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# Results of assessing the dynamics of ophthalmological complications in chronic kidney disease patients after kidney transplantation

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## Abstract

***Objective.*** *The study objective was to investigate the dynamics of opthalmological complications in the non-diabetic end-stage chronic kidney disease in patients after kidney transplantation.*

***Material and methods.*** *A long-term observation was conducted to assess the changes in morphofunctional parameters of eyes in patients of the study group (after kidney transplantation, n=135 (269 eyes)) and the comparison group (continued on hemodialysis, n=81 (162 eyes)) over 18 months. Both general and specialized ophthalmological investigation methods were employed.*

***Results.*** *The observation showed a positive trend in patients after kidney transplantation, which was manifested by reduced corneal and conjunctival calcification. In the comparison group, both an increase and decrease in qualitative signs of retinopathy were seen as based on optical*

*coherence tomography data, while in the study group, most retinopathy signs decreased, indicating a positive trend possibly brought about by the kidney transplantation. Analysis of optical coherence tomography quantitative parameters showed an improvement in central choroidal thickness and retinal nerve fiber layer thickness in the study group.*

***Conclusion.*** *Kidney transplantation in patients with the non-diabetic end-stage chronic kidney disease leads to a reduction in ophthalmological complications both in the anterior eye segment (reduced corneal and conjunctival calcification) and in its posterior segment (improved optical coherence tomography retinal parameters).*

**Keywords:** chronic kidney disease, kidney transplantation, ophthalmological complications

**Conflict of interests** Authors declare no conflict of interest

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AMD, age-related macular degeneration
BCVA, best-corrected visual acuity
CCT, central choroidal thickness
CKD, chronic kidney disease
CRF, chronic renal failure
HD, hemodialysis
KT, kidney transplant
NE, neuroepithelium/neuroepithelial
OCT, optical coherence tomography
OND, optic nerve disc
RNFL, retinal nerve fiber layer

## Introduction

Currently, the world is witnessing a steady increase in the number of patients with kidney pathology which outcome is a chronic renal failure (CRF). The deterioration of visual functions is a significant factor affecting the quality of life of patients with various somatic diseases, including a kidney disease. According to the latest data from world studies [1-3], structural changes in the organ of vision associated with uremic ophthalmopathy are observed in all patients with chronic kidney disease (CKD). Chronic program hemodialysis (HD), peritoneal dialysis and kidney transplantation (KT) remain the main methods of treating the patients suffering from end-stage chronic renal disease. And the optimal and definitive method of treating this patient population is KT, which eliminates uremic manifestations, promotes medical and social rehabilitation and ensures a high quality of life comparable to that of the general population [4].

Due to the limited possibilities in coping with the consequences of angioretinopathy and optic neuropathy in CKD, it is important to ensure the stability of unaffected retinal neurons and prevent their death in order to maximally preserve the patient's visual function [5–7]. In this case, it is especially important to monitor the dynamics of morphofunctional parameters of the visual organ by using appropriate special ophthalmological investigative techniques in patients with CKD who are on HD or have undergone KT surgery.

**The study objective** was to investigate the dynamics of ophthalmological complications pertinent to the end-stage chronic kidney disease of non-diabetic origin in patients after kidney transplantation.

## Material and methods

The study was conducted at the Republican Specialized Scientific and Practical Medical Center for Eye Microsurgery in the period from 2020–2023. The study included a comprehensive in-depth ophthalmological examination of the patients with end-stage CKD who were under continuous supervision and received hemodialysis at the nephrology center, urology center or private clinics in Tashkent, and the patients who underwent the surgical treatment (kidney transplant) at *V.Vakhidov Republican Specialized Scientific and Practical Medical Center for Surgery*.

The criteria for inclusion of patients in the study were as follows:

– The presence of the end-stage CKD confirmed by the results of relevant laboratory tests as per the proposed by KDOQI classification (2002) based on glomerular filtration rate data;

– A patient informed consent to participate in the study.

Exclusion criteria for the study were the following:

– Diabetes mellitus;

– Ophthalmological diseases (mature or complete cataract, hemophthalmos, uveitis, vitreoretinal interface pathology) preventing the fundus visualization and optical coherence tomography (OCT);

– Age-related macular degeneration (AMD), wet or dry form above AREDS category 2;

– Glaucoma or cases of true ocular hypertension;

– Poor outcome of kidney transplantation within 2 years of follow-up after surgery;

– Fatal outcome during a 2-year follow-up period in patients with chronic renal failure undergoing hemodialysis;

– Refraction anomalies in the form of myopia less than -4.0 Diopters (D) or hyperopia more than +3.0 D.

Based on the selection criteria, a total sample of 241 patients with end-stage CKD (KDOQI stage 4–5) (482 eyes) was formed. The distribution of patients by gender was as follows: 179 men (74.2%) and 62 women (25.8%). The age of patients ranged from 18 to 63 years, the mean age being 35.5±9.7 years.

The CKD development in patients was caused by chronic glomerulonephritis in 182 cases (75.5%), chronic pyelonephritis in 25 cases (10.3%), polycystic kidney disease in 20 cases (8.3%), and other forms of renal abnormal development in 14 cases (5.8%).

Patients of the study group underwent a planned surgical treatment by means of heterotopic kidney transplantation from a living related donor. In preparation for surgery and in the postoperative period, all patients underwent a comprehensive examination, including an objective clinical examination, laboratory tests (complete blood count and blood biochemistry, urinalysis, coagulogram), standard instrumental investigations (electrocardiography, ultrasonography), CYP3A5 genotyping, cross-test, genotyping of HLA class II subtypes.

All patients after KT were administered immunosuppressive therapy: tacrolimus 6 mg/day with monitoring the blood drug levels (normal 13–10 ng/mL for 3 months, 10–7 ng/mL for 3–6 months, 8–6 ng/mL for 6–12 months, 7–5 ng/mL after 12 months); mycophenolate mofetil 1000 mg/day; methylprednisolone 16 mg/day. All patients were also prescribed standard hypotensive, antibacterial and symptomatic therapy.

The ophthalmic examinations included general ophthalmological ones (visometry, biomicroscopy, ophthalmoscopy) and a special investigation, an optical coherence tomography (OCT). For grading and quantitative assessment of corneal and conjunctival calcification, we used the Ching-Hsi Hsiao scoring system (2011) (Fig. 1).

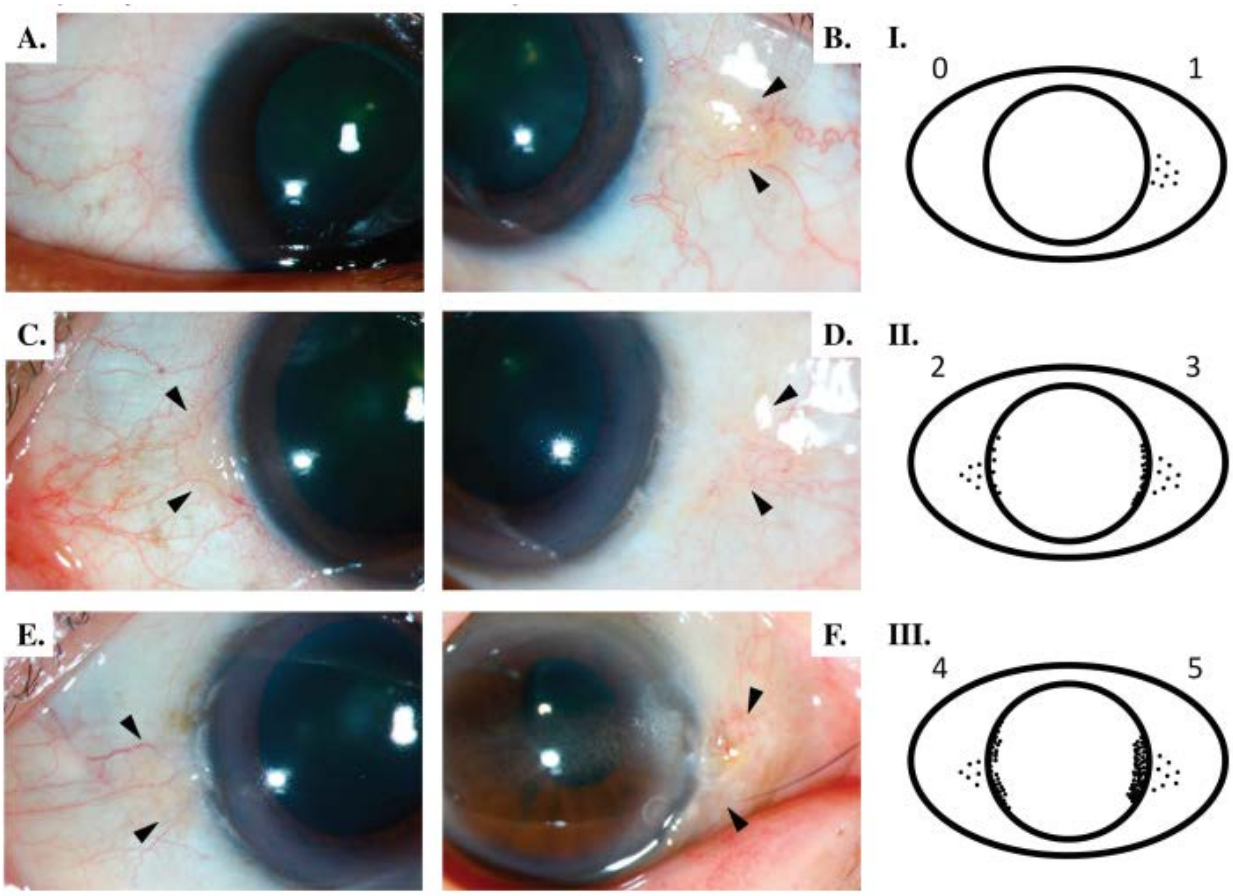


**Fig. 1. Scoring of conjunctival and corneal calcification. (Ching-Hsi Hsiao, 2011). The severity of conjunctival and corneal calcification was classified into six grades (0–5).** 0, no deposits; 1, conjunctival deposits only; 2, conjunctival and irregular corneal deposits; 3, conjunctival and single line of corneal deposits; 4, conjunctival and increased corneal deposits, often as two lines; and 5, conjunctival and extensive corneal deposits

The study materials were subjected to statistical processing using parametric and nonparametric analysis methods. The initial information was collected, adjusted, systematized and the obtained results were summarized as the tabulated data by using the Microsoft Office Excel 2016. Statistical analysis was performed using IBM SPSS Statistics software, v.26.

## Results

One of the most common ophthalmologic findings in patients with end-stage CKD who were on hemodialysis was corneal-conjunctival calcification visualized as the deposits of calcium phosphate salts detected on the conjunctiva and peripheral part of the cornea at biomicroscopy. Their development is usually associated with metabolic disorders in the human body manifested by the increased blood levels of calcium and phosphates as a result of CKD.

Studies have shown that initially only 7.68% of eyes showed no traces of deposits on the cornea and conjunctiva, while the remaining eyes showed signs of calcification of varying severity (Table 1).

**Table 1. Incidence rate of corneal and conjunctival calcification severities in the eyes (n=482) of patients with end-stage chronic kidney disease**

| Corneal and conjunctival calcification grade | n | % |
|---|---|---|
| 0 | 37 | 7.68 |
| 1 | 46 | 9.54 |
| 2 | 126 | 26.14 |
| 3 | 113 | 23.44 |
| 4 | 96 | 19.92 |
| 5 | 64 | 13.28 |
| **Total** | **482** | **100** |

Patient observations over time showed that those who had undergone KT, showed positive dynamics manifested by a decreased severity of corneal and conjunctival calcification in the eyes. The patients who continued receiving HD, showed negative dynamics with the progression of the ocular surface calcification (Table 2).

**Table 2. Dynamics of the corneal and conjunctival calcification grade on the ocular surface in the patients in the investigated groups**

| Grade | Patients with the end-stage CKD who continued to receive HD (81 patients, 162 eyes) | | | | Patients with end-stage CKD who underwent KT (160 patients, 320 eyes) | | | |
|---|---|---|---|---|---|---|---|---|
| | Baseline | | After 36 months | | Baseline | | After 36 months | |
| | n | % | n | % | n | % | n | % |
| 0 | 14 | 8.64 | 6 | 3.70 | 23 | 7.19 | 21 | 6.56 |
| 1 | 20 | 12.35 | 16 | 9.88 | 26 | 8.13 | 28 | 8.75 |
| 2 | 32 | 19.75 | 29 | 17.90 | 94 | 29.38 | 94 | 29.38 |
| 3 | 41 | 25.31 | 45 | 27.78 | 72 | 22.50 | 73 | 22.81 |
| 4 | 34 | 20.99 | 40 | 24.69 | 62 | 19.38 | 66 | 20.63 |
| 5 | 21 | 12.96 | 26 | 16.05 | 43 | 13.44 | 38 | 11.88 |

The data in Table 2 show that in the group of patients who continued to receive HD, the number of patients with more severe calcification (grades 3 and 4) increased. For example, the proportion of eyes with grade 3 increased from 25.31% to 27.78%, and that one with grade 4 increased from 20.99% to 24.69%. In the group of patients who underwent KT, the proportion of eyes with grade 0 calcification decreased from 7.19% to 6.56%, and that with grade 1, increased insignificantly from 8.13% to 8.75%. These data show that calcification progressed faster in the patients who continued to receive HD than in those who underwent KT.

A clinical example is shown in Fig. 2.

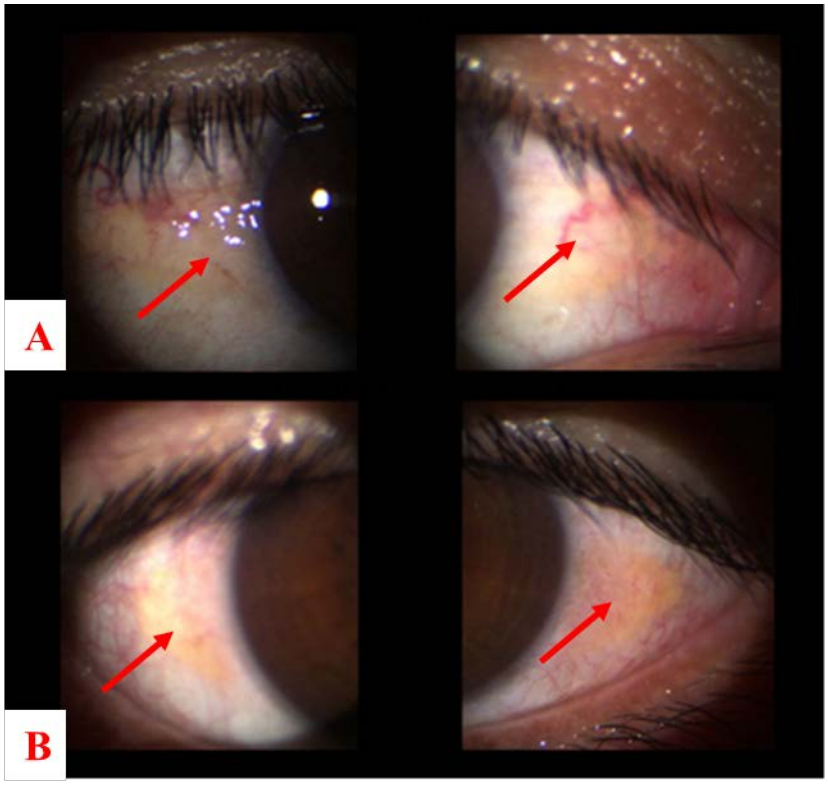


**Fig. 2. The view of the anterior segment of the eyeball before (A) and 18 months (B) after kidney transplantation**

The presented images (Fig. 2) show that before the kidney transplant, the right eye had grade 3 corneal and conjunctival calcification (deposits are marked with arrows), whereas 18 months after the kidney transplant, the deposits regressed and the degree of calcification was assessed as grade 1.

The effect of KT on the retinal status was assessed by investigating the qualitative and quantitative OCT parameters over time. A similar set of parameters was investigated in the group of patients who continued to receive HD. A longitudinal study was performed to evaluate the dynamics of morphofunctional characteristics of the visual organ in patients in the study group (KT, n=135 (269 eyes) (1 eye was excluded from the study due to the development of tacrolimus-induced optic neuropathy) and the comparision group (continuation of the program HD, n=81, 162 eyes) during 18-month observation period. The patients who developed the

visual organ changes associated with immunosuppressive therapy side effects in the form of ocular hypertension and tacrolimus-induced optic neuropathy were excluded from the comparative study, as were the cases where the detailed visualization of the retina by OCT was impossible due to severe lens opacity or the presence of hemophthalmos caused by malignant hypertension, so the total number of patients reduced to 216 (431 eyes).

The analysis of data on the incidence of the main OCT qualitative signs of retinal damage in patients over 18-month observation period is presented in Table 3.

**Table 3. The incidence rate dynamics (%) in the main qualitative signs of retinal damage according to optical coherence tomography data in the patients of the investigated groups over 18 months of observation**

| OCT signs | Comparison group (patients who continued to receive HD, 81 patients, 162 eyes) | Study group (patients who underwent KT, 135 patients, 269 eyes) |
|---|---|---|
| | *Δ%* | *Δ%* |
| Diffuse retinal edema | 39.1 | -91.7 |
| Foci of NE serous detachment | -12.5 | -93.36 |
| Macular edema | -21.4 | -92.83 |
| OND edema | -13.8 | -90.14 |
| Hyperreflective foci in the outer retinal layer | 14.3 | -80.4 |
| Areas of nerve fiber layer thickening | 19.92 | -17.81 |
| Areas of the DRILL type disorganization in the inner retinal layers | 24.98 | -7.61 |
| Focal thinning of the inner retinal layers with the elevation of the outer retinal layers | 30.42 | 1.95 |
| Areas of atrophic inner retinal layers | 36.83 | 1.04 |

Notes: OND, optic nerve disk; NE, neuroepithelium.

Table 3 demonstrates a significant improvement in all key OCT signs, especially in the incidence of retinal edema (decreased by 91.7%), serous NE detachment (decreased by 93.36%), macular edema (decreased by 92.83%) and optic disc edema (decreased by 90.14%), in the study group (patients who underwent transplantation). These changes differ significantly from the results in the comparison group, where the incidence of some signs even increased, indicating a less effective impact of conservative treatment. Kidney transplantation was more effective in improving the patient condition across most OCT signs, which was confirmed by a considerable decrease in the frequency of these signs in the study group.

There is a clinical example below, showing the OCT image changes over time in a patient with the end-stage CKD before and after KT. The OCT images are shown before and 15 months after KT (Fig. 3).

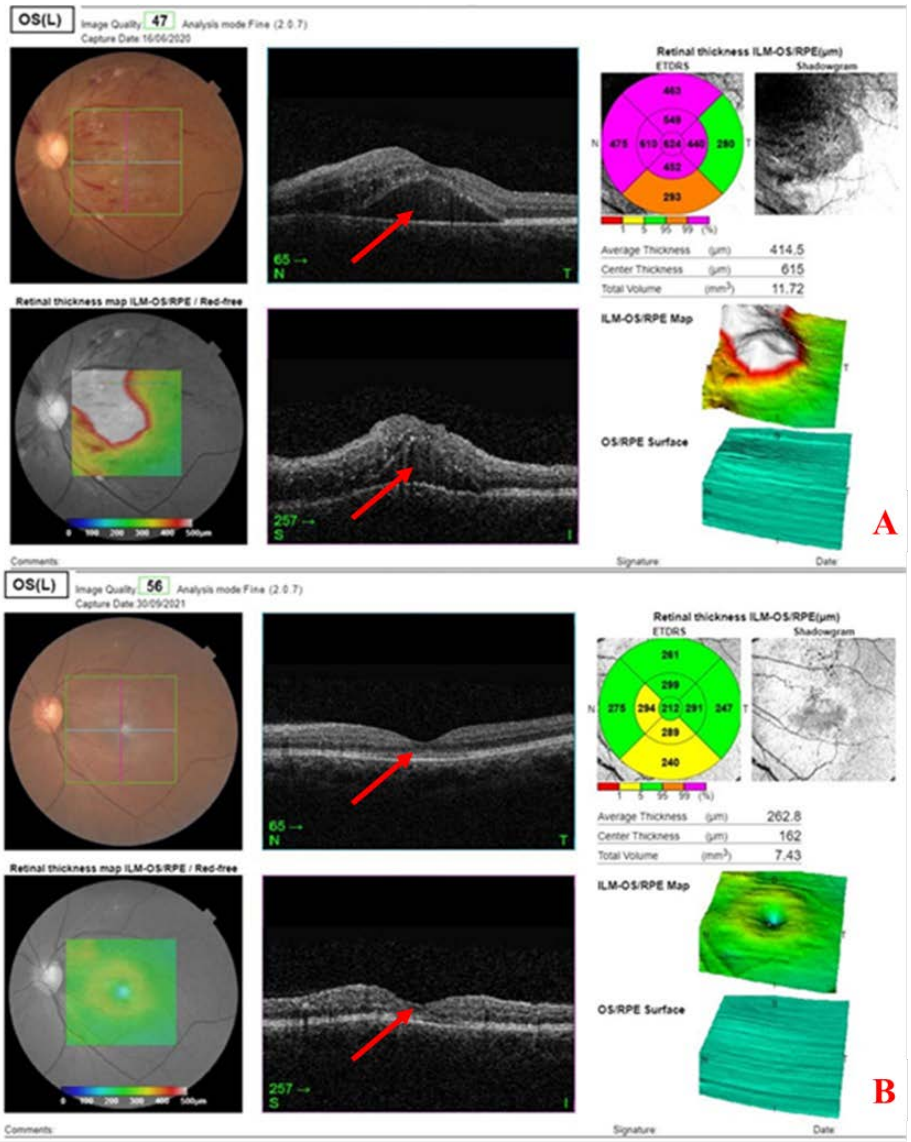


**Fig. 3. Dynamics of central exudative neuroepithelial detachment in chronic renal failure after kidney transplantation. A.** Initial optical coherence tomography image: a section in the macular region reveals the presence of serous exudative neuroepithelial detachment (arrows). **B.** Optical coherence tomography image after 18 months: a section in the macular region reveals positive dynamics as a cease of retinal detachment as a coped detachment of neuroepithelium and the adjacent retina) (arrows)

Among the quantitative variables presented in Figure 3, the particularly interested was the study of the changes in the central choroidal thickness and the thickness of the retinal nerve fiber layer (RNFL) over time.

The statistical analysis showed that the change of the central choroidal thickness in the comparison group over 18 months was statistically significant (p=0.0186), which suggested negative actual changes in the ophthalmic status of the patients in the hemodialysis group.

The change of the central choroidal thickness in the study group was statistically insignificant (p=0.7471), which meant that there were no significant changes in the patient ophthalmic status 18 months after KT and indicated its stability in the patients of the KT group (Table 4).

**Table 4. Dynamics of the central choroidal thickness parameter in the patients of the investigated groups during the first 18 months of observation**

| Parameter | Comparison group | Study group |
|---|---|---|
| | M±m | M±m |
| Baseline | 245.59±19.35 | 242.34±17.75 |
| After 18 months | 240.47±19.62* | 242.84±18.2 |
| p | 0.0186 | 0.7471 |

* Differences compared to baseline values were considered statistically significant at p<0.05

As can be seen from Table 5, the decrease in RNFL thickness in the comparison group may indicate a progressive loss of retinal nerve fibers. Meantime, we observed a statistically significant decrease in the RNFL parameter after 18 months (p<0.001). This indicates that the continuation of hemodialysis does not prevent a decrease in the thickness of the nerve fiber layer, which requires careful monitoring and possible changes in therapy (Table 5). The decrease in RNFL thickness in the study group was also statistically insignificant (p<0.05). The study group demonstrated the stability of the RNFL parameter, which could indicate a favorable effect of kidney transplantation in preventing progressive neurodegeneration.

**Table 5. Dynamics of the retinal nerve fiber layer thickness in patients of the investigated groups during the first 18 months of observation**

| Parameter | Comparison group | Study group |
|---|---|---|
| | M±m | M±m |
| Baseline | 93.55±2.75 | 94.46±2.46 |
| After 18 months | 90.01±2.84* | 93.9±2.68* |
| p | 0.0002 | 0.11 |

* Differences compared to baseline values were considered statistically significant at p<0.05

Table 6 presents the results of dynamic monitoring of the best-corrected visual acuity (BCVA) parameter in patients in the investigated groups.

**Table 6. Dynamics of best-corrected visual acuity in the patients of the investigated groups during 18 months of observation**

| Parameter | | Comparison group | Study group |
|---|---|---|---|
| | | M±m | M±m |
| BCVA, distance | Baseline | 0.73±0.11 | 0.73±0.12 |
| | After 18 months | 0.69±0.14* | 0.85±0.09*^ |
| BCVA, near | Baseline | 0.79±0.09 | 0.79±0.09 |
| | After18 months | 0.74±0.11 | 0.83±0.08*^ |

* Statistically significant in relation to the baseline value (p<0.05);

^ Statistically significant in relation to the value of the comparison group (p<0.05).

The data in Table 6 indicate that HD does not prevent the deterioration of visual acuity: both at a distance and near; a statistically significant decrease in the presented parameters is observed after 18 months. KT demonstrates a favorable effect on visual acuity with a significant improvement in both the distance and near vision in patients who underwent the procedure.

## Discussion

The analysis shows different trends in CCT changes in patients from the two groups. Patients who continued on hemodialysis showed a decrease in this parameter, while those who underwent KT showed a slight increase. The decrease in CCT may be associated with morphological changes in renal tissues, indicating the severity of glomerular damage [6–8]. Our study included patients with advanced stages of CKD, and we found a consistent association between a decrease in CCT and worsened glomerular filtration rate.

Our data indicate a general decrease in retinal thickness in patients on HD. In addition, an incomplete recovery of choroidal and retinal thickness was noted after dialysis. In addition, a decrease in the CCT parameter was a characteristic feature for the overall sample of patients with end-stage CKD, which may be associated with specific changes in the choroid. They may be due to a more significant decrease in serum osmolarity and total body weight in the patients.

The exact mechanism of neurodegeneration in patients with CKD has not yet been defined [8–12]. Patients with diabetes mellitus and true increase in intraocular pressure were excluded from the present study. In this regard, the obtained results showing a decrease in RNFL thickness can be interpreted as the signs of neurodegeneration, which is presumably associated with systemic processes caused by CKD. The results of the study have proven that patients at the end-stage of non-diabetic CKD who receive hemodialysis have a high rate of progression of RNFL loss over time.

## Conclusions

1. Kidney transplantation in patients with the end-stage chronic kidney disease of non-diabetic origin contributes to the reduction in the severity of ophthalmological complications both in the eye anterior

segment (reduced progression of corneal and conjunctival calcification) and the eye posterior segment (reduced incidences of retinal edema by 91.7%, serous detachment of neuroepithelium by 93.36%, macular edema by 92.83%, and the optic disc edema by 90.14%).

2. The study has demonstrated a statistically significant decrease of the central choroidal thickness and RNFL thickness, as per optical coherence tomography results, in the hemodialysis group of patients ($p=0.0186$ and $p=0.0002$) over an 18-month period, compared to no statistically significant changes in these parameters in the kidney transplantation group ($p=0.7471$ and $p=0.11$) over the similar observation period, which indicates the deterioration of the retinal quantitative parameters in patients on hemodialysis and these parameters being stable in kidney transplant recipients in the long term.

## References

1. Zhu Z, Liao H, Wang W, Scheetz J, Zhang J, He M. Visual impairment and major eye diseases in chronic kidney di-sease: the National Health and Nutrition Examination Survey, 2005–2008. *Am J Ophthalmol.* 2020;213:24–33. PMID: 31945332 https://doi.org/10.1016/j.ajo.2020.01.002

2. Fursova AZh, Derbeneva AS, Vasilyeva MA, Tarasov MS, Nikulich IF, Galkina EV. Development, clinical manifestations and diagnosis of retinal changes in chronic kidney disease. *Russian Annals of Ophthalmology.* 2021;137(1):107–114. (In Russ.). https://doi.org/10.17116/oftalma2021137011107

3. Ahsan MK, Alam MR, Khanam A, Ahmed A, Faroque M, Hadiuzzaman K, et al. Ocular fundus abnormalities in pre-dialytic chronic kidney disease patients. *J Biosci Med.* 2019;7:20–35. https://doi.org/10.4236/jbm.2019.711003

4. Chen H, Zhang X, Shen X. Ocular changes during hemodialysis in patients with end-stage renal disease. *BMC Ophthalmol.* 2018;18(1):208. PMID: 30139333 https://doi.org/10.1186/s12886-018-0885-0

5. Zeng X, Hu Y, Chen Y, Lin Z, Liang Y, Liu B, et al. Retinal neurovascular impairment in non diabetic and non-dialytic chronic kidney disease patients. *Front Neurosci.* 2021;15:703898. PMID: 34867144 https://doi.org/10.3389/fnins.2021.703898

6. Wu IW, Sun CC, Lee CC, Liu CF, Wong TY, Chen SY, et al. Retinal neurovascular changes in chronic kidney di-sease. *Acta Ophthalmol.* 2020;98(7):e848–e855. PMID: 32190993 https://doi.org/10.1111/aos.14395

7. Jung KI, Kim SJ, Park CK. Systemic vascular risk factors for multiple retinal nerve fiber layer defects. *Sci Rep.* 2018;8(1):7797. PMID: 29773842 https://doi.org/10.1038/s41598-018-26160-7

8. Yeung L, Wu IW, Liu CF, Lin YT, Lee CC, Sun CC. Accelerated peripapillary retinal nerve fiber layer degeneration in patients with chronic kidney di-sease: a 2-year longitudinal study. *Transl Vis Sci Technol.* 2022;11(12):10. PMID: 36515965 https://doi.org/10.1167/tvst.11.12.10

9. Gong X, Wang W, Li W, Jin L, Wang L, Meng J, et al. Association between renal function and retinal neurodege-neration in Chinese patients with type 2 diabetes mellitus. *Ann Transl Med.* 2021;9(7):560. PMID: 33987258 https://doi.org/10.21037/atm-20-6957

10. Chow JY, She PF, Pee XK, Muda WNW, Bastion M-LC. Comparison of peripapillary retinal nerve fiber layer and macular thickness in non-diabetic chronic kidney disease and controls. *PLoS One.* 2022;17(4):e0266607. PMID: 35385541 https://doi.org/10.1371/journal.pone.0266607

11. Rauscher FG, Wang M, Francke M, Wirkner K, Tönjes A, Engel C, et al. Renal function and lipid metabolism are major predictors of circumpapillary retinal nerve fiber layer thickness – the LIFE-Adult

Study. *BMC Med.* 2021;19(1):202. PMID: 34488766 https://doi.org/10.1186/s12916-021-02064-8

12. Demir MN, Eksioglu U, Altay M, Tok O, Yilmaz FG, Acar MA, et al. Retinal nerve fiber layer thickness in chronic renal failure without diabetes mellitus. *Eur J Ophthalmol.* 2009;19(6):1034–1038. PMID: 19882571 https://doi.org/10.1177/112067210901900621

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