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Peripapillary Microvascular Changes (Vascular Density) in Patients of Hypertension Using OCT Angiography

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ABSTRACT

Background: Funduscopy is utilized directly to detect vascular alterations in the eye. Arteriolar tightness is a distinctive feature of hypertensive retinopathy; this tightness can be diffuse or focal in nature. This happens when the blood pressure in the systemic circulation rises in order to maintain a consistent flow of blood through the process of autoregulation of the circulation in the retina.

Aim and objectives: To evaluate peripapillary microvascular alterations in hypertensive cases, focusing on vascular density by utilizing OCT angiography.

Patients and Methods: This research is a prospective comparative case control research at Benha University Hospital outpatient clinics between July 2022 and July 2023 on 60 subjects (120 eyes), who were divided into three groups and were examined for the peripapillary microvascular changes including vascular density using OCT angiography; Group A: twenty normal subjects, Group B: 20 subjects who had hypertension for more than ten years, and Group C: 20 subjects with hypertension for less than 10 years.

Results: A significant variance was observed among participants under study regarding best corrected visual acuity (BCVA), uncorrected visual acuity (UCVA), superior temporal vascular density and no significant difference was found regarding peripapillary of vascular thickness.

Conclusion: Our results showed that there was significant change in peripapillary microvascular density in cases who had hypertension lasting more than ten years.

Keywords: Peripapillary microvascular changes, vascular density, hypertension, OCT angiography.

INTRODUCTION

Uncontrolled hypertension is responsible for vascular alterations in many organs, like the brain, kidneys, eyes and heart, because of increased arterial pressure and elevated peripheral resistance. Funduscopy is utilized directly to detect vascular alterations in the eye. Arteriolar tightness is a distinctive feature of hypertensive retinopathy; this tightness can be diffuse or focal in nature. This happens when the blood pressure in the systemic circulation rises in order to maintain a consistent flow of blood through the process of autoregulation of the circulation in the retina [(1, 2)].

Utilizing dependable and replicable imaging methods to identify early microvascular modifications could thus serve as a screening modality, particularly in regard to the rapid identification of systemic and ocular complications associated with hypertension [(3)].

Cotton wool spots, bleeding within the retina, and lipid deposits within the retina can result from the deterioration of vascular endothelial structure and the inner blood-retinal barrier. Fluorescein angiography (FA), optical coherence tomography and funduscopy can be useful in the diagnosis and assessment of retinal pathological alterations associated with hypertension [(4)].

OCTA **(Optical** coherence tomography angiography**)** has significantly transformed the criteria employed by scientists and clinicians in retinal vascular analysis in recent times [(5)].

OCTA provides precise structural assessments from the major retinal vessels to the capillaries and allows visualization of the superficial and deep macular capillary plexus independently [(6)].

In recent times, noninvasive diagnostic imaging has been revolutionized with OCTA. This method generates depth-resolved images of the choroidal, high-resolution and retinal vasculature with no need for dye injection by utilizing motion contrast obtained from high-speed optical coherence tomography imaginings [(7, 8)]. Adding to that, OCTA instruments that are widely available for the assessment of vessel density (VD), the area of the foveal avascular zone (FAZ) and perfusion density (PD) [(2)].

This research objected to assess the peripapillary microvascular alterations especially vascular density in patients of hypertension using OCT angiography.

PATIENTS AND METHODS

This research is a prospective comparative case control research performed at Benha University Hospital outpatient clinics between July 2022 to July 2023 on 60 subjects (120 eyes) who were separated to 3 groups:

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Group A: twenty normal individuals.

Group B: twenty cases with hypertension for more than 10 years; included patients with both controlled and uncontrolled hypertension who were examined for peripapillary microvascular changes including vascular density. Group C: 20 subjects with hypertension for less than 10 years; included patients with both controlled and uncontrolled hypertension who were examined for peripapillary microvascular changes including vascular density.

Inclusion criteria

Age was more than eighteen years old and less than sixty years to avoid vascular changes in elderly, patients who were diagnosed with hypertension and under regular follow up in the outpatient clinics of Benha University.

Exclusion criteria

Exclusion criteria included diabetic retinopathy, retinal vasculopathy, occurrence of media opacities prohibiting fundus assessment and reliable retinal imaging, (age-related macular deterioration, foveal hypoplasia, epiretinal macular membrane, macular hole and foveoschisis) and cases with optic disc changes prohibiting peripapillary optical coherence tomography angiography assessment (pathologic myopia, history of optic neuritis and diagnosed glaucoma).

The following were done for all subjects:

Detailed medical history and local assessment of the two eyes (involving assessment of slit lamp assessment, visual acuity, pupil function, fundus examination, intraocular pressure and refraction of the eye).

OCTA Scans Evaluation

By AngioVue software (Optovue Inc., Fremont, CA, USA), (ReVue software, version 2017) and 3 × 3 mm, SSADA technology) were done to all subjects.

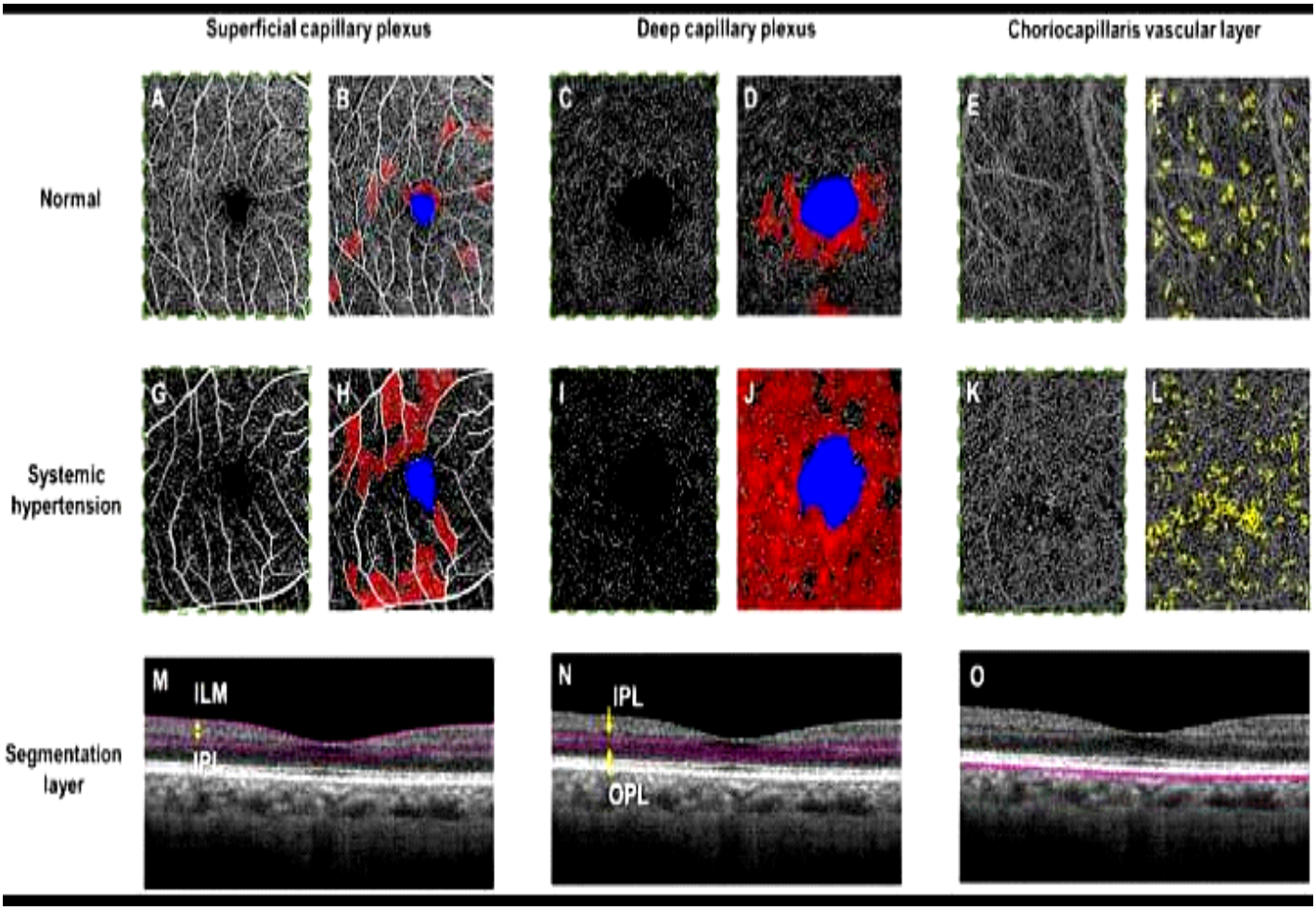

Figure 1: Optical coherence tomography angiography and color-coded maps of a healthy control individual (Top panel; A–F) and a case who had hypertension with slightly controlled blood pressure (Middle panel; G–L) and corresponding layer's horizontal B-scan photos (bottom row, M–O).

Sample size

Using STATA 14.2 software, sample size was calculated based on the following parameters, mean vascular density in normal populations 59.23 ± SD 1.5 mm, mean vascular density in hypertensive populations 57.85 ± SD 2.64 mm as reported in previous studies [(3)]. Power was 80%, with 95% confidence interval and 0.05 level of significance. Sample size was $N_{per\ group}$= 40 subjects.

Ethical Considerations:

For the purpose of taking part in the study, the patient gave written informed consent to Ophthalmology Department, Benha University, Egypt, and the Research Ethics Committee of the Benha University Faculty of Medicine authorized the research's conduct. The purpose of this study was to perform research on humans in compliance with the Declaration of Helsinki, the code of ethics of the World Medical Association.

Statistical analysis

The SPSS 22nd edition was utilized to perform the statistical analysis. The numerical information was reported as the mean ± standard deviation and were contrasted by utilizing either the one-way ANOVA or the student T test for normal distribution data and Kruskal wallis and mann whitney u test for abnormal distribution data. Frequencies and percentages were used to show categorical information, which were compared via the Chi^2 method. A p-value less than 0.05 was deemed to consider significance.

RESULTS

No significant variance was obtained among the groups according to age, gender and BMI **[Table 1]**.

Table (1): Characteristic and clinical information of the 3 groups.

		Group A (n=20)	Group B (n=20)	Group C (n=20)	F	P
Age (years), Mean ± SD		51.78 ± 7.68	53.75 ± 6.04	51.9 ± 7.95	0.582	0.561
Gender	Female	18 (90%)	19 (95%)	17 (85%)	□² 1.11	0.574
	Male	2 (10%)	1 (5%)	3 (15%)		
BMI (kg/m^2) Mean ± SD		25.17 ± 2.45	26.43 ± 1.67	25.21 ± 2.16	2.42	0.095
HTN duration (years) Mean ± SD		---	13.95 ± 5.21	3.9 ± 2.1	**U 0.76**	**<0.001**

SD: standard deviation F: ANOVA test, □2: chi square test U: mann whitney u test BMI: Body Mass Index, HTN: Hypertension

There was a significant variance among the 3 groups according to UCVA and BCVA **[Table 2]**.

Table (2): Uncorrected and best-corrected visual acuity among the 3 groups.

	Group A (n=20)	Group B (n=20)	Group C (n=20)	KW	P
UCVA					
OD Mean ± SD	0.22 ± 0.207	0.41 ± 0.215	0.23 ± 0.27	**9.1**	**0.011**
OS Mean ± SD	0.21 ± 0.18	0.4 ± 0.205	0.3 ± 0.247	**8.6**	**0.014**
BCVA					
OD Mean ± SD	0.12 ± 0.146	0.18 ± 0.17	0.06 ± 0.135	**6.88**	**0.032**
OS Mean ± SD	0.07 ± 0.113	0.205 ± 0.161	0.12 ± 0.179	**8.39**	**0.015**

KW: Kruskal wallis test F: ANOVA test, OD: Oculus dexter (right eye), OS: Oculus sinister (left eye), UCVA: Uncorrected visual acuity, BCVA: Best corrected visual acuity, KW: Kruskal-Wallis test.

A significant variance was found among the 3 groups according to rim area. There was no significant variance among the groups regarding C/D area ratio, C/D H. ratio, cup volume (mm^2), C/D V. ratio, disc area (mm^2) and RNFL thickness **[Table 3]**.

Table (3): ONH analysis among the 3 groups.

	Group A (n=40 eyes)	Group B (n=40 eyes)	Group C (n=40 eyes)	KW	P
C/D area ratio, Mean ± SD	0.015 ± 0.048	0.023 ± 0.062	0.01 ± 0.044	1.32	0.517
C/D V. ratio, Mean ± SD	0.191 ± 0.384	0.119 ± 0.288	0.133 ± 0.335	0.795	0.672
C/D H. ratio, Mean ± SD	0.025 ± 0.089	0.05 ± 0.135	0.081 ± 0.204	2.01	0.366
Rim area (mm^2), Mean ± SD	1.88 ± 0.335	1.61 ± 0.488	1.74 ± 0.629	**6.01**	**0.049**
Disc area (mm^2), Mean ± SD	1.95 ± 0.389	1.85 ± 0.483	1.95 ± 0.504	1.07	0.586
Cup volume (mm^2), Mean ± SD	0.001 ± 0.006	0.005 ± 0.018	0.002 ± 0.011	0.789	0.674

F: ANOVA test, RNFL: Retinal nerve fiber layer, KW: Kruskal-Wallis test.

The 3 groups didn't show any significant variance regarding RCP (Retinal capillary plexuses) density distribution **[Table 4]**.

Table (4): RCP density distribution among the 3 groups.

	Group A (n=40 eyes)	Group B (n=40 eyes)	Group C (n=40 eyes)	F	P
Superior hemi small Mean ± SD	52.59 ± 2.67	51.63 ± 4.76	52.51 ± 3.41	0.828	0.439
Superior hemi all Mean ± SD	59.1 ± 2.64	58.45 ± 4.4	59.12 ± 3.26	0.470	0.626
Inferior hemi small Mean ± SD	51.91 ± 2.32	51.88 ± 4.37	52.16 ± 3.27	0.079	0.924
Inferior hemi all Mean ± SD	58.35 ± 2.47	57.98 ± 4.29	58.18 ± 3.16	0.121	0.886

F: ANOVA test,

The 3 groups showed significant variance among the studied groups according to superior temporal vascular density **[Table 5]**.

Table (5): Small vessels density distribution among the 3 groups.

Vascular density	Group A (n=40 eyes)	Group B (n=40 eyes)	Group C (n=40 eyes)	F	P
Superior hemi, Mean ± SD	52.59 ± 2.67	51.64 ± 4.7	52.51 ± 3.41	0.813	0.446
Inferior hemi, Mean ± SD	51.91 ± 2.32	51.85 ± 4.37	52.16 ± 3.28	0.090	0.914
Nasal superior, Mean ± SD	48.8 ± 3.97	48.94 ± 4.83	49.84 ± 4.22	0.664	0.517
Nasal inferior, Mean ± SD	47.28 ± 4	47.98 ± 4.36	48.37 ± 5.2	0.576	0.567
Inferior Nasal, Mean ± SD	50.57 ± 3.6	52.1 ± 6.63	51.37 ± 5.19	0.814	0.445
Inferior temporal, Mean ± SD	57.48 ± 4.01	56.82 ± 7.02	57.79 ± 4.58	0.324	0.711
Temporal Inferior, Mean ± SD	53.96 ± 3.96	52.07 ± 4.16	52.46 ± 4.14	2.38	0.097
Temporal superior, Mean ± SD	55.99 ± 3.63	55.99 ± 5.06	55.6 ± 4.09	0.108	0.898
Superior Temporal, Mean ± SD	56.88 ± 3.78	53.87 ± 6.13	55.7 ± 4.74	**3.7**	**0.028**
Superior nasal, Mean ± SD	50.66 ± 3.71	48.76 ± 6.45	49.99 ± 5.39	1.32	0.272

F: ANOVA test,

The three groups didn't show any significant variance according to peripapillary vascular density [**Table 6]**.

Table (6): Peripapillary vascular density distribution among the 3 groups.

	Group A (n=40 eyes)	**Group B** (n=40 eyes)	**Group C** (n=40 eyes)	**F**	**P**
Peripapillary vascular density Mean ± SD	113.38 ± 13.55	111.63 ± 16.23	114.23 ± 14.64	0.319	0.728

F: ANOVA test.

DISCUSSION

As a quick identification method of the ocular and systemic consequences of HTN, the recognition of early microvascular alterations via reliable and reproducible imaging methods can serve as a screening modality [(3)].

By utilizing non-invasive optical methods, a person's eye provides direct optical entry to the retina and its vasculature. Because of availability, pathological alterations of the retinal vessels were extensively examined and regarded as biomarkers for systemic vascular disorders. Concurrently, developments in diagnostic equipment have allowed for an ever-improving ability to observe the retinal vascular network. Usage of exogenous contrast agents, like fluorescein, was the only restriction on these assessments till recently [(9, 10)].

The criteria of physicians and scientists to retinal vascular assessment has been significantly progressed in recent years due to the advent of OCTA. OCTA is capable of visualizing superficial and deep capillaries in the peripapillary region independently and providing precise structural assessments from the capillaries to the greatest retinal vessels [(11, 12)].

Our results observed that a significant variance was shown among the studied groups regarding UCVA and BCVA. Unlike, **Lim *et al.*** [(4)] who aimed to analyze the connection among the inner retinal alterations and assess retinal blood flow and retinal microcirculation in cases with hypertensive via OCT angiography. There were two hundred and one cases in the research in total, divided into one hundred and seventeen healthy controls, thirty-two in hypertension group one (hypertension ≥5 years), and fifty-two in hypertension group two (hypertension ≥5 years). They demonstrated that there was no significant difference among the groups in the research according to BCVA.

Our findings observed that a significant variance was obtained between the studied groups regarding rim area, while no significant difference was found among the 3 groups regarding C/D area ratio, C/D V. ratio, rim area, disc area, cup volume, and RNFL thickness. Corresponding to our research **Lim *et al.*** [(4)] indicated no significant difference among the 3 groups was found regarding cup volume, and cup disk ratio, otherwise they obtained no significant difference among the 3 groups according to rim area.

In disagreement with our study, **Lee *et al.*** [(13)] who enrolled a total of fifty-eight eyes from fifty-eight cases comprised the healthy control group (Group A), thirty-seven eyes from thirty-seven cases belonged to the chronic hypertension with no retinopathy group (Group B), which comprised cases with the condition for a minimum of ten years, and additionally, thirty-one eyes from thirty-one cases with recovered hypertensive retinopathy (Grade IV hypertensive retinopathy one year ago or greater than one year, but at the duration of the research there was no evidence of the condition; Group C). They reported that group B exhibited significantly reduced average thicknesses of the central macula, RNFL, and GCIPL layers compared to Group A (P, 0.001, 0.001, and 0.001, respectively). Group C exhibited 3 layers with less thicknesses (P, 0.001, 0.001, and 0.001, respectively) than Group B. Group C exhibited the least average thicknesses of the central macula, RNFL, and GCIPL (P = 0.001, 0.001, and 0.001, respectively) among the 3 groups. They also concluded that the central macula, GCIPL and RNFL in Group B were significantly lower in thickness than participants with normal eyes, and these retinal alterations were extra prominent in Group C. So, it is important to take into account the impact of hypertension-related retinal alterations on the thicknesses of the GCIPL, central macular and RNFL layers for those diagnosed with eye problems such as neuro-ophthalmological diseases, glaucoma, and retinal pathologies.

Our study showed that a significant variance was observed among the studied groups regarding inside disc small, in contrast with our results **Lim *et al.*** [(4)] who demonstrated no significant difference among the 3 groups according to inside disc small.

Our study observed that no significant variance was found among the studied groups according to superior hemi small, superior hemi all, inferior hemi small, and superior hemi all and peripapillary. While there was a significant variance among the 3 groups according to inside disc and superior temporal density.

Shin *et al.* [(14)] utilized OCT angiography to examine modifications in the peripapillary microvasculature in

cases with hypertension and to estimate the connections among peripapillary OCT angiography parameters. The cases in the research were separated to 3 distinctive groups: A group control (no evidence history of systemic disorder and no ocular disorder, ninety eyes), hypertension group one (cases who had HTN less than ten years, thirty-eight eyes), and hypertension group two (cases who had HTN less than or equal ten years, forty eyes). They reported that no significant variance among the groups in the research according to Peripapillary microvascular.

CONCLUSION

Our findings reported a significant change in peripapillary microvascular density in cases diagnosed with hypertension for a duration exceeding ten years. Additional research with larger scales is required to validate our results.

DECLARATIONS

- **Consent for publication:** I certify that each author has granted permission for the work to be submitted.
- **Funding:** No fund
- **Availability of data and material:** Available
- **Conflicts of interest:** No conflicts of interest.
- **Competing interests:** None.

REFERENCES

1. **Niro A, Sborgia G, Lampignano L *et al.* (2022):** Association of neuroretinal thinning and microvascular changes with hypertension in an older population in Southern Italy. J Clin Med., 11(4):1098. 1-13. doi: 10.3390/jcm11041098.
2. **Hua D, Xu Y, Zeng X *et al.* (2020):** Use of optical coherence tomography angiography for assessment of microvascular changes in the macula and optic nerve head in hypertensive patients without hypertensive retinopathy. Microvasc Res., 129:103969. doi: 10.1016/j.mvr.2019.103969.
3. **Donati S, Maresca A, Cattaneo J *et al*. (2021):** Optical coherence tomography angiography and arterial hypertension: A role in identifying subclinical microvascular damage? Eur J Ophthalmol., 31(1):158-165.
4. **Lim H, Lee M, Park J *et al.* (2019):** Changes in ganglion cell-inner plexiform layer thickness and retinal microvasculature in hypertension: An optical coherence tomography angiography study. Am J Ophthalmol., 199:167-176. doi: 10.1016/j.ajo.2018.11.016.
5. **Pellegrini M, Cozzi M, Staurenghi G, Corvi F (2019):** Comparison of wide field optical coherence tomography angiography with extended field imaging and fluorescein angiography in retinal vascular disorders. PLoS One, 14(4), e0214892.
6. **Debuc D, Somfai G, Koller A (2017):** Retinal microvascular network alterations: potential biomarkers of cerebrovascular and neural diseases. Am J Physiol Heart Circ Physiol., 312(2): H201–H212. https://doi.org/10.1152/ajpheart.00201.2016.
7. **de Carlo T, Romano A, Waheed N, Duker J (2015):** A review of optical coherence tomography angiography (OCTA). Int J Retina Vitreous, 1:5. doi: 10.1186/s40942-015-0005-8.
8. **Kashani A , Chen C, Gahm J *et al* . (2017):** Optical coherence tomography angiography: a comprehensive review of current methods and clinical applications. Progress in retinal and eye research, 60, 66-100.
9. **Qin Z, He S, Yang C *et al.* (2020):** Adaptive optics two-photon microscopy enables near-diffraction-limited and functional retinal imaging in vivo. Light Sci Appl., 9:79. doi: 10.1038/s41377-020-0317-9.
10. **Criqui M, Matsushita K, Aboyans V *et al.* (2021):** Lower extremity peripheral artery disease: contemporary epidemiology, management gaps, and future directions: A scientific statement from the American Heart Association. Circulation, 144(9): e171-e191. doi: 10.1161/CIR.0000000000001005.
11. **Chan K, Tang F, Tham C *et al.* (2017):** Retinal vasculature in glaucoma: a review. BMJ Open Ophthalmol., 1(1): e000032. doi: 10.1136/bmjophth-2016-000032.
12. **Chui T, Mo S, Krawitz B *et al*. (2016):** Human retinal microvascular imaging using adaptive optics scanning light ophthalmoscopy. Int J Retina Vitreous, 2:11. doi: 10.1186/s40942-016-0037-8.
13. **Lee S, Lee W, Lim H *et al.* (2019):** Thicknesses of central macular, retinal nerve fiber, and ganglion cell inner plexiform layers in patients with hypertension. Retina, 39(9):1810-1818.
14. **Shin Y, Nam K, Lee W *et al*. (2020):** Peripapillary microvascular changes in patients with systemic hypertension: An optical coherence tomography angiography study. Scientific reports, 10(1), 1-8. DOI: 10.1038/s41598-020-63603-6.