

Quantitative Assessment of Foveal Avascular Zone in Patients with Early and Intermediate Nonexudative Age-Related Macular Degeneration Using Optical Coherence Tomography-Angiography

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Abstract

Optical coherence tomography-angiography (OCT-A) is a relatively new non-invasive imaging technique which provides three-dimensional visualization of the retinal and choroidal microvasculature. Recently, OCT-A is widely used in the diagnosis of age-related macular degeneration (AMD). **Purpose:** To compare 3 quantitative indexes of foveal avascular zone (FAZ)—area (A), perimeter (Pm), and circularity (C) in patients with early and intermediate nonexudative AMD and healthy subjects using OCT-A. **Methods:** Eighty-nine patients with nonexudative AMD (n = 89 eyes) were enrolled in the study. They were compared with sex- and age-matched control group of 66 healthy subjects (n = 66 eyes). The patients with nonexudative AMD were divided into 2 subgroups—early AMD (n = 42 eyes) and intermediate AMD (n = 47 eyes). All participants underwent OCT-A (3 × 3 mm scans, Cirrus HD-OCT, Angioplex, Carl Zeiss Meditec, Dublin, CA). **Results:** There was no statistically significant difference in all 3 assessed indexes between the early AMD subgroup and the control group (A – P = 0.139; Pm – P = 0.230; and C – P = 0.191). There was also no statistically significant difference in all 3 assessed indexes between the intermediate AMD subgroup and the control group (A – P = 0.106, Pm – P = 0.124, and C – P = 0.102, respectively). **Conclusions:** According to our results from the assessment of FAZ in patients with early and intermediate AMD, we hypothesize that macular perfusion remains fairly unchanged in the nonexudative stages of the disease. OCT-A is a reliable technique for visualizing and quantifying FAZ in patients with nonexudative AMD.

Keywords

Age-Related Macular Degeneration, Optical Coherence Tomography-Angiography, Foveal Avascular Zone

1. Introduction

Age-related macular degeneration (AMD) is the leading cause of visual impairment in individuals over the age of 55 years worldwide [1]. The clinical classification of AMD defines 3 stages according to the size of drusen, pigmentary abnormalities, and/or choroidal neovascularization (CNV) assessed within 2 disc diameters of the fovea—early, intermediate, and late AMD, including geographic atrophy (GA) and CNV [2].

The traditional multimodal imaging modalities in AMD include fluorescein angiography (FA), indocyanine green angiography (ICGA), and optical coherence tomography (OCT) [3]. OCT-angiography (OCT-A) is a relatively new non-invasive imaging technique. It provides three-dimensional visualization of the retinal and choroidal microvasculature, without the need of an intravenous dye [4]. A motion contrast is generated by differentiating between moving erythrocytes in the vessels and static surrounding tissue [5]. Each OCT-A-scan is simultaneously obtained along with the corresponding standard OCT B-scan. Thus, both functional and morphological images are acquired [6].

Recently, OCT-A has been used in many vascular and degenerative diseases (AMD, diabetic retinopathy, central/branch retinal vein occlusion, etc.) to visualize and examine microvasculature, as well as foveal avascular zone (FAZ), in different vascular plexuses separately [7] [8]. FAZ is a non-vascular area within the central part of the macula—fovea. Its dimensions vary among normal individuals [8] [9]. In addition, in various retinal diseases FAZ may be altered or deformed which may correlate with decreased best-corrected visual acuity (BCVA) [10] [11] [12].

The purpose of the recent study was to compare 3 quantitative indexes of the superficial FAZ—area (A), perimeter (Pm), and circularity (C) in a Caucasian cohort with early and intermediate nonexudative AMD, and healthy subjects using OCT-A.

2. Materials and Methods

This prospective study was approved by Ethics Committee of Medical University of Plovdiv, Bulgaria, and conducted in accordance with the requirements of Declaration of Helsinki. A total of 89 consecutive patients (48 female, 41 male) with nonexudative AMD ($n = 89$ eyes) were enrolled in the study (**Table 1**). The age (mean \pm standard deviation, SD) was 67.8 ± 6.4 years (range, 56 - 81). According to the clinical classification of AMD, they were divided into 2 subgroups—early AMD with drusen $\geq 63 - < 125 \mu\text{m}$ ($n = 42$ eyes) and intermediate

Table 1. Characteristics of the examined groups.

| | Early AMD (n = 42 eyes) | Intermediate AMD (n = 47 eyes) | Control group (n = 66 eyes) | Overall patients (n = 155 eyes) |
|-------------------|----------------------------|--------------------------------------|--------------------------------|------------------------------------|
| Age | | | | |
| (mean ± SD) Range | 66.5 ± 6.1 56 - 76 | 69 ± 6.3 57 - 81 | 64 ± 4.8 55 - 74 | 66 ± 6 55 - 81 |
| Gender | | | | |
| Male | 20 | 21 | 30 | 71 |
| Female | 22 | 26 | 36 | 84 |

AMD = age-related macular degeneration, SD = standard deviation.

AMD with drusen $\geq 125 \mu\text{m}$ and/or pigmentary abnormalities (n = 47 eyes). Criteria for inclusion in AMD patients group were age ≥ 55 years old, drusen and/or retinal pigment epithelium (RPE) abnormalities (hyper-/hypopigmentation) secondary to AMD, a spherical equivalent of $\geq -3\text{D}$ to $\leq +3\text{D}$. Exclusion criteria were presence of CNV, GA, and other ocular degenerative, vascular or traumatic diseases. They were compared with sex- and age-matched control group of 66 healthy subjects (n = 66 eyes, 36 female and 30 male). The age was 64 ± 4.8 years, range 55 - 74. The inclusion criteria for the healthy volunteers were age ≥ 55 years old, BCVA of ≥ 1.0 , and no history or evidence of ocular or systemic disease.

All participants underwent a complete ophthalmologic examination, including BCVA (Snellen charts), slit-lamp biomicroscopy with fundus examination, tonometry, and OCT-A (Cirrus HD-OCT, Angioplex, Carl Zeiss Meditec, Dublin, CA). OCT-A has automatic algorithms that provide estimates of the “non-flow” area in the center of the macula, defining the FAZ (**Figure 1**). Quantitative analyses of the FAZ were performed using the $3 \times 3\text{-mm}$ en face OCT-A images. In this study we used only the preset settings for the superficial FAZ because of software limitations. We measured 3 indexes of the superficial FAZ-A in mm^2 , Pm in mm, and C. OCT-A scans with low quality of images were excluded. Written informed consent was obtained from all participants.

All statistical analyses were performed using statistical software (IBM SPSS software Version 19; SPSS, Inc., Chicago, IL, USA). The correlation between healthy subjects and each AMD subgroup was generated by independent-samples T-test. P values less than $P < 0.05$ were considered statistically significant.

3. Results

Our study analyzed 89 eyes of AMD patients and 66 eyes of healthy volunteers (n = 155 eyes, 66 ± 6 years, range: 55 - 81). In the early AMD subgroup the following FAZ values (mean \pm SD) were established: A— $0.27 \pm 0.09 \text{ mm}^2$, Pm— $2.28 \pm 0.55 \text{ mm}$, and C— 0.66 ± 0.08 . In the intermediate AMD subgroup the registered values were: A— $0.28 \pm 0.08 \text{ mm}^2$, Pm— $2.28 \pm 0.34 \text{ mm}$, and C— 0.65 ± 0.04 , and in the control group: A— $0.24 \pm 0.08 \text{ mm}^2$, Pm— $2.16 \pm 0.44 \text{ mm}$, and C— 0.68 ± 0.05 , respectively. The values are summarized in **Table 2**. There was no statistically significant difference in all 3 assessed indexes between the early

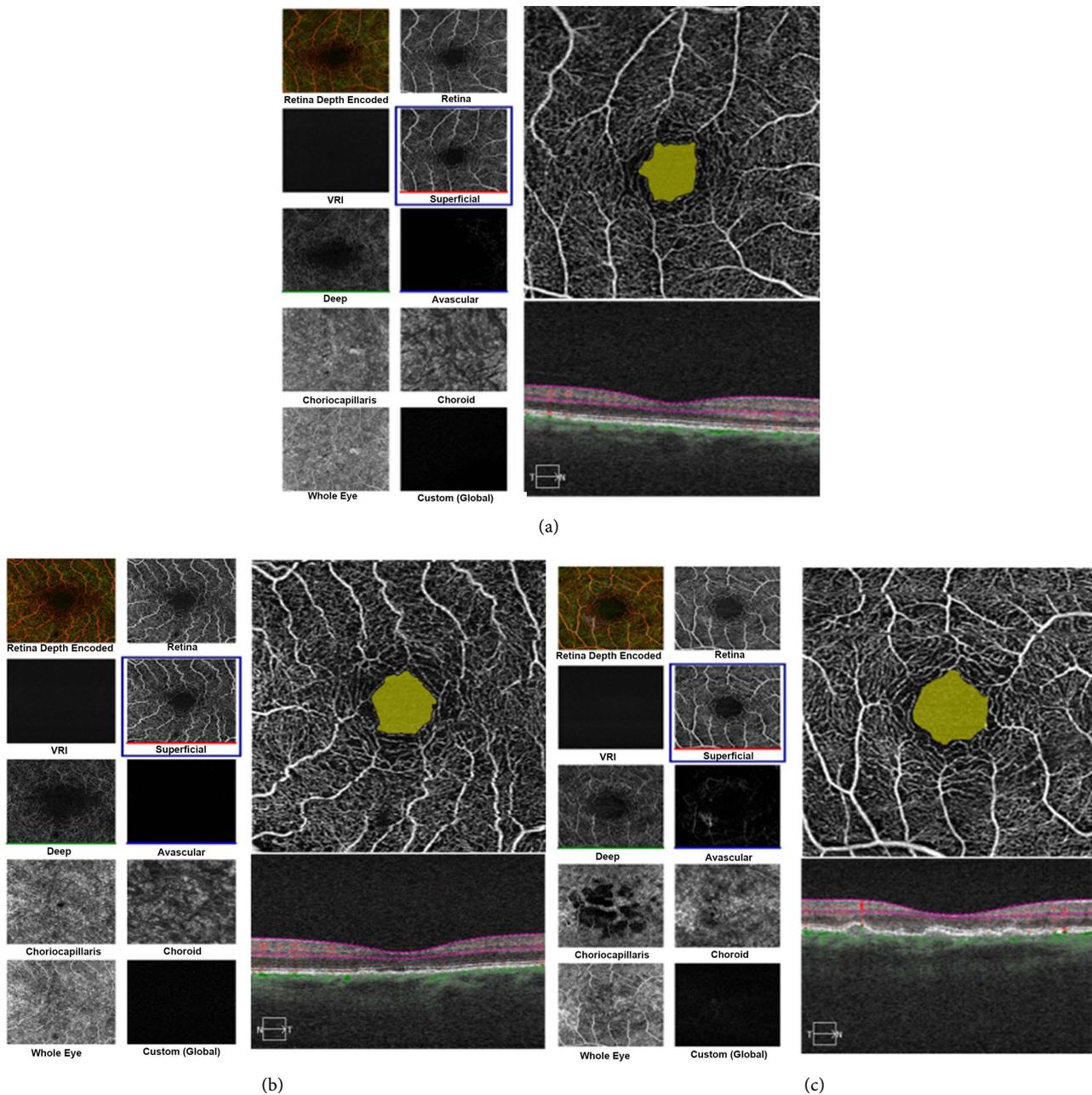


Figure 1. Superficial foveal avascular zone in healthy subject (a), in early AMD (b), and in intermediate AMD (c).

AMD subgroup and the control group: $A - P = 0.139$, $Pm - P = 0.230$, and $C - P = 0.191$. No statistically significant correlation was found in all 3 assessed indexes between the intermediate AMD subgroup and the control group as well: $A - P = 0.106$, $Pm - P = 0.124$, and $C - P = 0.102$, respectively.

4. Discussion

OCT-A enables precise evaluation and quantification of the retinal microvasculature at different levels, without the need of a dye. OCT-A has automatic algorithms defining the FAZ. A relation of FAZ with the age and gender in normal

Table 2. Quantitative indexes of superficial foveal avascular zone (FAZ) in early and intermediate age-related macular degeneration (AMD), and in control group.

| Superficial FAZ indexes | Early AMD (n = 42 eyes) | Intermediate AMD (n = 47 eyes) | Control group (n = 66 eyes) |
|-------------------------|----------------------------|-----------------------------------|--------------------------------|
| Area (mm ²) | 0.27 ± 0.09 | 0.28 ± 0.08 | 0.24 ± 0.08 |
| Perimeter (mm) | 2.28 ± 0.55 | 2.28 ± 0.34 | 2.16 ± 0.44 |
| Circularity | 0.66 ± 0.08 | 0.65 ± 0.04 | 0.68 ± 0.05 |

eyes has been previously described by various studies. Samara *et al.* [8] and Tan *et al.* [13] reported no correlation between FAZ area and age in normal eyes whereas Iafe *et al.* [14] found a significant difference in the examined variables. In our study we did not find any statistically significant correlation between age and FAZ area in the group of healthy volunteers ($P > 0.354$). FAZ area and gender remain a controversial topic which has to be confirmed or rejected by additional studies [8] [13].

In the analysis of superficial FAZ and examined parameters (A, Pm, and C) on 3×3 -mm scans, our results did not show any statistically significant difference between patients with different stages of nonexudative AMD and control group of healthy volunteers. According to that, we hypothesize that FAZ area and shape, as well as macular perfusion remain fairly unchanged in the nonvascular form of the disease. As far as we know this is the first study which compares FAZ variables such A, Pm, and C in patients with nonexudative AMD using OCT-A.

There are some limitations in this study. We did not evaluate deep FAZ because of the software version limitations. In all conducted studies deep FAZ was measured with a wider range compared to superficial FAZ [9] [14] [15]. Furthermore, central foveal thickness and axial length were not included in the overall assessment. Some authors describe negative correlation of superficial FAZ area with central retinal thickness [8] [13].

5. Conclusion

In conclusion, OCT-A is an appropriate non-invasive and reliable method for evaluating superficial FAZ that provides automatic quantitative measurement of this “nonflow” area in the center of the macula. According to our results, we hypothesize that macular perfusion remains fairly unchanged in the nonexudative stages of the disease. Additional studies are needed to confirm its application and importance in nonexudative stages of AMD.

Conflict of Interest

The authors declare no conflict of interest.

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