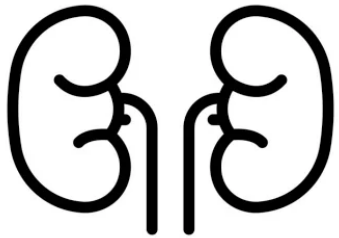
HELLENIC SOCIETY OF NEPHROLOGY
MEETING & SEMINAR
Combined with:
18th BANTAO CONGRESS
October 19-22, 2023
Makedonia Palace Hotel THESSALONIKI, GREECE

Quantifying Microvascular Abnormalities in Chronic Kidney Patients

Damir Rebić, MD, PhD
Clinic for nephrology
Clinical Center University of Sarajevo
Bosnia and Herzegovina

Cardiovascular diseases (CVD) is the headmost cause of death and counts the cardiac, metabolic risk, and chronic kidney disease (CKD) among its accelerating factors.

CVD and CKD are narrowly interrelated: they both divide common traditional risk factors, such as diabetes mellitus, obesity, smoking, and hypertension

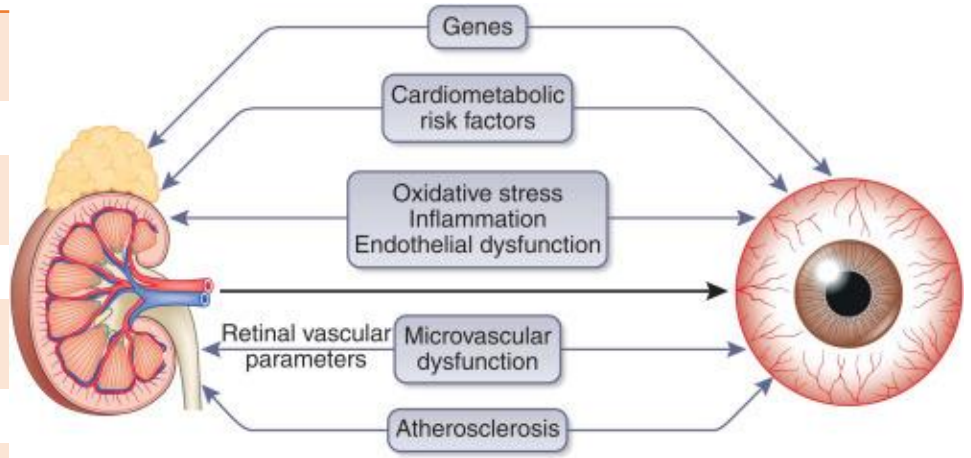


CKD is a common comorbidity in ophthalmologic patients.

Patients with CKD have higher risks of cataracts, glaucoma, retinopathies, and visual exacerbation

What about
the mechanism
behind increased ocular diseases
in patients with CKD ?!?!

Mechanisms of CKD	Associated eye diseases
Atherosclerosis	Cataract, AMD, DR, glaucoma, retinal vascular damage
Endothelial dysfunction	AMD, cataract
Oxidative stress	Cataract, DR, AMD, glaucoma, retinal vascular damage
Inflammation	AMD, DR, retinal vascular damage
Renin–angiotensin system dysfunction	DR, retinal vascular damage, glaucoma
Genetic polymorphisms	AMD, retinal venular diameter
Klotho	AMD, cataract, retinopathy



** Risk factors

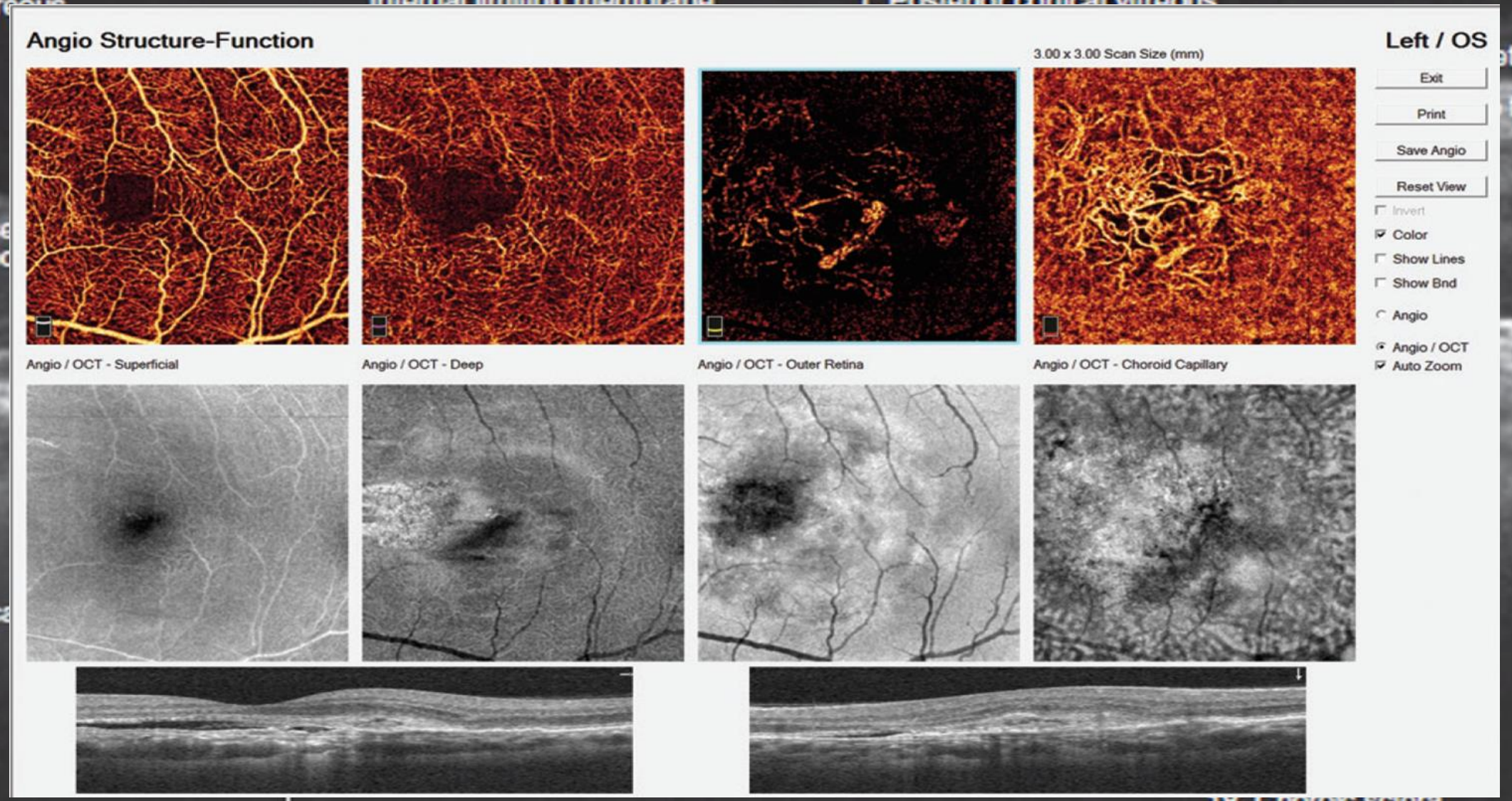
** increased oxidative stress

** microvascular alterations

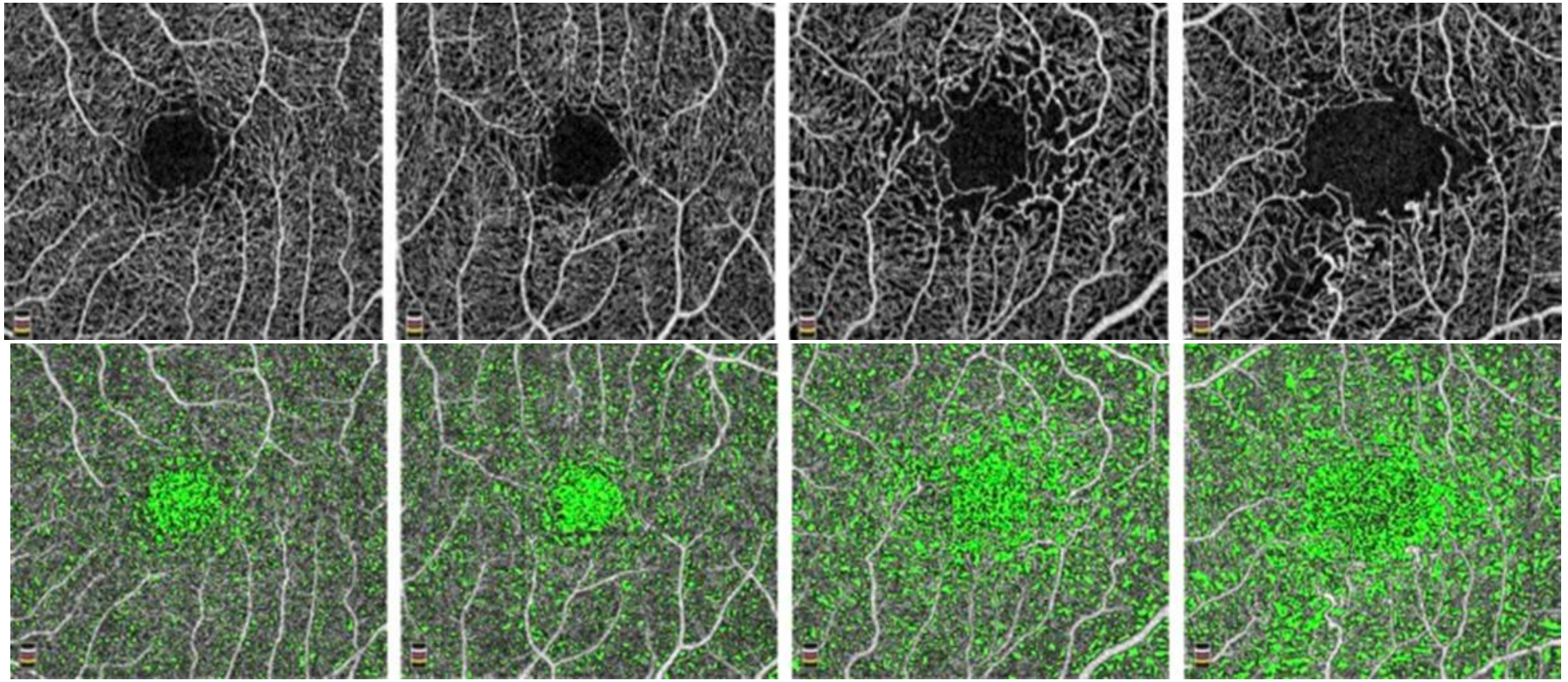
** embryogenesis,

Vascular changes of retina in CKD					
Author, year	Type of study and location	Sample size	Retinal vascular measure	Definition of CKD	Results
Risk of retinal vascular changes in individuals with/without CKD					
Liew et al., 2012[117]	Population-based cross-sectional study (BMES), Australia	n=2971	CRVE	eGFR <60ml/min per 1.73m^2	CKD was associated with the presence of retinal venular (CRVE) dilation,
Myers et al., 2012[153]	Population-based prospective study (BDES), Wisconsin, USA, follow-up=15 years	n=4600	CRVE	eGFR <45ml/min per 1.73m^2	CKD was associated with a greater decrease in CRVE over time
Ooi et al., 2011[138]	Hospital-based case–control study, CKD stage 3–5 vs. CKD stage 1–2, Australia	Cases: 126, controls: 126	CRAE, CRVE	eGFR <60ml/min per 1.73m^2	Patients with CKD stage 3–5 had a smaller mean CRAE and CRVE than hospital controls
Sabanayagam et al., 2011[145]	Population-based prospective study (BDES) of adults aged 43–84 years, Wisconsin, USA, follow-up=15 years	n=3199	CRAE, CRVE	eGFR <60ml/min per 1.73m^2 accompanied by a 25% decrease in eGFR, during follow-up	Baseline eGFR was not associated with 15-year risk of incident retinal arteriolar narrowing or retinal venular widening
Risk of CKD in individuals with/without retinal vascular changes					
Yau et al., 2011[144]	Population-based prospective study (MESA) of whites, African-Americans, Chinese, and Hispanics aged 45–84 years, USA, follow-up=5 years	n=4594	CRAE, CRVE	eGFR <60ml/min per 1.73m^2	CRAE was associated with incident CKD stage 3 in whites only. comparing lowest with highest CRAE tertile
Sabanayagam et al., 2011[145]	Population-based prospective study, adults aged 43–84 years, BDES, Wisconsin, USA, follow-up=15 years	n=3199	CRAE, CRVE	eGFR <60ml/min per 1.73m^2 accompanied by a 25% decrease in eGFR, during follow-up	Baseline CRAE and CRVE were not associated with 15-year risk of incident CKD

International nomenclature for OCT meeeting consensus normal OCT terminology



OCTA healthy eye - vascularity



- Vessel density decreases and PAN increases with increasing disease severity. **Top Row**: En face OCTA of full retinal thickness angiograms for a healthy patient (left), a patient with diabetes without CKD (middle left), a patient with CKD eGFR>60ml/min (middle right), and eGFR<60ml/min (right). **Bottom Row:** Areas of nonperfusion are shown in green. PAN is reported as a percentage of the area of nonperfusion to the total retinal area and increases from left to right.

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.

The inclusion criteria :

- 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,
- 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.

	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

	GFR≤60ml/min	GFR>60ml/min	p	CKD without albuminuria	CKD with albuminuria	p
Antihypertensive 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

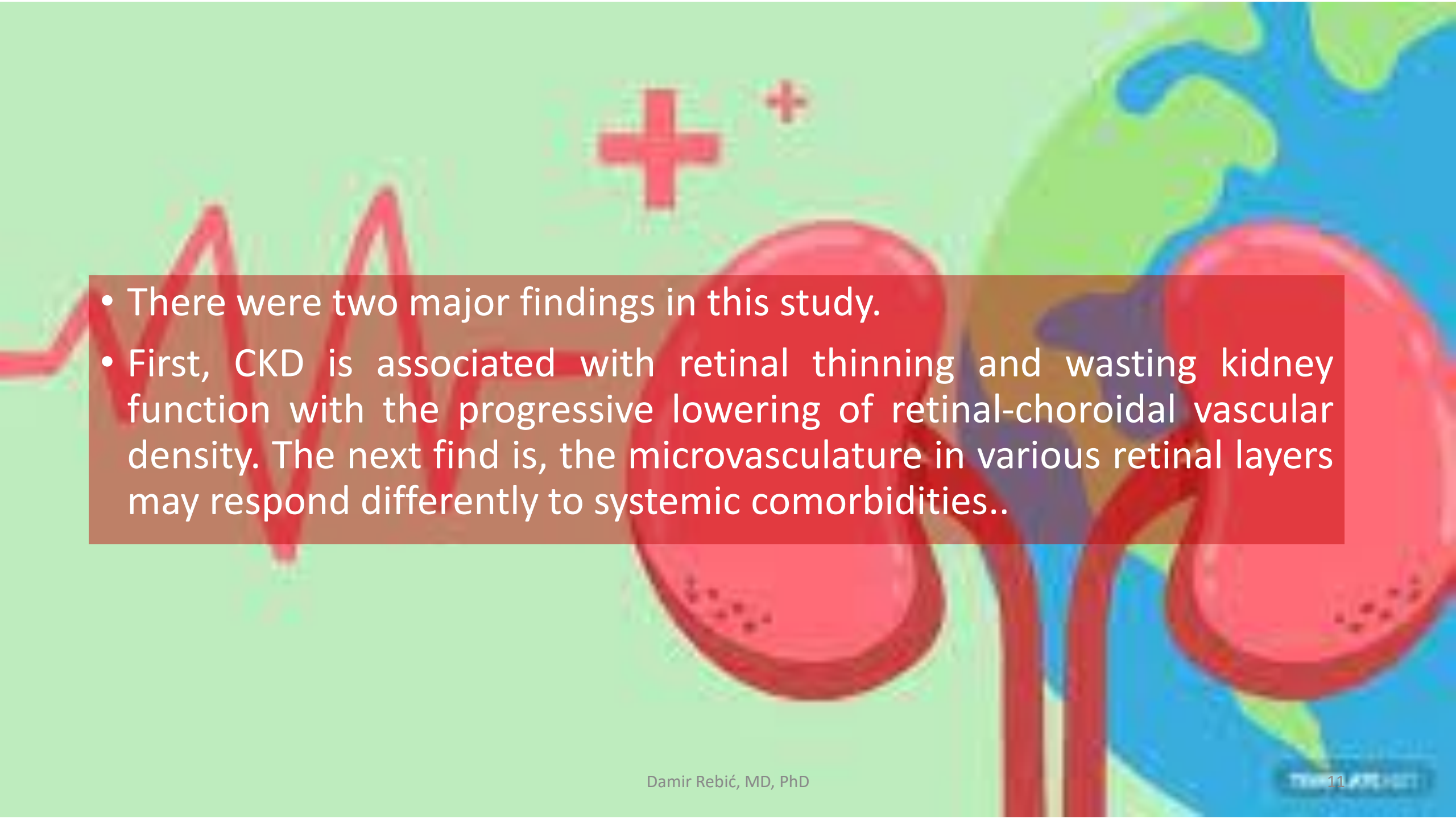
	GFR≤60 ml/min	GFR>60 ml/min	p	CKD without albuminuria	CKD with albuminuria	p
RT total area (µ)	274.4±10.7	275.7±9.7	0.52	277.2 (271.2-280.5)	273.4 (266.8-280.6)	0.116
RT central ring (µ)	245.3 (240.7-247.8)	246(241.6-247.7)	0.462	246.3 (242.2-247.9)	244.8 (240.6-247.5)	0.312
ChT central ring (µ)	286.2 (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- choriodal thickness; FAZ- foveal avascular zone; SVD-superficial vascular density; DVD-deep vascular density; MA-microaneurysms

Table : 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- Choriodal thickness; FAZ-foveal avascular zone; SVD- superficial vascular density; DVD- deep vascular density; *p<0.05; **p<0.01



- 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..

- 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.

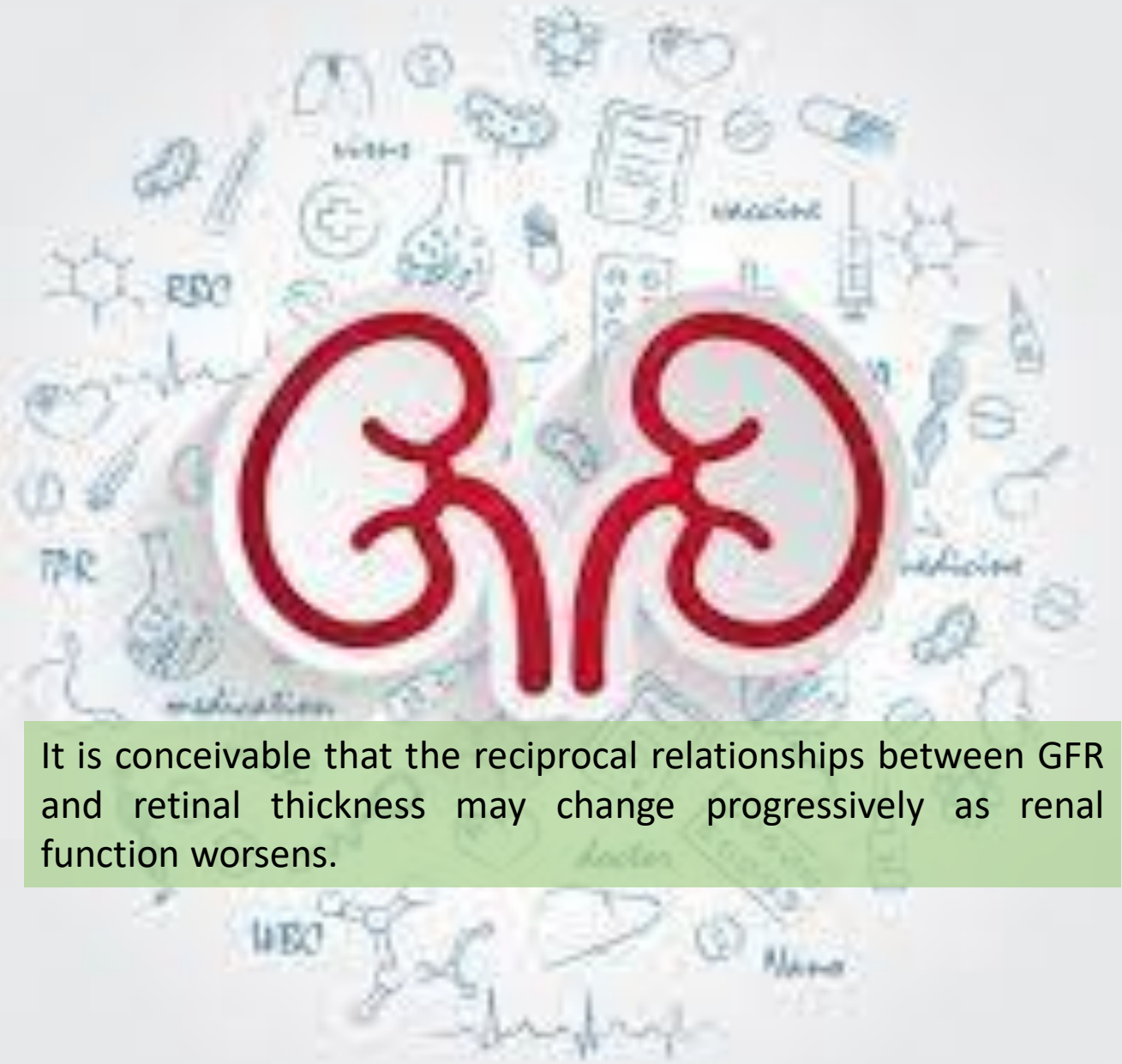
In the comparison between patients with high eGFR without albuminuria, and low GFR with albuminuria, there was a significant difference between some microvascular parameters such as the FAZ area, FAZ perimeter, and radial peripapillary capillary density.

Wasting renal function is accompanied by progressive diluting of the choroid.

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

Study by Balmforth et al.**

Albuminuria revealed significant inverse associations with retinal-choroidal thicknesses



It is conceivable that the reciprocal relationships between GFR and retinal thickness may change progressively as renal function worsens.

- No correlation between the blood pressure values and the retinal-choroidal thicknesses, nor the SVD anf DVD assesed by OCTA.

- Study limitations: small sample size and cross sectional design
- Longitudinal follow-up data were not available. Like that, 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 needed to understand whether the information obtained with the imaging techniques like OCTA can ensure prognostic indications on the progression of CKD.

SOCIETY OF NEPHROLOGY, DIALYSIS AND KIDNEY TRANSPLANTATION BOSNIA AND HERZEGOVINA

It is our great pleasure to invite you to participate at the 6th Congress of the Society of Nephrology, Dialysis and Kidney Transplantation in Bosnia and Herzegovina (SNDT BH) which will be held from 9th to 12th May 2024 in Sarajevo, one of the most beautiful cities in the Bosnia and Herzegovina, Europe, and world.

Congress will be organized with the support of the Society of Nephrology, Dialysis and Transplantation of Bosnia and Herzegovina.

We will be glad to see you at this meeting, in the embracing atmosphere of the 6th Congress of SNDT BH, where scientists in the regional countries can update their knowledge and share their experiences.

We heartily hope that the 6th Congress of the Society of Nephrology, Dialysis and Kidney Transplantation in Bosnia and Herzegovina will be an event to remember with your contribution and participation.

We are looking forward to seeing you in Sarajevo.

Yours Sincerely,

Congress President
Prof. Damir Rebić, MD, PhD

You can find more about the 6th Congress of the Society of Nephrology, Dialysis and Kidney Transplantation in Bosnia and Herzegovina and registration at the following link or by scanning the QR code.

www.nefrobih.ba

Scientific Committee SNDT Bosnia and Herzegovina

Congress President
Damir Rebic

e-mail:
damir.rebic@gmail.com
info@undt.ba

nefrobih.ba