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Assessment of Retinal Microangiopathy in Chronic Kidney Disease Patients

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ABSTRACT

Introduction: Optical coherence tomography angiography (OCT-A) is a useful diagnostic tool for assessing eyes' health in patients with chronic diseases, such as diabetes, hypertension, Parkinson's disease and chronic kidney disease (CKD). **Aim:** To detect changes in macular structure and retinal vascular meshwork in the macular area and peripapillary in patients with chronic kidney disease (CKD). **Methods:** This cross-sectional study included 80 eyes of patients with CKD in stages 2, 3 or 4, who were followed-up in the Nephrology Clinic of University Clinical Center Sarajevo. All patients were categorized according to the stage of CKD. All patients were scanned by a high-speed 840-nm-wavelength spectral-domain optical coherence tomography instrument (RTVue XR Avanti; Optovue, Inc, Fremont, California, USA). Blood flow was detected using a split-spectrum amplitude-decorrelation angiography algorithm. A fully automated microstructural analysis of the foveal avascular zone (FAZ), FAZ perimeter, foveal vessel density in a 300-µm area around the FAZ (FD), nonflow area, flow index in superficial and deep vascular plexus, choriocapillary flow, vascular density, radial peripapillary capillary density was performed. **Results:** When comparing patients with CKD stage 2 and stage 3 there were no statistically significant changes in microvascular parameters on OCT angiography, as well as when comparing patients with CKD stage 3 and stage 4. But in the comparison between patients with less developed CKD (stage 2) and terminal CKD (stage 4) there was a significant difference between some microvascular parameters such as FAZ area, FAZ perimeter, choriocapillary flow. **Conclusion:** Many studies demonstrated that evaluation of the microvascular changes in different retinal layers using SS-OCTA may be considered as a key to assessing the systemic perfusion status. Evaluation of retinal microvasculature may ease the management and approach of patients with CKD, having in mind that the retinal and the kidney vascular network are, concerning structure, development and the function, very similar.

Keywords: retinal angiopathy, microangiopathy, optical coherence tomography angiography, chronic kidney disease.

1. INTRODUCTION

Optical coherence tomography angiography (OCT-A) is a useful diagnostic tool for assessing eyes' health in patients with chronic diseases, such as diabetes, hypertension, Parkinson's disease and chronic kidney disease (CKD) (1). CKD is a medical term for heterogeneous disorders of kidney structure and function. Disease stages are assessed from the glomerular filtration rate (GFR) and albuminuria, as well as clinical diagnosis (2). According to Guideline for the Evaluation and Management of CKD, five stages of disease are classified as follows: Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 m^2); Stage 2: Mild reduction in GFR (60-89 mL/min/1.73 m^2); Stage 3a: Moderate reduction in GFR (45-59 mL/min/1.73 m^2); Stage 3b: Moderate reduction in GFR (30-44 mL/min/1.73 m^2); Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 m^2); Stage 5: Kidney failure (GFR<15 mL/min/1.73 m^2 or dialysis) (3).

Renal and retinal circulations have similar pathways of development, anatomy, physiology and pathology (4). In diabetic patients without diabetic retinopathy signs, changes in capillary network have been detected using OCT-A (5). Several studies have reported the connection between retinopathy (microaneurisms and retinal hemorrhages) and renal impairment, as well as changes in the caliber of retinal vessels due to CKD (6, 7). It is possible to examine the smallest vessels by OCT-A, which can detect patients with risk for progressive kidney dysfunction (8).

2. AIM

To detect changes of macular structure and retinal vascular meshwork in the macular area and peripapillary in patients with chronic kidney disease (CKD).

3. METHODS

This cross-sectional study included 95 eyes of 95 patients with CKD who were followed-up in the University Clinical Center Sarajevo, Nephrology Clinic. All patients were categorized according to the stage of CKD in stages 2, 3 or 4, due to glomerular filtration rate, albuminuria and clinical diagnosis. CKD stage 2 counted 12 eyes in total, of which 10 male and 2 female eyes, CKD stage 3 counted 48 eyes, of which 31 male and 17 female eyes, CKD stage 4 counted 20 eyes, of which 14 male and 6 female eyes, as well as 15 healthy control eyes, of which 10 male and 5 female eyes. Approximate age of patients in CKD stage 2 group was 66,5 years (62-74 years), of patients in CKD stage 3 group 67 years (62-71 years), of patients in CKD stage 4 group 70 years (67-76 years), and 70 years in the group of healthy controls (60-80 years).

All patients were scanned in Eye polyclinic „Dr. Sefić" by a high-speed 840-nm-wavelength spectral-domain optical coherence tomography instrument (RTVue XR Avanti; Optovue, Inc, Fremont, California, USA). Blood flow was detected using a split-spectrum amplitude-decorrelation angiography algorithm. A fully automated microstructural analysis of the foveal avascular zone (FAZ), FAZ perimeter, foveal vessel density in a 300-µm area around the FAZ (FD), nonflow area, flow index in superficial and deep vascular plexus, choriocapillary flow, macular vascular density, radial peripapillary capillary density was performed.

Inclusion criteria for the study were: male and female older than 18, patients with diagnosed CKD in stages 2, 3 or 4, who were followed-up in the Nephrology Clinic of University Clinical Center Sarajevo.

Exclusion criteria for the study were: younger than 18, acute ocular pathology, patients with previous ocular surgery, pregnancy, high myopia, amblyopia.

Statistical analysis

Results were analyzed using standard statistical methods, using the SPSS computer program for statistical analysis (SPSS Statistical Package for Social Sciences) version 13.0. Results are presented as the median and interquartile range (25-75 percentile), as mean ± SEM, and a percentage value (%). To test the significance of the difference in deviation from the normal distribution, the Kolmogorov-Smirnov test was used. The results are analyzed by appropriate non-parametric tests (Wilcoxon and Friedman Tests). Values of $p<0.05$ are considered as statistically significant, and values of $p<0.001$ as statistically highly significant.

4. RESULTS

FAZ area was significantly higher in patients with CKD grade 4 (0.29 mm^2 [0.24-0.36]) compared to CKD grade 2 patients (0.23 mm^2 [0.19-0.49]) (p=0.01). There was no statistically significant difference in these parameters between other groups.

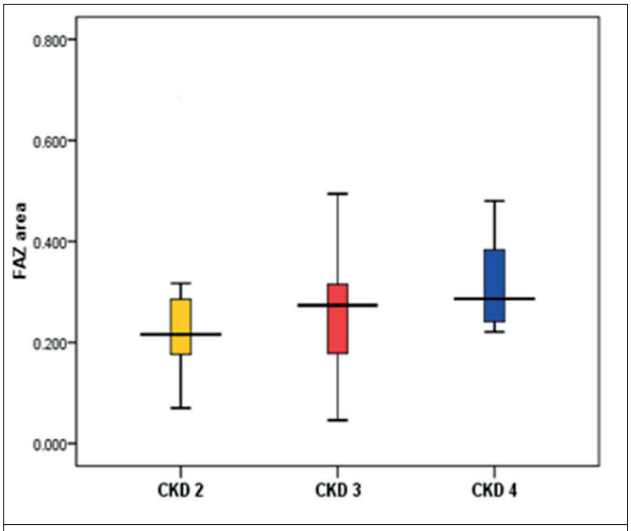
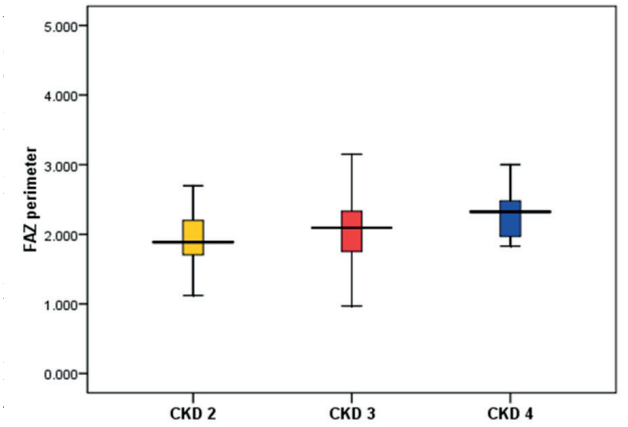


Figure 1. Foveal avascular zone area in chronic kidney disease patients

FAZ perimeter was significantly higher in patients



grade 3 (50,5% ± **0,65**) (p=0,002), with no difference detected between other groups.

RPC density in inferior quadrant was significantly

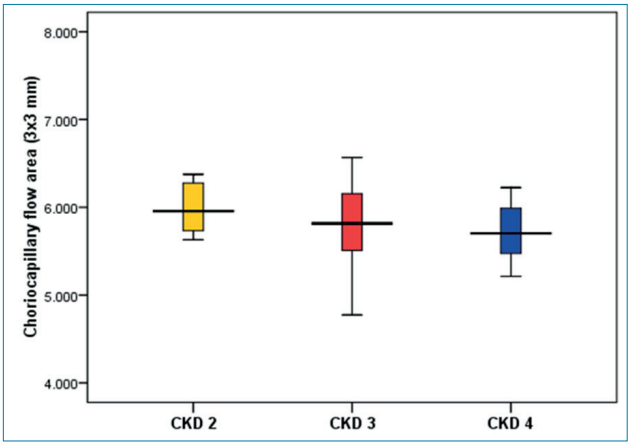


Figure 3. Choriocapillary flow area (3x3 mm) in chronic kidney disease patients

higher in patients with chronic kidney disease grade 4 (55.9% ± **1.37**) compared to chronic kidney disease grade 3 (52.4% ± **0.57**) (p=0.009), with no difference detected between other groups.

While analyzing central foveal thickness (CFT), macular volume, foveal vessel density in a 300 µm area around the FAZ, flow index, the nonflow area around FAZ, parafoveal vessel density (%) in temporal, superior,

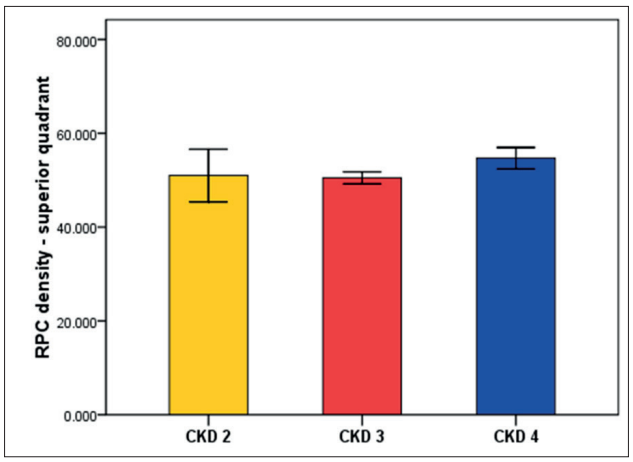


Figure 4. Retinal peripapillary capillary density – superior quadrant in chronic kidney disease patients

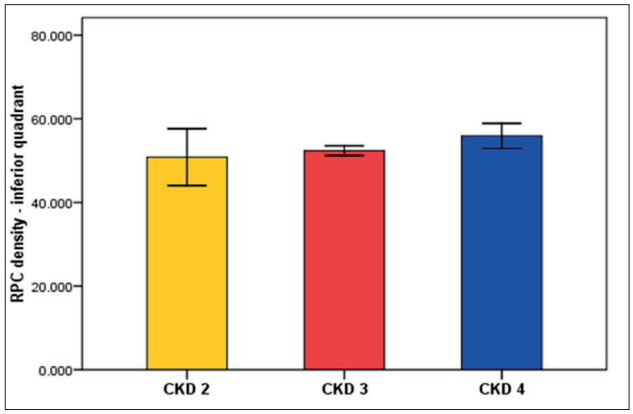


Figure 5. Retinal peripapillary capillary density – inferior quadrant in chronic kidney disease patients

nasal and inferior quadrant between groups, there was no statistically significant difference detected.

5. DISCUSSION

Changes in structure and function of microvasculature are a well known long-term consequence of diabetic disease and are usually present in the retina, as well as in kidney and neural tissue. To follow the course of chronic kidney disease, independently of what causes it, practicians usually need invasive procedures, such as kidney biopsy. As ophthalmologists, we have a useful tool such as OCT-A that can promptly detect changes in the microvasculature of retina, which may reflect systemic circulation and kidney function, among other things.

So far, only a small number of studies compared OCT-A metrics such as FAZ, FAZ perimeter, FD, non-flow area, flow index in superficial and deep vascular plexus, choriocapillary flow, macular vascular density and radial peripapillary capillary density in patients with CKD between stages of the disease. In our study, in the comparison between patients with less developed CKD (stage 2) and terminal CKD (stage 4), there was a significant difference between some microvascular parameters such as the FAZ area, FAZ perimeter and choriocapillary flow, as well as in radial peripapillary capillary density.

Several studies strongly showed the association of retinal microvascular abnormalities and renal impairment, as well as caliber changes related to CKD (9-13).

In 2010 Sng C. et al. investigated the relationship between retinal vasculature measurements and chronic kidney disease. They found that deviations from optimal microvascular architecture may reflect kidney damage (14).

Cheung et al. conducted a study in 2018. with 184 patients with diabetes and demonstrated that capillary rarefaction in the retina is connected with coexisting microcirculatory damage in the kidney. Their OCT-A findings reflected previous histopathologic studies in diabetic eyes of endothelium changes and capillary dropout in retinal capillaries. These authors showed that average and largest 10 intercapillary areas had a significant association with glomerular filtration, and they mentioned previous studies that demonstrated how other OCT-A metrics (FAZ, FAZ perimeter, vessel density) were associated with diabetic retinopathy. In our study, we demonstrated that the FAZ area, FAZ perimeter and choriocapillary flow area were significantly changed with disease progression (8).

In 2018 Yu Z. et al. reported about changes in retina and choroid after hemodialysis in patients with end-stage kidney disease, assessed using OCT-A, and found that the retinal thickness and vascular density decreased after hemodialysis. They showed that ocular perfusion pressure after hemodyalisis was significantly lower, as well as vascular density of outer retina (from 38.8 ± 5.5% to 37.5 ± 3.4%; $p<0.05$) (15).

Ling Y. et al. conducted a study in 2019. where they showed that patients in the CKD group had reduced parafoveal vessel density (46.7 ± 4.3%; $p<0.001$), compared to healthy individuals (16).

In our study we did not found any statistically significant difference in VD between patients in different CKD stages.

Sabanayagam et al. (17) conducted a study on the Asian population and found an association between retinal arteriolar narrowing and decreased glomerular filtration. They also mentioned how early retinal microvascular caliber changes may predict the development of many systemic conditions such as hypertension, cardiovascular disease, diabetes and CKD.

In the opposite of our study, where we found no difference in FD between groups, Zhang Y. et al. showed that vascular density in outer retina had significantly lower values ($p<0.05$) in all patients with end-stage kidney disease after hemodyalisis (15).

In summary, we demonstrated that retinal microvasculature changes may reflect reductions in kidney function, such as peritubular capillary flow reduction and ischemia. Also, in this study we showed that a noninvasive way of observing and measuring retinal microvasculature by OCT-A can reflect coexisting changes and damages in kidney's microcirculation, which can be a good way to predict the course of the chronic kidney disease, as well as its outcome, and to avoid invasive diagnostic procedures such as kidney biopsy. We also suggest that observations of retinal circulation may aid in evaluating and estimating CKD risk in patients with various systemic diseases.

The limitation of this study is a small sample of patients, as well as different diagnostic locations, which led to losing some patients and data.

If supported by future studies and researches, our findings have the ability to help in kidney function evaluation in patients with retinal microvasculature changes, as well as prompt and appropriate diagnosis and treatment.

6. CONCLUSION

Many studies demonstrated that evaluation of the microvascular changes in different retinal layers using SS-OCTA may be considered as a key to assessing the systemic perfusion status. Evaluation of retinal microvasculature may ease the management and approach of patients with CKD, having in mind that the retinal and the kidney vascular network are, concerning structure, development and the function, very similar. Our study showed that the assessment of microvascular changes in the retina can predict a progressive reduction in kidney function. The retinal microvascularity is a useful indicator of at-high-risk individuals and a good way of avoiding aggressive kidney biopsy.

- **Author's contribution**: Each author gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. Each author have role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **Conflicts of interest**: There are no conflicts of interest.
- **Financial support and sponsorship**: Nil.

REFERENCES

1. De Carlo TE, Romano A, Waheed NK, Duker JS. A review of optical coherence tomography angiography (OCTA). International Journal of Retina and Vitreous. 2015; 1(1).
2. Levey AS, Coresh J. Chronic kidney disease. The Lancet. 2012; 379(9811): 165-180.
3. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013; 3: 1-150. https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf (Accessed: 16.03.2019.)
4. Wong CW, Wong TY, Cheng CY, Sabanayagam C. Kidney and eye diseases: common risk factors, etiological mechanisms, and pathways. Kidney Int. 2014; 85(6): 1290-1302.
5. de Carlo TE, Chin AT, Bonini Filho MA, et al. Detection of microvascular changes in eyes of patients with diabetes but not clinical diabetic retinopathy using optical coherence tomography angiography. Retina. 2015; 35(11): 2364-2370.
6. Sabanayagam C, Shankar A, Koh D. et al. Retinal microvascular calibre and chronic kidney disease in an Asian population. Am J Epidemiol. 2009; 169: 625-632.
7. Sabanayagam C, Tai ES, Shankar A. et al. Retinal arteriolar narrowing increases the likelihood of chronic kidney disease in hypertension. J Hypertens. 2009; 27: 2209-2217.
8. Cheung CY, Tang F, Ng DS, Wong R, Lok J, Sun Z, Tham CC. The Relationship of Quantitative Retinal Capillary Network to Kidney Function in Type 2 Diabetes. American Journal of Kidney Diseases. 2018; 71(6): 916-918.
9. Wong TY, Coresh J, Klein R. et al. Retinal microvascular abnormalities and renal dysfunction: the Atherosclerosis Risk in Communities Study. J Am Soc Nephrol. 2004; 15: 2469-2476.
10. Edwards MS, Wilson DB, Craven TE et al. Associations between retinal microvascular abnormalities and declining renal function in the elderly population: the Cardiovascular Health Study. Am J Kidney Dis. 2005; 46: 214-224.
11. D'souza YB, Short CD. The eye - a window on the kidney. Nephrol Dial Transplant. 2009; 24: 3582-3584.
12. Hocking S, Bhandari S, Duggin G. An eye for the diagnosis of chronic renal failure in young patients. Nephrol Dial Transplant. 2002; 17: 166-168.
13. Colville D, Dagher H, Miach P. et al. Ocular clues to the nature of disease causing end-stage renal failure. Nephrol Dial Transplant. 2000; 15: 429-432.
14. Wessing A. Diabetic retinopathy: update on diagnosis and treatment. Nephrol Dial Transplant. 1997; 12: 2013-2018.
15. Sng C, Sabanayagam C, Lamoureux E, Liu E, Lim S, Hamzah H. et al. Fractal analysis of the retinal vasculature and chronic kidney disease. Nephrol Dial Transplant. 2010; 25(7): 2252-2258.
16. Yu Z, Huan W, Quingjian L, Zhiliang W. Changes in retina and choroid after haemodialysis assessed using optical coherence tomography angiography. Clinic and Exp Opt. 2018; 101(5).
17. Ling Y, I-Wen W, Chi-Chin S, Chun-Fu L, Shin-Yi C, Chun-Hsin T, et al. Early retinal microvascular abnormalities in patients with chronic kidney disease. Microcirculation. 2019.
18. Sabanayagam C, Shankar A, Koh D, Chia K, Saw S, Lim S. et al. Retinal Microvascular Caliber and Chronic Kidney Disease in an Asian Population. American Journal of Epidemiology. 2008; 169(5): 625-632.