Foveal Avascular Zone Area Quantification with OCT Angiography Following Successful Rhegmatogenous Retinal Detachment Repair

Quantificação da Área da Zona Avascular Foveal com OCTA Após Reparação Bem Sucedida de Descolamento de Retina Regmatogéneo

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ABSTRACT

INTRODUCTION: Visual prognosis after a rhegmatogenous retinal detachment (RRD) may relate to the vascular status of the macula. Recent works have demonstrated that optical coherence tomography angiography (OCTA) can reproducibly evaluate foveal avascular zone (FAZ) dimensions. The aim of this research was to study the FAZ area at the superficial and deep capillary plexus using OCTA after successful RRD repair and correlate this data with postoperative visual recovery.

METHODS: This was a prospective case-control study that included all patients diagnosed between January and March of 2021 with an RRD that was successfully repaired with a single, uncomplicated surgical procedure (pars plana vitrectomy with gas tamponade). Two groups were created according to macula involvement (macula-on and macula-off) and control data was obtained from the fellow healthy eye. FAZ areas were independently measured by manually outlining the inner border of foveal capillaries of superficial (SCP) and deep capillary plexus (DCP) using OCTA system software.

RESULTS: We included 12 eyes (6 macula-on and 6 macula-off) and 12 controls (12 patients). All eyes with RRD had significantly larger FAZ areas of both SCP (study group: 0.30 ± 0.09 mm^2; control group: 0.26 ± 0.09 mm^2; $p<0.001$) and DCP (study group: 0.37 ± 0.06 mm^2; control group: 0.33 ± 0.05 mm^2; $p=0.002$). In the macula-off group this difference was greater than in the macula-on group for both superficial (macula-off group=+0.051 mm^2; macula-on group=+0.027 mm^2; $p=0.027$) and deep (macula off group=+0.062 mm^2, macula-on group=+0,023 mm^2, $p=0.062$) FAZ areas. Postoperative best corrected visual acuity was significantly higher in the macula-on group (macula-on group=0.81; macula-off group=0.55; $p=0.029$).

CONCLUSION: FAZ area enlargement observed after a retinal detachment demonstrates that the latter may lead to an ischemic injury. When the macula is involved this damage may be greater which could explain a larger FAZ area. Slighter changes in FAZ area in macula-on RRDs may explain a better visual prognosis associated with this type of detachment.

KEYWORDS: Angiography; Fovea Centralis; Retinal Detachment; Tomography, Optical Coherence.

RESUMO

INTRODUÇÃO: O prognóstico visual após descolamento de retina regmatogéneo (DRR) pode relacionar-se com o estado vascular da mácula. Alguns trabalhos recentes demonstraram que a angiografia por tomografia de coerência óptica (OCTA) avalia de forma reprodutível as dimensões da zona avascular foveal (ZAF). O objetivo deste trabalho foi estudar a área da ZAF, através de OCTA, após cirurgia de DRR e correlacioná-la com a recuperação visual pós-operatória.

MÉTODOS: Este foi um estudo prospetivo, caso-controlo, que incluiu todos os doentes diagnosticados entre Janeiro e Março de 2021 com um DRR tratado com vitrectomia via pars plana com tamponamento com gás. Criaram-se dois grupos de acordo com o envolvimento macular (mácula *on* e mácula *off*) e o olho adelfo saudável foi utilizado como controlo. As áreas da ZAF foram calculadas através de *software* do OCTA após delineação manual do bordo interno dos capilares foveais do plexo capilar superficial (PCS) e profundo (PCP). Resultados e Discussão: Foram incluídos 12 olhos (6 mácula *on* e 6 mácula *off*) e 12 controlos (12 doentes). Todos os olhos com DRR tinham áreas da ZAF significativamente maiores no PCS (grupo DRR: 0,30 ± 0,09 mm^2; grupo controlo: 0,26 ± 0,09 mm^2; p<0,001) e no PCP (grupo DRR: 0,37 ± 0,06 mm^2; grupo controlo: 0,33 ± 0,05 mm^2; p=0,002). No grupo mácula off esta diferença foi maior que no grupo mácula on para o plexo superficial (grupo mácula *off* =+0,051 mm^2; grupo mácula *on*=+0,027 mm^2; p=0,027) e também para o plexo profundo (grupo mácula *off*=+0,062 mm^2, grupo mácula *on*=+0,023 mm^2, p=0,062). A acuidade visual pós-operatória foi significativamente maior no grupo mácula on (grupo mácula *on*=0,81; grupo mácula *off*=0,55; p=0,029).

CONCLUSÃO: O alargamento da área da ZAF após descolamento de retina demonstra que este pode causar dano isquémico. Quando a mácula está envolvida, esta lesão pode ser maior o que pode explicar uma área mais larga da ZAF. Um menor alargamento da área da ZAF em DRRs com mácula *on* pode explicar o melhor prognóstico visual associado a este tipo de descolamento.

PALAVRAS-CHAVE: Angiografia; Descolamento da Retina; Fóvea Central; Tomografia de Coerência Óptica.

INTRODUCTION

Rhegmatogenous retinal detachment (RRD) refers to the separation of the neurosensory retina from the underlying retinal pigment epithelium that results from the passage of fluid from the vitreous cavity, through a retinal break, into the subretinal space.[1] This is the most common form of retinal detachment and has been associated with a growing incidence, mainly due to the rising age of many populations and the increasing global prevalence of myopia.[2] Visual prognosis after successful RRD repair has been largely studied, and with modern surgical techniques a fairly high success rate can be expected.[3] However, especially when the macula is involved, it can cause severe visual impairment. The anatomical explanation is still yet to be fully understood, but, according to recent literature, it may be related with the vascular status of the retina.[4,5] The human retinal capillary network is composed of distinct layers including the superficial and the deep capillary plexus (SCP and DCP, respectively) that surround the foveal avascular zone (FAZ).[6] The FAZ is a region within the fovea, devoid of retinal vessels, which shape and size may be altered and correlated with visual acuity, in eyes with retinal disease.[7-10] Optical coherence tomography angiography (OCTA) is a fairly recent imaging modality which can accurately characterise retinal and choroidal blood flow.[11] Recent works have demonstrated that OCTA can reproducibly evaluate FAZ dimensions.[12]

The aim of this research was to study the FAZ area at the superficial and deep capillary plexus using OCTA after successful RRD repair and correlate this data with postoperative visual recovery.

METHODS

STUDY DESIGN

This was a prospective, observational, case-control study. The research conformed to the ethical standards of the Declaration of Helsinki.

STUDY POPULATION

All patients diagnosed between January and March of 2021, at the department of ophthalmology of Centro Hospitalar Lisboa Ocidental, with a primary unilateral RRD, that was successfully repaired with a single uncomplicated surgical procedure were included. Only patients submitted to

a pars plana vitrectomy (PPV) with gas tamponade with or without scleral buckling were eligible for the study. Patients surgically treated with other techniques, such as PPV with silicone oil tamponade, were not included. We also excluded patients with a prior history of ocular surgery of the posterior segment in at least one eye, and patients with preexisting ocular disease in at least one eye, such as diabetic retinopathy, any kind of maculopathy, glaucoma, uveitis or high myopia (> 6D). Patients with postoperative complications such as recurrence of retinal detachment, cystoid macular edema, persistent subfoveal fluid, epiretinal membrane proliferation or patients with severe media opacities hindering high-quality imaging were also excluded. All patients were submitted to a detailed ophthalmic exam, 6 to 9 months after surgery, including best-corrected visual acuity (BCVA), complete anterior and posterior segment slit-lamp ocular examination, and imaging with spectral domain optical coherence tomography (SD-OCT) and OCTA. Control data was obtained from the fellow healthy eye. The study group was further divided into two groups according to macula involvement (maculaon and macula-off).

OCTA

At 6 to 9 months postoperatively, all patients were submitted to pupil dilatation and an OCTA volume scan was generated using OCT Spectralis® (Heidelberg). En face images of the SCP and the DCP were obtained after automated layer segmentation with the preset settings achieved by Heidelberg Eye Explorer system software. FAZ was considered the avascular space limited by the inner margin of the respective vascular network. One independent masked researcher delineated this border manually, using software "draw region" tool, after which the FAZ area was automatically estimated in mm^2.

Furthermore, according to recent works, FAZ area may correlate with central macular thickness (CMT) in eyes without disease.[13] We therefore noted and analysed CMT which was obtained from an automated measurement performed by the system software.

SURGERY

All surgeries were performed by one of three vitreoretinal surgeons. Surgical technique consisted of PPV with gas tamponade with or without scleral buckling. A standard three-port, 23 gauge PPV was performed with vitreous traction release, subretinal fluid drainage, and endolaser photocoagulation around the breaks. Scleral buckling consisted of passing and anchoring an encircling episcleral band around the circumference of the globe. This technique was added to the PPV in cases of inferior DRR, multiple inferior retinal breaks or presence of severe proliferative vitreoretinopathy.

Phacoemulsification was associated in some cases according to media opacity. All surgeries were concluded with gas tamponade with either SF 6 or C3 F8.

STATISTICAL ANALYSIS

Continuous variables were presented as mean ± standard deviation and qualitative variables were expressed as number and percentages. Two-tailed, paired Student t-test was used to compare FAZ areas between the study and the control eye. All statistical analyses were performed using SPSS statistical software. A *p*-value of <0.05 was considered statistically significant.

RESULTS

PATIENTS DEMOGRAPHICS

A total of 24 eyes from 12 patients were included in the study and underwent FAZ area measurement. Twelve were study eyes and 12 were controls. The mean age was 61.1±11.6 years (range 44 - 82 years) and the majority of the patients were male (58%). Surgery and lens status

All patients underwent PPV with gas tamponade and four patients (33%) were also submitted to scleral buckling. Three patients (25%) were pseudophakic at the time of surgery and 5 patients (42%) either underwent phacoemulsification at the time of vitrectomy or posteriorly during follow-up. At 6 months postoperatively, 7 study eyes (58%) were pseudophakic.

VISUAL FUNCTION

Preoperative BCVA in study eyes was on average 0.36. The difference between preoperative BCVA in the macula-on group (0.72) and the macula-off group (0.01) was statistically significant (p=0.001). Postoperative BCVA improved in both groups when compared to preoperative BCVA, and was significantly better in the macula-on group than in the macula-off group (macula-on group=0.81; macula-off group=0.55; p=0.029).

CENTRAL MACULAR THICKNESS

In our sample, the CMT was larger in the study group when compared to the control group (study group: 306.8 ± 30 μm; control group: 286.3 ± 24 μm; p=0.052). However, there was no significant difference between macula-on and macula-off groups regarding CMT (macula-on: 306.5 ± 35 μm; macula-off: 307.2 ± 27 μm; p=0.971).

MACULA STATUS AND FOVEAL AVASCULAR ZONE AREA

Six eyes had a macula-on RRD, and six eyes had a macula-off RRD. The mean macula-off duration, from RRD diagnosis to surgery procedure, was 6.17±4.07 days. We tested similarity between FAZ areas of control eyes of the macula-on and macula-off groups to understand if we could draw correct conclusions from differences between this group and the study group. There was no difference regarding FAZ areas between controls of the macula-on and macula-off groups (p=0.785). All

eyes that had suffered an RRD had significantly larger FAZ areas than their fellow healthy eyes, of both superficial capillary plexus (study group: 0.30 ± 0.09 mm^2; control group: 0.26 ± 0.09 mm^2; p<0.001) and deep capillary plexus (study group: 0.37 ± 0.06 mm^2; control group: 0.33 ± 0.05 mm^2; p=0.002). In the macula-off group this difference was greater than in the macula-on group for both superficial (macula-off group=+0.051 mm^2; macula-on group=+0.027 mm^2; p=0.027) and deep (macula off group=+0.062 mm^2, macula-on group=+0.023 mm^2, p=0.062) vascular plexus. Fig. 1 shows the detailed SCP and DCP analysis and measurements of one patient from our study.

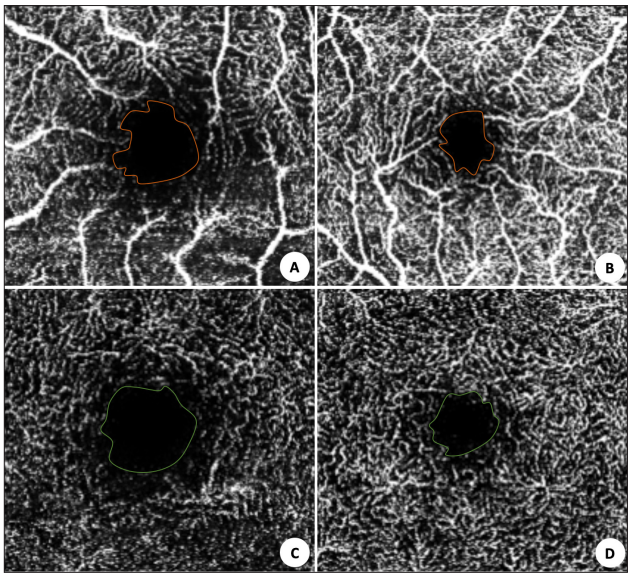

Figure 1. FAZ area of one patient. (A) SCP of affected eye; (B) SCP of healthy eye; (C) DCP of affected eye; (D) DCP of healthy eye.

DISCUSSION

The purpose of our work was to study the FAZ area at the superficial and deep capillary plexus using OCTA after successful RRD repair and correlate this data with postoperative visual recovery.

Taking into account that the FAZ area is similar between both eyes in healthy individuals,[13] we used the fellow healthy eye as a control to the eye that suffered a RRD.

The FAZ status, namely its area, has already been implicated in the possible etiopathogenesis of some retinal diseases. In diabetic retinopathy, a statistically significant FAZ enlargement has been documented when compared with healthy eyes.[7] Also, in eyes with glaucoma, a decreased macular vascular density with an increased FAZ area have been revealed and the FAZ circularity index has been suggested as a possible biomarker.[8] Furthermore, in patients with retinal vein occlusion, a decrease in vascular perfusion at the DCP and a larger mean FAZ area have also been observed.[9,10] These results support the theory that in retinal vascular diseases there is an ischemic injury to the retinal capillary plexus which may contribute to visual impairment. Recent works have analysed and interpreted the FAZ changes after a retinal detachment and tried to correlate this with postoperative visual prognosis.[9,14-17] However, the results are still inconsistent. Some studies reported strong correlations between FAZ and BCVA[18,19] whereas other did not find any correlation.[16] To the best of our knowledge, this is however the first study that tries to identify a difference in FAZ are between macula-on and macula-off RRDs and that tries to correlate anatomical differences with the worse visual prognosis associated with macula-off RRDs. In fact, the microvasculature of the retina, especially the capillary plexus within its thickness, constitute a complex and very important provider of nourishment and carrier of waste products to and from the retinal cells. This network is distributed in different layers, including the SCP and the DCP, and recent evidence has suggested that these two plexus may be excessively disturbed by retinal vascular disease.[7-10] When the macula detaches this damage may be greater, as demonstrated in our sample by a FAZ area enlargement of 0.051 mm^2 in the SCP and 0.062 mm^2 in the DCP compared a smaller enlargement of 0.027 mm^2 in the SCP and 0.023 mm^2 in the DCP if the macula is not involved.

As for limitations, our study has a small sample size and a short postoperative observation period. Further works are needed to confirm our results and evaluate FAZ changes over a longer postoperative time. Also, FAZ area calculation included a manual delineation which, although being made by a masked independent researcher, is still a subjective process. And finally, the fact that not all study eyes were pseudophakic may have influenced visual acuity outcome. On the other hand, FAZ area measurement in OCTA was probably not affected by this fact, because, as it has been demonstrated,[20] it is not strongly altered by cataract.

CONCLUSION

In conclusion, our study results suggest that after a retinal detachment there is a FAZ area enlargement. This change may be due to an ischemic injury to the retinal capillary plexus. When the macula is involved this ischemic damage may be greater which could explain a larger FAZ area. Our work also shows that changes in FAZ area may correlate with visual acuity and that smaller changes in FAZ area in macula-on RRDs may be on the basis of a better visual prognosis associated with this type of detachment. The FAZ area may be predictive of visual outcomes following surgery in eyes with RRDs.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

MP, PA: Data collection, literature review, writing of first draft.

MP and SD: Critical analysis and revision.

FV: Critical analysis, supervision and guidance.

All authors approved the final version to be published.

RESPONSABILIDADES ÉTICAS

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Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.

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Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2013).

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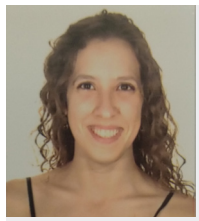

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