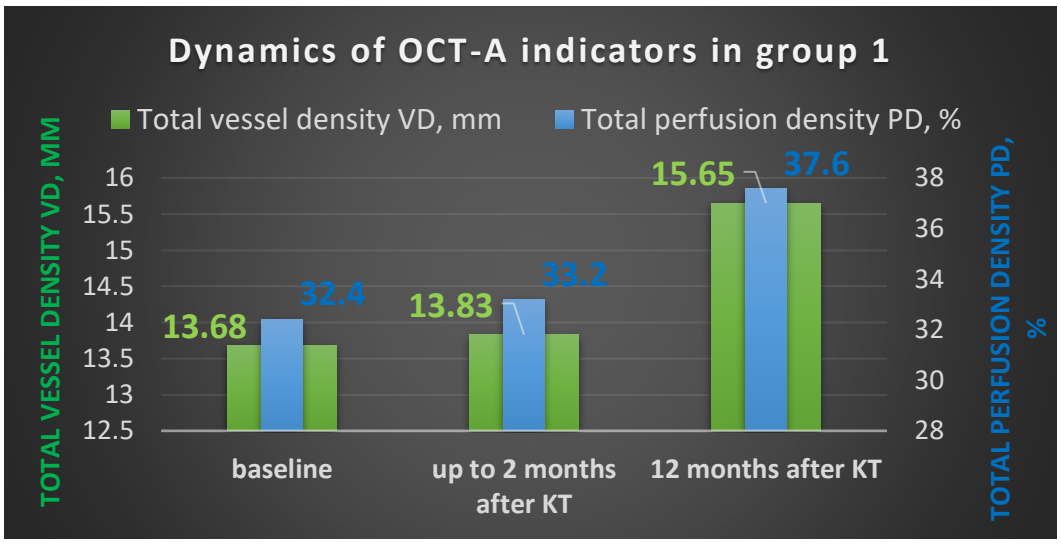

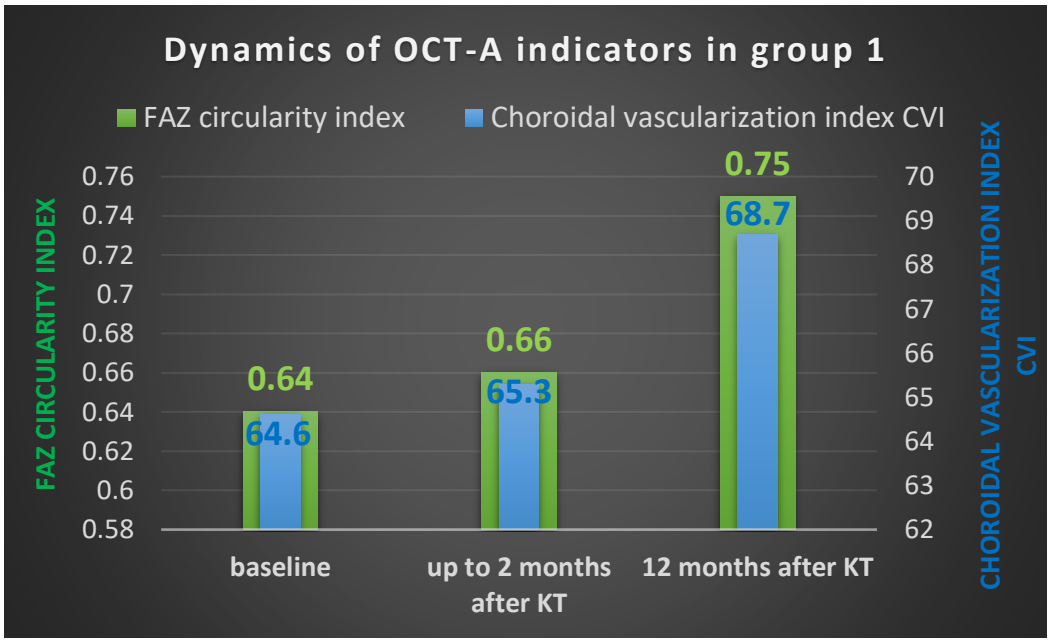

Figure 1. Dynamics of OCT-A indicators in patients of the main group after kidney transplantation.

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The dynamics of OCTA parameters showed that after kidney transplantation (KT), there was a restoration of average values for FAZ area, perimeter, and circularity index over the 12-month observation period, reflecting a positive trend in the macular region. A similar trend was observed in terms of overall vessel density, perfusion, and CVI (fig. 1).

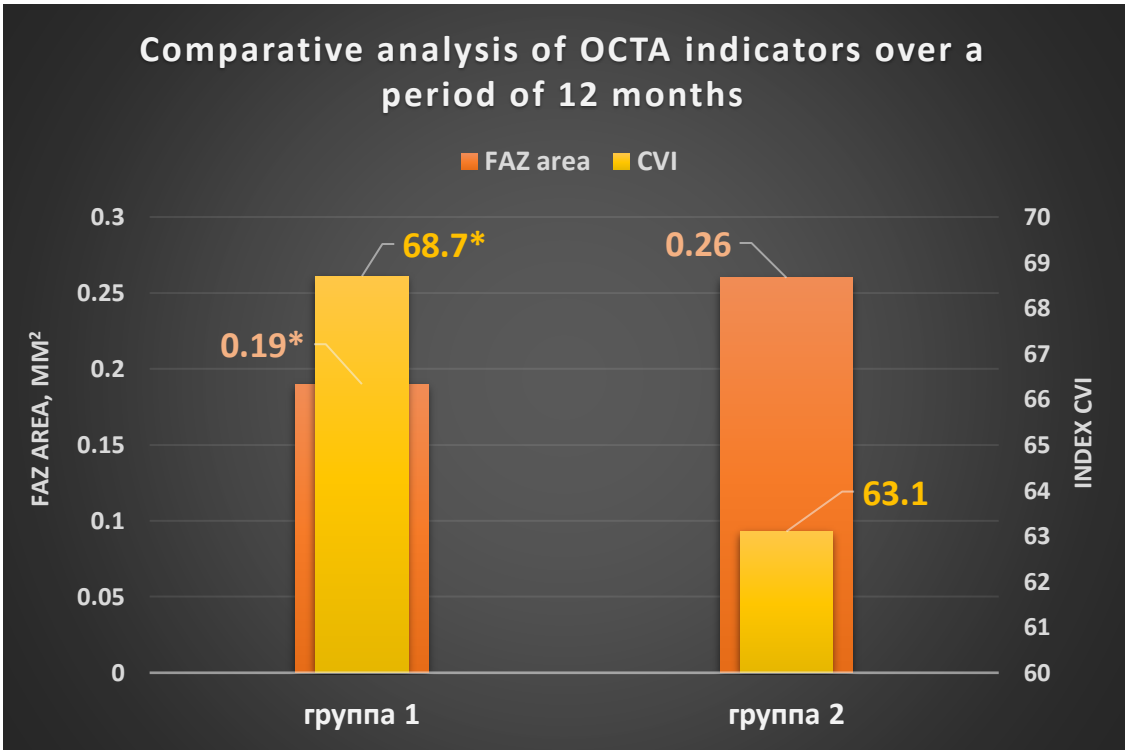

Figure 2. Comparative analysis of key OCT-A indicators in patients from the studied groups after 12 months of observation. ***(* - differences compared to the indicators of group 2 are statistically significant at p < 0.05)***

Figure 2 graphs present the results of a comparative analysis of key OCT-A parameters in the study groups during the 12-month postoperative observation period. A positive dynamic pattern of key parameters in Group 1 was evident when comparing OCT-A parameters such as FAZ area and CVI. In this case, statistically significant differences ($p<0.05$) between the parameters in the study groups were also identified.

The research results indicate a significant reduction in the density of outer retinal vessels after hemodialysis. However, the vessel density in the superficial capillary layer (SCL), deep capillary layer (DCL), and choriocapillaris layer did not show significant changes.

DISCUSSION

The microvascular network with a lumen diameter of less than 300 µm regulates blood supply to tissues and maintains peripheral resistance. Structural and functional disturbances in this network contribute to the development and progression of chronic kidney disease (CKD). Researchers are interested in non-invasive diagnostic possibilities, visualization of retinal and choroidal vessels, and quantitative determination of perfusion volume [1,3,4,7].

The study based on OCT-A allowed us to hypothesize that the reduction in the thickness of the ganglion cell layer and nerve fibers in CKD may be associated with impaired retinal microcirculation and capillary density, affecting perfusion volume. Our research results confirm previously published data [2,4,6,14], which indicated that the level of capillary density in the retina may serve as a prognostic indicator of CKD and may also predict the severity of this condition. This study also underscores the importance of early diagnosis of retinal microcirculation disorders in patients, as it may be a significant risk factor for more severe kidney damage. Similar correlations between the degree and frequency of macular microvascular changes and glomerular filtration rate (GFR) have been noted by other researchers, who found that narrower retinal arterioles and lower fractal dimension of retinal vessels correlate with lower GFR. It has also been demonstrated that narrowing of retinal arterioles is associated with advanced stages of chronic kidney disease (CKD) [6,8].

Most previous studies [2,5,7,11] utilized fundus photography, allowing for the quantitative assessment of only the diameter of large vessels in the retina. In our OCTA-based study, we were able to conduct a more detailed analysis of retinal capillaries and identify a connection between changes in retinal microcirculation and kidney function. We found that GFR levels correlate with impaired retinal perfusion.

These results can be explained by differences in the architecture of vascular structures in the retina. Deep capillary layers of the retina (DCL) are surrounded by a large number of pericytes, while arterioles in the superficial capillary layers (SCL) are freer from such surrounding tissue. Apoptosis (programmed cell death) of pericytes, known to play a crucial role in the

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development of diabetic retinopathy (DR), occurs as CKD progresses, accompanied by increased levels of endothelin-1 and activation of the renin-angiotensin-aldosterone system (RAAS). This can lead to arteriolar constriction and thinning of the vascular intima in response to inflammatory cytokines and growth factors during CKD progression [3,8,9,12].

Our study has also expanded on previous findings, showing that patients with CKD experience a decrease in capillary density in both SCL and DCL. Including patients with more advanced forms of CKD, high proteinuria, and serious kidney function impairments in our study explains pronounced perfusion disturbances and a greater number of sparse capillaries in the retina. All these factors collectively lead to serious microcirculation impairments in CKD.

It is worth noting that our data also demonstrated a correlation between decreased vessel density, increased area and perimeter of foveal avascular zone (FAZ) non-perfusion areas, and the degree of retinopathy, emphasizing the importance of this marker in patients with CKD. Our results also confirm conclusions drawn based on multiple regression analysis, showing that CKD is independently associated with reduced capillary density in both SCL and DCL. The decrease in capillary density is a consequence of capillary rarefaction, which we were able to visualize using OCTA. The degree of capillary rarefaction in the retina of CKD patients varies and depends on various factors. Our results highlight the importance of early diagnosis and monitoring of microcirculation disorders in CKD patients.

CONCLUSION

The main structural changes in the retina and choroid in patients with end-stage CKD is accompanied by a reduction in vessel density and perfusion volume in the superficial capillary layer. These changes become more pronounced with the progression of CKD and are associated with impaired kidney function. The study results showed that kidney transplantation with full compensation of kidney function leads to partial improvement in the condition of the retina, stabilizing the microcirculation.

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