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Original Scientific Paper

QUANTIFYING MICROVASCULAR ABNORMALITIES IN CHRONIC KIDNEY PATIENTS

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SUMMARY – *Introduction.* Ocular microvascular changes can be related to kidney deterioration in chronic kidney disease (CKD). We aimed to identify the association between retino-choroidal parameters and kidney deterioration in diabetics and non-diabetics.

Methods. The study group consisted of CKD patients (cross-sectional study) with arterial hypertension with different stages of CKD. Complete eye examination was completed with optical coherence tomography angiography (OCTA) scans of the macular region. According to the value of glomerular filtration rate (GFR) and albuminuria, patients were divided into groups: low GFR (<60ml/min) and high GFR (>60ml/min) and CKD patients without albuminuria and CKD with micro or macroalbuminuria.

Results. One hundred and six eyes of 106 chronic kidney disease patients were evaluated. The mean retinal thickness in GFR <60 ml/min group was 275,73±9,65 micron (μ), whereas in a GFR >60 ml/min group was 274,36±10,77 μ. OCTA showed lower deep vascular density (DVD) in CKD with albuminuria versus CKD without albuminuria group ($p < 0.001$). Albuminuria was inversely related to choroidal and retinal thickness measures of superficial (SVD) and DVD.

Conclusions. CKD is associated with retinal diluting and decreasing kidney function with reduction of retinal and choroidal vascular density.

Key words: *Microvasculature; Chronic kidney disease; OCTA; Chorioretinal thickness; Vascular density*

Introduction

Cardiovascular diseases (CVD) are a severe medical issue due to the progressive increase in their incidence and prevalence. CVD is also the headmost cause of death and includes cardiac, metabolic risk, and chronic kidney disease (CKD) among its accelerating factors. CVD and CKD are narrowly interrelated: they both share common traditional risk factors, such as diabetes mellitus, obesity, smoking, and hypertension (1). CKD is a common comorbidity in ophthalmologic patients, especially among old aged, hypertensive patients, and diabetics. The prevalence is estimated to be as high as 30.8% at age 70 or more (2). It can also be found in 15% of non-diabetic hypertensive patients and in 43%-53% of patients with diabetes. Patients with CKD have higher risks of cataracts, glaucoma, retinopathies, and visual exacerbation (3).

The mechanism behind increased ocular diseases in patients with CKD is still being discussed. It may be due to CKD and ocular diseases, dispensing many systemic risk factors such as aging, diabetes, hypertension, obesity, and smoking. This is primarily due to mechanisms related to CKD, such as increased oxidative stress or increased inflammation (4). The microvascular changes of the retina may be valuable biomarkers

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for predicting CVD, cognitive deterioration, and aggravation of kidney function in patients with CKD (5,6). However, there is limited information on microvascular alterations at the capillary level. It is also unclear what role other systemic comorbidities play in these microvascular changes (7).

Recent studies also emphasize the analogy existing between the eye and the kidney, detectable in their embryogenesis, on a structural level, and also in the pathogenic pathways that involve them. There is a structural analogy between the kidney vascular network and the choroidal circulation, the glomerular membrane and blood-retinal barrier share similar pathways too. A specific RAS has also been found, which acts selectively on various retinal components as the microcirculation, Müller cells, ganglion cells, and retinal pigment epithelium cells (4). The ocular microcirculatory system is easily accessible to clinical and morphological evaluation and can be studied in a repeatable and noninvasive manner, offering a unique condition to observe the vascular network when affected by systemic diseases such as hypertension, diabetes mellitus, and CKD (8).

The introduction into clinical practice of optical coherence tomography angiography (OCTA) offers a reliable tool for studying retinal and choroidal circulation from a morphological point of view. OCTA is a newly developed noninvasive diagnostic tool that provides a depth-resolved three-dimensional image to visualize the different layers of the retinal vascular plexuses. OCTA is easily performing, noninvasive, and repeatable; it ensures high-resolution images and information about retinal and choroid thickness and vascular network. (9).

The purpose of this study was to evaluate the retina-choroid in patients with different stages of kidney dysfunction, using OCTA, and to analyze associations, if any, between retinal-choroidal parameters and CKD. We also evaluated systemic factors associated with these changes.

Methods

This is a cross-sectional study that was selected from hypertensive patients with different stages of kidney deterioration consecutively attending the Clinic for Nephrology. The research followed the tenets of the Declaration of Helsinki. Informed consent was obtained, and the research was approved by the Ethics Committee of the University Clinical Center Sarajevo.

The inclusion criteria were: patients with arterial hypertension with different stages of kidney dysfunction, age ≥21 years, and no visual symptoms. The exclusion criteria were as follow: the presence of dense cataract, vascular occlusion, macular hole, maculopathies or choroidal neovascularisation, and glaucoma, as well as the presence of an uncontrolled systemic condition able to cause an ocular involvement, GFR <15 ml/ min/ 1.73 m2, hemodialysis, peritoneal dialysis, and heart failure.

Clinical data, urine analysis, and quantitative urine analysis for albuminuria were obtained from all subjects. Only the subjects with albuminuria >30 mg/day, identified on reliable 24-h urine collections, were defined as albuminuria. The entire study cohort was divided into four subgroups based on two different criteria: subjects with a GFR value above (high GFR) or below (low GFR) 60 ml/min/1.73 m^2 and CKD patients with or without albuminuria as previously defined.

We used the new OptoVue OCTA (Optical coherence tomography angiography) machine, AngioVue system (Optovue Inc., Fremont, CA, USA,) to examine superficial and deep vascular density (SVD and DVD) on macular OCTA scans (3 × 3mm) centered on the fovea in a cross-sectional study in 106 eyes of 106 patients with different stages of CKD. Using the machine's AngioVue software, the vascular area was automatically segmented into four layers: the superficial, deep, outer retina, and choroidal. The default segmentation for the SVD includes vasculature between the internal limiting membrane and 10 μm above the inner plexiform layer. For the DVD, this includes the vasculature between 10 μm above the inner plexiform layer and 10 μm below the outer plexiform layer. The vessel density is defined as the percentage area occupied by all vessels in a particular region. The AngioVue software automatically calculates the vessel density of the SVD and the DVD, respectively. We also evaluated other foveal parameters provided by the machine software, including the foveolar avascular zone (FAZ) size, FAZ perimeter, and microaneurysms. The foveal parameters were determined from an OCTA image of the inner retina microvasculature, which contained both SVD and DVD.

Table 1. Main clinical characteristics of patients with different stages of kidney dysfunction

	GFR≤60ml/min (n=69)	GFR>60ml/min (n=37)	p	CKD without albuminuria	CKD with albuminuria	p
Age (years)	66 (60-74.5)	64 (56.5-71.5)	0.262	63 (58.3-72.8)	66.5 (60-73.3)	0.354
Gender (M/F)	47 (68.1%) / 22 (31.9%)	26 (70.3%) / 11 (29.7%)	0.819	30 (69.8%) / 13 (30.2%)	43 (68.3%) / 20 (31.7%)	0.869
Smoking (yes)	31 (45.6%)	11 (30.6%)	0.137	15 (34.9%)	27 (44.3%)	0.337
SBP (mm Hg)	130 (120-140)	130 (120-140)	0,868	130 (120-140)	135 (120-140)	0.854
DBP (mm Hg)	80 (70-90)	80 (70-90)	0,819	80 (77.5-82.5)	80 (70-80)	0.1
Diabetes (yes)	24 (34.8%)	18 (48.6%)	0.164	7 (16.3%)	35 (55.6%)	**<0.001**
Glycemia(mmol/L)	5.1 (4.6-7.1)	5.95 (4.7-8.4)	0.126	5 (4.5-5.7)	6.4 (4.9-8.8)	**0.002**
Chol (mmol/L)	5.5±1.4	5.4±1.4	0.6	5.4±1.3	5.6±1.4	0.253
Tg (mmol/L)	1.9 (1.6-2.5)	1.9 (1.4-2.9)	0.808	1.8 (1.4-2.5)	2 (1.7-2.6)	0.303
Hb (g/L)	129.14±20.5	137.54±18.8	**0.041**	134.6±17.3	130.2±21.9	0.433
Proteinuria (g/day)	0.51 (0.2-1.5)	0.45 (0.16-1.82)	0.627	0.19 (0.13-0.28)	1.06 (0.44-2.7)	**<0.001**
Albuminuria(mg/L)	39.5 (23-247.8)	61.5 (21.5-297)	0.703	21 (16.5-27)	204 (75-282.3)	**<0.001**
Cr. clear. (ml/min)	39.7 (31.7-48.9)	74.8 (65.7-94)	**<0.001**	52.6 (36.3-64.1)	46.7 (36.1-72.4)	0.762

Abbreviations: GFR-glomerular filtration rate; CKD-chronic kidney disease; SBP-systolic blood pressure; DBP-diastolic blood pressure; Tg-triglyceride; Chol.-cholesterol; Hb-hemoglobin; Cr. clear. - creatinine clearance

Statistical analysis

All statistical calculations were performed with the SPSS 16 software (version 16.0, SPSS Inc, Chicago, Illinois, USA). The distribution of variables was tested by the Kolmogorov–Smirnov and the Shapiro-Wilk test. Values with normal distribution were expressed as mean ± standard deviation, while those without normal distribution were shown as median and interquartile range. Depending on the distribution of variables, a comparison between the groups was performed by the t-test or Mann-Whitney U-test. In the analysis of the dependence between categorical variables, the chi-square test was performed. Depending on the distribution of variables, correlations were assessed by Pearson's correlation analysis or Spearman's test. *P* values of less than 0.05 were considered statistically significant.

Results

Baseline characteristics and data of the study population are summarised in Table 1.

One hundred-six eyes of 106 CKD patients with different stages of kidney dysfunction were evaluated. Sex, age, presence of glycemia, and systolic and diastolic blood pressure were recorded. Total cholesterol, triglycerides, hemoglobin, GFR, and urinary excretion of protein were evaluated as health status parameters. Low GFR with albuminuria group included patients with kidney impairment; the High GFR with albuminuria group included the remaining ones. These groups enrolled patients with comparable clinical characteristics ($p > 0.05$) except for some parameters (presence of diabetes, glycemia, and urinary albumin). When evaluating subgrouping according to GFR values, in the high GFR group (>60 ml/min), there were 37 subjects, 26 of which are males (70.3%); the low GFR (≤60 ml/min) group collected 69 subjects, 47 of which are males (68.1%). In CKD without albuminuria group, there were 43 subjects, 30 of which are males (69.8%). CKD with albuminuria group collected 63 subjects, 43 of which are males (68.3%). Age was no significantly different in group high GFR than in group low GFR, as well as in patients CKD groups with or without albuminuria. The CKD group with albuminuria or gross proteinuria showed a mean higher value of plasma glucose and urine albumin than the CKD without albuminuria group ($p<0.001$ respectively).

Table 2. shows pharmacological treatment distribution, also categorised according to kidney function. CKD group with albuminuria and low GFR were more often treated with anti-hypertensive drugs (ACE

Table 2. Distribution of the patients pharmacologically treated for hypertension and of other cardiovascular drugs among the groups with different stages of kidney dysfunction

	GFR≤60ml/min	GFR>60ml/min	p	CKD without albuminuria	CKD with albuminuria	p
Anti-hypertensive drugs (%)						
ACE inhibitors	43 (62.3)	18 (48.6)	0.175	22 (51.2)	39 (61.9)	0.272
AT1 blockers	12 (17.4)	8 (21.6)	0.596	7 (16.3)	13 (20.6)	0.574
Calcium antagonists	34 (49.3)	19 (51.4)	0.839	24 (55.8)	29 (46.0)	0.323
Diuretics	38 (55.1)	15 (40.5)	0.154	20 (46.5)	33 (52.4)	0,553
β-blockers	22 (31.9)	11 (29.7)	0.819	12 (27.9)	21 (33.3)	0,554
Other cardiovascular drugs (%)						
Antiplatelet drugs	21 (30.4)	16 (43.2)	0.187	16 (37.2)	21 (33.3)	0.681
Statins	33 (47.8)	20 (54.1)	0.541	18 (41.9)	35 (55.6)	0.166

Table 3. OCTA among the groups with different stages of kidney dysfunction

	GFR≤60 ml/min	GFR>60 ml/min	p	CKD without albuminuria	CKD with albuminuria	p
RT total area (μ)	274.4±10.7	275.7±9.7	0.52	277.2 (271.2-280.5)	273.4 (266.8-280.6)	0.116
RT central ring (μ)	245.3 (240.7-247.8)	246(241.6-247.7)	0.462	246.3 (242.2-247.9)	244.8 (240.6-247.5)	0.312
ChT central ring (μ)	286.2 (246.4-290.1)	276.6 (250.2-292.6)	0.36	290.2 (286.1-294.1)	264.5 (245.1-288.7)	**<0.001**
ChT total area (μ)	271.2 (249.7-276.7)	270.3 (264.5-275.9)	0.59	273.5 (269.8-278.1)	266.9 (249.4-273.9)	**0.001**
Area of FAZ (mm^2)	0.29 (0.27-0.33)	0.28 (0.25-0.31)	0.06	0.28 (0.26-0.3)	0.3 (0.3-0.34)	**0.03**
SVD (%)	46.6 (44.9-47.9)	47.3 (45.9-49.6)	**0.03**	47.3 (46.3-48.3)	46.3 (44.8-48.6)	0.06
DVD (%)	48.7 (47.3-49.3)	48.7 (47.7-49.2)	0.44	49.1 (48.6-49.4)	48.1 (47.1-48.9)	**<0.001**
MA (up to 10)	20 (29%)	24 (64,9%)	**<0.001**	21 (48.8%)	23 (36.5%)	0.206
FAZ (μm) perimeter	2197 (2168.5-2267)	2177 (2157-2259)	0,263	2177 (2156-2201)	2199 (2166-2285)	**0.009**

Abbreviations: GFR - glomerular filtration rate; CKD - chronic kidney disease; RT - retinal thickness; ChT - choroidal thickness; FAZ - foveal avascular zone; SVD - superficial vascular density; DVD - deep vascular density; MA - microaneurysms

inhibitors and AT1 blockers) than the counterpart. The systemic conditions and classes of anti-hypertensive drugs are summarized in Table 2.

Table 3. elucidates data referring to OCTA features. Regarding choroidal thickness, comparing these data according to the subgrouping for GFR values, low GFR, and CKD with albuminuria groups showed greater choroidal thinning values than GFR>60 ml/min and CKD without albuminuria groups (p <0.001). These differences remained significant even after the adjustment for treatment with anti-hypertensive drugs. OCTA comparison, according to subgrouping, revealed differences in vascular density of both SVD and DVD in the parafoveal area. SVD was significantly lower in the GFR≤60 ml/min group than in the GFR>60 ml/min group (p=0.03), but not in the CKD

Table 4. Correlates of the chorioretinal parameters using OCTA features assessed in the overall study population

	GFR	Albuminuria	Glycemia	Chol.	Tg	Hb	SBP	DBP
	Rho							
RT total area (μ)	0.180	**-0.223***	**-0.595****	0.047	-0.029	**0.254****	**-0.197***	0.072
RT central ring (μ)	0.184	-0.167	**-0.431****	0.110	-0.036	0.177	0.140	0.127
ChT central ring (μ)	0.184	**-0.542****	**-0.686****	0.093	-0.158	0.158	-0.082	0.160
ChT total area (μ)	0.187	**-0.398****	**-0.636****	0.109	-0.149	**0.232***	-0,083	0.168
Area of FAZ (mm^2)	**-0.26****	**0.291****	**0.411****	0.041	**0,234***	**-0.27****	0.168	-0.047
SVD (%)	**0.32****	**-0.275****	**-0.581****	0.017	-0.110	**0.352****	-0.095	0.143
DVD (%)	**0.203***	**-0.490****	**-0.683****	0.010	-0.177	0.185	-0.088	0.114
FAZ perimeter (mm)	**-0.233***	**0.389****	**0.467****	0.051	0.136	-0.081	-0.103	-0.058

Abbreviations: GFR - glomerular filtration rate; Chol. - cholesterol; Tg-trygliceride; Hb - hemoglobin; SBP - systolic blood pressure; DBP - diastolic blood pressure; RT - Retinal thickness; ChT - Choroidal thickness; FAZ - foveal avascular zone; SVD - superficial vascular density; DVD - deep vascular density; *p<0.05; **p<0.01

without albuminuria group versus the CKD with albuminuria (p=0.059). Deep vascular density analysis revealed a lower density in the CKD without albuminuria group than in the CKD with albuminuria (p<0.001). No differences were observed for FAZ perimeters in the GFR≤60 ml/min and GFR>60 ml/min groups.

In bivariate analyses of correlation, kidney function, albuminuria, and glycemia were the strongest correlate of choroidal measures (Table 4). Furthermore, the same analysis disclosed a significant association of choroidal, but not of retinal thickness measures, with GFR, as well as of SVD and DVD. (Table 4). As far as the OCTA, the parafoveal density of both SVD and DVD showed an inverse association with albuminuria and glycemia. Also, the foveal density of SVD and DVD, area of FAZ, and FAZ perimeter are related to GFR, albuminuria, and glycemia. Other associations were inconsistent with other clinical data. The Spearman correlation analyses revealed that albuminuria was inversely related to the choroidal thickness (central ring and total area) in the subjects in whom the albuminuria was positive.

Discussion

There were two major findings in this study. First, CKD is associated with retinal thinning and wasting kidney function with the progressive lowering of retinal-choroidal vascular density. The next find is, the microvasculature in various retinal layers may respond differently to systemic comorbidities.

Changes in structure and function of microvasculature are well known long-term repercussions of diabetes mellitus and are usually present in the retina, as well as in neural and kidney tissue. To follow CKD's rate, independently of what causes it, doctors typically need invasive procedures, such as kidney biopsy. Retinal microvascular abnormalities may be regarded as signs of systemic microangiopathy in kidney vascular diseases and arterial hypertension, and their objective evaluation represents a current topic of interest (10). The possible connection between systemic microangiopathy and changes in the choroid is less investigated, even if choroid is a highly vascular structure with an important role in controlling ocular volume and metabolism (11).

Chronic kidney disease has been associated with increased visual impairment and ocular diseases in prior epidemiology studies (9,12,13).

OCTA technology permits us to get repeatable and detailed measurements of the retinal-choroid volume and thickness (3). Furthermore, recent studies have been conducted regarding the vascular flow of ocular microcirculation in a noninvasive mode, without the use of contrast funds (14). As nephrologists, we have a valuable apparatus such as OCTA that can rapidly detect changes in the microvasculature of the retina, which may reflect condition systemic circulation and kidney function, among other things.

So far, only a small number of studies compared OCTA metrics in patients with CKD between stages of the disease. Our research uses OCTA to analyze the possible relationships between kidney function param-

eters, the presence of albuminuria, and retinal and choroidal morphological features in CKD groups. In the comparison between patients with high eGFR without albuminuria and low GFR with albuminuria, there was a significant difference between some microvascular parameters such as the FAZ area, FAZ perimeter, and radial peripapillary capillary density.

The GFR failed to show an immediate association with retinal-choroidal thickness, unlike albuminuria and glycemia in the study groups. Chronic kidney disease is associated with the diluting of the retina. This relation involved every studied area except the central ring, due to avascular anatomical characteristics of this area, and was mostly explained by the older age of CKD patients. Likewise, wasting renal function is accompanied by progressive diluting of the choroid.

Also, a similar relation was shown between GFR and retinal vascular density in the paracentral area assessed by OCTA both at the SVD and the DVD. CKD group with albuminuria presented a reduction in vascular density in the deep parafoveal network.

In patients with albuminuria, an inverse connection was observed between urinary albumin excretion and thicknesses choroid- retina, as well as a negative association with vascular density in the SVD and DVD parafoveal network of the retina. This is not an unexpected finding since urinary albuminuria excretion is a well-known marker of endothelial function (15).

Our findings appear partially in agreement with the study by Balmforth et al. (16). The authors reported a direct relationship between GFR and choroidal thickness and a negative relationship between the latter and proteinuria. The authors also observed a thinning of the retinal and choroidal thicknesses in patients with CKD compared to both healthy and hypertensive patients. At variance with this study, we did not find a correlation between retinal thicknesses and estimated kidney function. It is conceivable that the reciprocal relationships between GFR and retinal thickness may change progressively as renal function worsens.

Several studies strongly showed the association of retinal microvascular abnormalities and renal impairment, as well as caliber changes related to CKD (17,18). One of these studies was conducted in 2018. 184 patients with diabetes demonstrated that capillary rarefaction in the retina is connected with coexisting microcirculatory damage in the kidney (18). Their OCTA findings reflected previous histopathologic studies in diabetic eyes of endothelium changes and capillary dropout in retinal capillaries. These authors showed that the average and largest 10 intercapillary areas had a significant association with glomerular filtration, and they mentioned previous studies that demonstrated how other OCTA metrics (FAZ, FAZ perimeter, vessel density) were associated with diabetic retinopathy. In our study, we showed that the FAZ area, FAZ perimeter, and choroidal capillary flow area were notably modified with disease progression.

It is remarkable that unlike GFR, albuminuria revealed significant inverse associations with retinal-choroidal thicknesses. The design of our study has not allowed us to explain this different behavior of GFR and albuminuria. On the other hand, there is evidence that microalbuminuria has a closer relationship with the progression of diabetic retinopathy compared with moderate GFR reduction (19).

It is important to emphasize the independent relationship we found between the GFR value and retinal vascular density index evaluated in the SVD and DVD parafoveal area assessed by OCTA.

The cross-sectional design of the study does not permit us to clear up the reasons for our findings. However, a hypothesis that oxidative stress, inflammation, and endothelial damage, which characterize CKD since its initial stages, can deteriorate with the worsening of kidney function, may explain how diluting of the choroid is associated with the lower GFR value and, especially in patients with albuminuria (16).

In our study, there was no correlation between the blood pressure (BP) values and the retinal-choroidal thicknesses nor the SVD and DVD assessed by OCTA. This study deficiency the control group of subjects with normal blood pressure since the aim of this investigation was centered on the evaluation of kidney function related to ocular parameters. In our nephrology clinic, BP measurement was performed and considered for analysis of results. Therefore, it cannot be ruled out that the use of out-of-office BP measurement techniques, for example, 24-h ambulatory BP monitoring, may reveal a correlation between ophthalmic variables and BP parameters. The results we obtained verify that patients with CKD showed higher serum lipid and glycemic levels than patients without CKD. These findings are in consent with previous literature data and the concept that progressive kidney

dysfunction is associated with an increase of insulin resistance and with the related metabolic changes (20,21).

There are several limitations to this study. The study is limited by its small sample size and cross-sectional design of the study. Longitudinal follow-up data were not available. Consequently, our results may reflect early microvascular alterations of the retina rather than late-stage retinopathies.

Conclusion

OCTA proposes an interesting apparatus to investigate the connection between retinal-choroidal circulation and another vascular area. Our study showed that patients with CKD had significant dilution of retinal microvasculature in both SVD and DVD. In summary, these results confirm the close connection between changes in ocular microcirculation and kidney function, as assessed by resources of OCTA. The microvasculature in different retinal layers may respond differently to various systemic factors. Further studies are needed to explain the results we have obtained in this study. Also, further research is required in order to understand whether the information obtained with the imaging techniques like OCTA can ensure prognostic indications on the progression of CKD.

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Sažetak

KVANTIFICIRANJE MIKROVASKULARNIH PROMJENA U KRONIČNIH BUBREŽNIH BOLESNIKA

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Uvod. Korioretinalne mikrovaskualrne promjene mogu biti povezane s bubrežnim oštećenjem u kroničnoj bubrežnoj bolesti (KBB). Rad istažuje udruženost korioretinalnih parametara i bubrežnog oštećenja u hipertoničara, dijabetičara i nedijabetičara s KBB.

Metode. Presječna studija KBB pacijenata s arterijskom hipertenzijom različitog stupnja oštećenja funkcije u KBB. Skeniranje makularne regije na očima je izvedeno pomoću optičke koherentne tomografije angiografije (OCTA). Pacijenti su podijeljeni na grupe prema stopi glomerularne filtracije na GFR<60ml/min i GFR >60ml/min, kao i na KBB pacijenti s albuminurijom i KBB pacijenti bez albuminurije.

Rezultati. Evaluirano je 106 očiju KBB pacijenata. Srednja vrijednost retinalnog zadebljanja u grupi s GFR <60ml/min je 275,73±9,65 mikrona (μ), dok je u grupi s GFR>60ml/min 274,36±10,77μ. Pomoću OCTA skena prikazana je značajno niža duboka vaskularna gustoća (DVD) retine u grupi KBB s albuminurijom u odnosu na grupu KBB bez albuminurije ($p<0.001$). Albuminurija je bila u negativnom odnosu s mjerama debljine koroida i retine, kao i indeksima površne vaskularne gustoće (SVD) i DVD-a.

Zaključak. KBB je povezan s retinalnim zadebljanjima, a opadajuća funkcija bubrega s progresivnom redukcijom korioretinalnom vaskularnom gustoćom.

Ključne riječi: *mikovaskularne promjene, kronična bubrežna bolest, OCTA, korioretinalna zadebljanja, vaskularna gustoća*