

Research Article

Current Trends in Ophthalmology

Foveal Avascular Zone in Hypertension as Measured by Optical Coherence Tomography Angiography

Dantas de Sá LG, Gadelha DNB, Cavalcanti Melo MCS and Brandt CT*

Department of Ophthalmology- UNIFACISA- Medical School- Campina Grande, Brazil

***Correspondence:** Carlos Teixeira Brandt, Department of Ophthalmology- UNIFACISA- Medical School- Campina Grande, Av. Sen Argemiro de Figueiredo, 1901 - Itararé, Campina Grande - PB, CEP: 58411-020, Brazil, E-mail: carlosbrandt@bol.com.br

Received: February 14, 2019; Accepted: March 13, 2019; Published: March 18, 2019

Abstract

Purpose: To investigate the Foveal Avascular Zone (FAZ) area in patients with arterial hypertension using optical coherence tomography angiography (OCT-A).

Material and methods: The study was performed at the School Clinic of UNIFACISA and at the Eye Care Center. It was included 21 hypertensive patients (study group) and 19 individuals without hypertension (control group). It was excluded patients with diabetes or glaucoma. The measurement of the FAZ areas was performed by the DRI OCT-1Triton/Plus. For the quantitative variables, the results were expressed by their means and standard deviations. Qualitative variables were expressed by their absolute and relative frequencies. Student's *t*-test was used to verify differences between means and Fisher's exact test for differences between frequencies. For evaluating the correlation between the superficial and deep plexus areas, the Pearson correlation test was used. *P* value ≤ 0.05 , rejected the null hypothesis. The research was approved by the Ethics Committee of the Medical School from Campina Grande -UNIFACISA and all individuals signed the free and informed consent form.

Results: The means of the superficial FAZ of both eyes was significantly higher in the study group (right eye $410.7 \pm 160.7 \mu\text{m}^2$ - $319.1 \pm 108.2 \mu\text{m}^2$ - $p = 0.0433$); (left eye: $405.4 \pm 144.8 \mu\text{m}^2$ versus $309.4 \pm 87.7 \mu\text{m}^2$ - $p = 0.0174$). The means of the deep FAZ areas of the right and left eyes were similar between the study and control groups (right eye: $559.6 \pm 253.28 \mu\text{m}^2$ versus $605.1 \pm 226.8 \mu\text{m}^2$ - $p = 0.5548$); (left eye: $673.2 \pm 170.8 \mu\text{m}^2$ versus $585.6 \pm 171.2 \mu\text{m}^2$ - $p = 0.1142$). The relationships between the superficial and deep plexus areas of both eyes showed a weak correlation between the two plexuses. ($r = 0.4734$), left eye ($r = 0.2287$), study group - right eye: ($r = 0.4374$), left eye ($r = 0.3580$).

Conclusion: The area of superficial FAZ of the right and left eyes was significantly higher in the hypertensive patients. The deep FAZ area of both eyes, however showed similar mean areas between the study and control groups.

Keywords: Central fovea, Retinal microvasculature, Systemic arterial hypertension, Optical coherence tomography

Introduction

In Brazil, the prevalence of arterial hypertension varies according to the studied population and the measurement method, reaching about 36 million adult individuals [1,2].

The retina microvasculature, choroid and optic disc undergoes patho-physiological alterations secondary

to hypertension, whose main representation is by hypertensive retinopathy [3]. In addition, since its arterial circulation is similar to cerebral, its evaluation (through funduscopy, fluorescence angiography and color retinography) is useful and sensitive with regard to the stratification of cardiovascular risk in hypertensive patients [4,5].

The foveal avascular zone (FAZ) is a structure sensitive to retinal microvasculature disorders, and may indicate events of ischemic nature [4-12]. The imaging gold standard investigation of the retina vascularization is fluorescein angiography, but it is limited in the depth of analyzed structures, viewing only the superficial vascular plexus [13,14].

Noninvasive methods of angiography based on Optical Coherence Tomography Angiography (OCT-A) have been developed, aiming at reproducing the three-dimensional image and the retina vascular mapping. Through this method it is possible to evaluate the perfusion indices of four zones in-face of the retina: the superficial and deep plexus, the outer layer of the photoreceptors and the choriocapillary. In addition, it is possible to investigate and measure the FAZ area of the superficial and deep plexuses [15].

Recently, fovea vascular density was used as an objective method to evaluate retinal microvasculature in the progression of systemic arterial hypertension [10,16].

Screening and appropriate interventions for the chronic and sustained effects of elevated blood pressure levels can prevent complications and sequelae of retina vascularization. In addition, findings regarding its microvasculature may determine the acquisition of new therapies that satisfactorily reach the posterior portion of the eye and its structures, since this aspect is still challenging, despite advances in ocular pharmacology [17]. Thus, the purpose of the study was to investigate the presence of FAZ area changes in patients with systemic arterial hypertension using OCT-A.

Material and Methods

The prospective, observational and analytical study was carried out at the Department of Ophthalmology of the UNIFACISA - School Clinic and the Eye Care Center.

It was enrolled in the investigation: hypertensive patients, with or without signs of hypertensive retinopathy (study group). In the control group, individuals without arterial hypertension and signs of hypertensive retinopathy were included. Diabetic and glaucoma patients were excluded.

The individuals, initially, underwent a comprehensive ophthalmologic examination, biomicroscopy, funduscopy and intraocular pressure (IOP) measurement. After this evaluation, they were submitted to OCT-A, using 3x3

mm digitized images of Topcon's DRT OCT-1Triton/Plus device, whose software allows the manual measurement of areas to be studied, as the FAZ area measured in this investigation. Three measurements were performed and the mean area was taken as estimated precision.

The sample was of convenience and involved 21 patients with systemic arterial hypertension - SAH (study group), and 19 without SAH (control group). For the quantitative variables, the results were expressed by their means and standard deviations. Qualitative variables were expressed by their absolute and relative frequencies. Student's t-test was used in order to verify differences between means for independent samples when the parameters had passed the normality test.

Fisher's exact test was used to verify differences between frequencies. To evaluate the correlation between the superficial and deep plexus areas, the Pearson correlation test was used. The rejection of the null hypothesis was done when the p value was ≤ 0.05 . The project was approved by the ethics committee of the Faculty of Medical Sciences of Campina Grande - UNIFACISA and the approval letter had the number 2,982,410.

All subjects in the study and control groups received information about the type of study and signed the informed consent form. There was no harm or embarrassment to any of the individuals included in the study.

Results

The mean age of the study group (52.6 ± 8.1 years) was significantly higher than the mean age of the control group (48.1 ± 5.6 years - $p = 0.0494$). The assessment of the frequency of male and female gender in both groups was homogeneous (Fisher's exact test - $p = 0.7411$).

It was observed that the mean area of the right FAZ eye was significantly greater in the study group when compared to the control group ($410.7 \pm 160.7 \mu\text{m}^2 - 319.1 \pm 108.2 \mu\text{m}^2$ - $p = 0.0433$). Similarly, the mean superficial FAZ of the left eye was significantly greater in the study group ($405.4 \pm 144.8 \mu\text{m}^2$ versus $309.4 \pm 87.7 \mu\text{m}^2$ - $p = 0.0174$).

The mean area of deep FAZ of the study group right eye was similar to that of the control group ($559.6 \pm 253.28 \mu\text{m}^2$ versus $605.1 \pm 226.8 \mu\text{m}^2$ - $p = 0.5548$). In the left eye, the mean area of the ZAF was similar ($673.2 \pm 170.8 \mu\text{m}^2$ versus $585.6 \pm 171.2 \mu\text{m}^2$ - $p = 0.1142$).

The relationship between the superficial and deep right eye plexuses areas showed a weak correlation between the two groups ($r = 0.4734$). For the left eye, the correlation was even weaker ($r = 0.2287$) (Figure 1A and B).

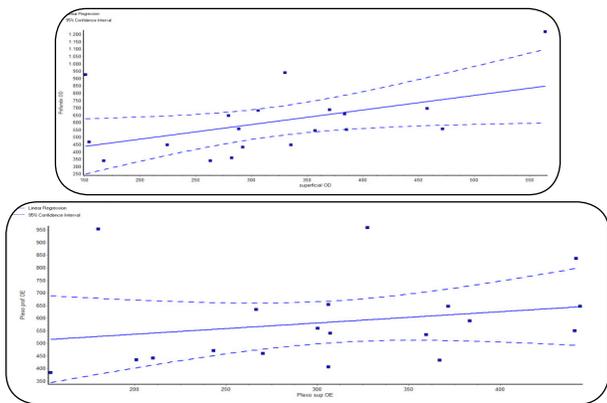


Figure 1A and B: Graphic representations of the correlations between the superficial and deep plexus of the right and left eyes of the control group. In the right and left eyes, 6 (31.6%) measurements are outside the limits of the confidence interval.

The relationship between the superficial and deep plexus areas of the right eye of the study group revealed a correlation of $r = 0.4374$. For the left eye, the correlation was $r = 0.3580$ (Figure 2A and B).

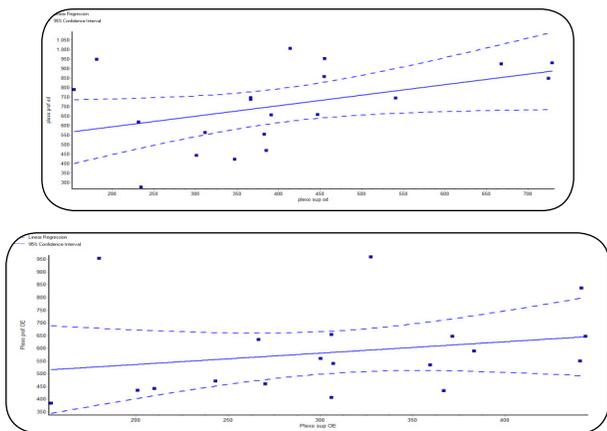


Figure 2A and B: Graphic representation of the correlations between the superficial and deep plexus of the right and left eyes of the study group. In the right eyes, 10 (47.6%) measurements are outside the limits of the confidence interval. In the left eyes, 9 (42.8%).

There were no differences among the outsiders points of the graphic confidence intervals from both eyes of the two groups.

Discussion

The search for a biological marker with accuracy and precision that can effectively demonstrate the effect of systemic arterial hypertension on retinal microcirculation is a current issue, which may facilitate the handling of this disease, assessment of hemodynamic status of the retina and its relation to physiology of vision, helping the specialist's assistance in the integral care of these patients [5,6].

Although there are studies investigating the relationship of ZAF and hypertension [8,9] to date and the best of our knowledge, this is the first study to find an increase in FAZ in the superficial plexus in hypertensive patients.

In this study, the area of the FAZ measured by OCT-A, was statistically significant greater in the superficial plexus of both eyes in the study group when compared to the control group. However, in the deep plexus, the mean FAZ areas were similar between the two groups. Such discrepancy between the findings of the superficial and deep FAZ plexuses could be explained by the difficulty of delimiting this plexus when compared to the superficial one. There is a possibility that the measurement, done manually, and by a single observer, even being the mean of three measurements of the same structure, does not contain the accuracy and precision required for the comparison of the obtained results.

The fact that there is a weak correlation between the superficial and deep plexus areas in all eyes, both in the control and in the study groups, with r values that do not exceed 0.50, may mean that the impact of systemic arterial hypertension is of different intensity when compared to the superficial and deep plexuses.

Another fact that should be highlighted is the occurrence of variation of retinal capillary density and age-related FAZ dimensions [12,13], highlighting the importance of new findings from OCT-A. This has been reported in other ischemic diseases, such as diabetic retinopathies [11,14,18,19] and sickle cell disease [20,21], in addition to glaucoma [22], with possible involvement at the level of the deep plexus, in addition to the histological variation found in this plexus, with greater distancing of the fovea and increased dimensions compared to the superficial plexus [23]. However, such enlargement is not easily interpreted, since there is variation in the size of this area also in the general population, since in a single individual this measurement can usually be large or abnormally increased. Thus, given its individual

variation, a personalized evaluation of the same and its relationships with the other layers of the retina is suggested [24].

It was observed in the present study that the mean age of the patients in the study group was significantly higher than in the control group, as well as the means of the superficial FAZ areas of both eyes. Thus, it can not be affirmed that the increase in FAZ was observed due to arterial hypertension, since with increasing age there is a decrease in vascular density of the retina and an increase in FAZ in both the superficial and deep plexuses [24-26].

The limitations of this research concern to the fact that there is reduced convenience sample size for more consistent evaluations. Moreover, the fact that a single observer performs the FAZ measurements makes the method less accurate and precise. Measurements made manually, not in an automated way, may also have interfered with the data, which should be taken, cautiously, into account when interpreting them.

Another limiting factor is that the patients complains of hypertensive symptoms for a given time, referred to by them, does not mean that they effectively have this disease for the period of time mentioned, since the most frequent is that this disease can go for a long time without symptoms. Moreover, among those individuals in the control group, considered without hypertension, there could be those with occasional hypertensive peaks when submitted to daily stress may have been included, which may induce probable focal ischemia.

Conclusion

The mean area of superficial foveal avascular zone (FAZ) of the right and left eyes was significantly greater in the hypertensive patients. The deep FAZ area of both eyes, meanwhile, showed similar average areas between the two groups.

In addition, the mean age of the study group was also significantly higher than in the control group. However, although systemic arterial hypertension is the probable cause of the increased in the superficial FAZ area, better delimitation and measurement is necessary when comparing deep FAZ in different settings, including hypertension. This association should not be recognized until studies with larger and homogeneous sample size, and better and reliable instruments, which will enable more precise and accurate FAZ measurements.

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