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Relationship between the Presence of a Cilioretinal Artery and Subretinal Fluid in Neovascular Age-Related Macular Degeneration

Adel Ebraheem, MD, MS,[1,2] *Akihito Uji, MD, PhD,*[1,2] *Nizar Saleh Abdelfattah, MD,*[1,2] *Muneeswar Gupta Nittala, MPhil Opt,*[1,2] *Srinivas Sadda, MD,*[1,2] *Phuc V. Le, MD, PhD*[1,2]

Purpose: To evaluate the relationship between presence of a cilioretinal artery (CRA) and the extent of subretinal fluid (SRF) in eyes with treatment-naïve neovascular age-related macular degeneration (nAMD). Eyes with nAMD have varying amounts of SRF, and factors affecting exudation volume are not well established. We hypothesize that presence of CRA may affect the extent of SRF by affecting the hemodynamics of blood flow supplying the choroidal neovascular membrane.

Design: Retrospective case-control study.

Participants: Two hundred twelve patients with treatment-naïve nAMD in at least 1 eye from anonymized datasets available at the Doheny Image Reading Center.

Methods: Color fundus photographs and fluorescein angiograms of the study eyes were reviewed to identify those with a CRA (cases) and those without (controls). Spectral-domain OCT data were evaluated by 2 masked graders to identify presence and volume of SRF. We identified subtypes of CNV and evaluated other OCT features that could affect SRF, such as presence of subretinal hyperreflective material (SHRM), cystoid macular edema (CME), and pigment epithelial detachment (PED). Nonparametric Mann−Whitney *U* test and univariate and multivariate analyses were performed to identify significant differences between cases and controls and to evaluate the relationship between these factors and SRF volume.

Main Outcome Measures: Presence and volume of SRF, presence of CME, PED types, and CNV types.

Results: We identified 44 cases and 168 controls. Mean SRF volume was significantly lower in cases than controls (0.72 ± 0.9 mm^3 vs. 1.60 ± 2.36 mm^3; $P = 0.03$). Univariate regression analysis showed a weakly significant correlation between presence of CRA and SRF volume ($r = -0.15$; $P = 0.03$) and OCT parameters, including SHRM ($r = 0.16$; $P = 0.023$), CME ($r = -0.20$; $P = 0.004$), and type 2 CNV ($r = 0.16$; $P = 0.02$). Multivariate analysis demonstrated that the presence of a CRA ($r = -0.17$; $P = 0.02$) was correlated independently with the presence of SRF.

Conclusions: Presence of a CRA was correlated negatively with the volume of SRF in eyes with nAMD. These findings may draw insights into the potential hemodynamic effect of the CRA, which warrants further investigation. *Ophthalmology Retina 2017;■:1−6 © 2017 by the American Academy of Ophthalmology*

Age-related macular degeneration (AMD) is a major cause of blindness and the most common cause of vision loss in the Western world.[1] In the United States, more than 8 million people are estimated to have some features of AMD.[1] Approximately 1.3 million of these will demonstrate the advanced stage of AMD, including either neovascular AMD (nAMD) or geographic atrophy, during the next 5 years.[2] Approximately 10% of AMD patients demonstrate choroidal neovascularization (CNV),[3] which can manifest as subretinal fluid (SRF), cystoid macular edema (CME), retinal pigment epithelial detachment (PED), fibrovascular disciform scar with atrophy, hemorrhage, or a combination thereof.[4−6] Choroidal neovascularization occurs as result of neovascular growth under or through the retinal pigment epithelium through breaks in Bruch's membrane. Different growth factors, such as vascular endothelial growth factor, are involved in the development of CNV.[7,8] The immature endothelial cells of the CNV do not demonstrate the barrier function of more mature choroidal blood vessels.[7−9] Therefore, CNV tends to leak, bleed, or both. This can result in fluid beneath the retinal pigment epithelium (PED), beneath the neurosensory retina (SRF), or within the retina itself (CME).

The primary blood supply of the inner retina of the macula normally originates from branches of the central retinal artery. In some eyes, a cilioretinal artery (CRA) arises from the choroidal circulation as a branch of the short ciliary artery and provides an additional blood supply to the macula (Fig 1). It usually is located on the temporal side of the optic disc, but sometimes appears on the nasal side. It has a characteristic sharp, diagnostic hook-like appearance.[10]

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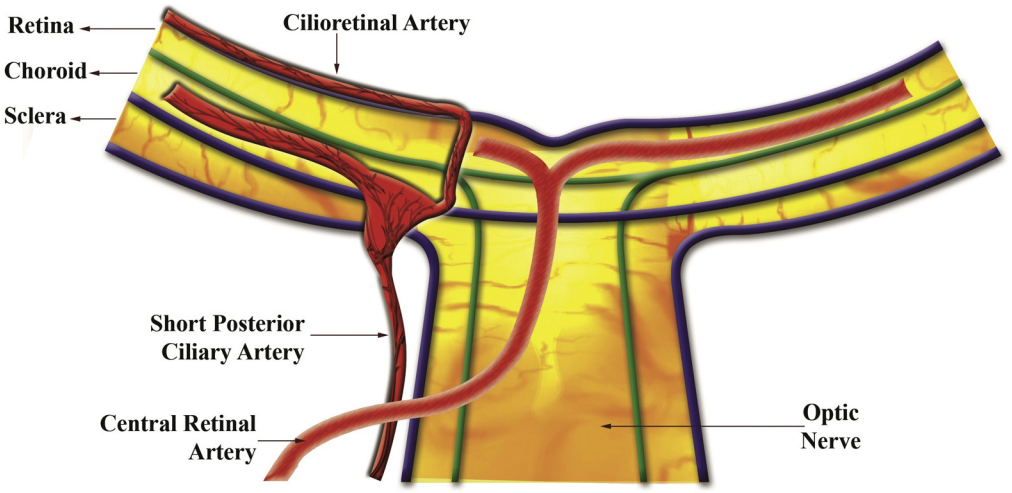

Figure 1. Diagram of the retinal blood supply showing the cilioretinal artery as a branch of short ciliary artery.

Fluorescein angiography (FA; Fig 2) is the most accurate method for determining whether CRA is present. Using a nonmydriatic fundus camera, Liu et al[11] found a CRA in 35% of their 2500 Han Chinese participants. In another study, clinical fundus examination of 921 Indian patients revealed that a CRA was present in 22.8% of the studied population.[12] However, Mann[13] reported that the incidence of a CRA in various studies ranged from 6.9% to 25%.

Inan et al[14] investigated the influence of the presence of a CRA on AMD and suggested that the presence of CRA prevented accumulation of drusen, which can act as a barrier to metabolic exchange between the choriocapillaris and photoreceptors. They concluded that the presence of a CRA may help to prevent the development of AMD. Another study, conducted by Meister et al,[15] showed that in matched populations, more eyes without a CRA had evidence of age-related maculopathy or AMD than did those with a CRA. Similar to Inan et al, they also concluded that the presence of a CRA could be a protective factor against age-related macular diseases.

The CRA belongs to the posterior ciliary artery system. It usually arises from the peripapillary choroid or directly from one of the short posterior ciliary arteries and supplies the inner retina. Because the CRA redirects a percentage of blood volume from the outer retina to the inner retina, we hypothesize that the volume of SRF will be less in patients with a CRA than a control group. To assess this, we analyzed OCT images of treatment-naïve nAMD from 212 patients.

Methods

Study Design

In this retrospective case-control study, patients with treatment-naïve nAMD in 1 eye were identified from anonymized datasets available at the Doheny Image Reading Center. Patients were required to have color fundus photographs, FA images, and spectral-domain (SD) OCT scans for each study eye to ensure multimodal imaging assessment of all study eyes at baseline.

Two qualified trained graders reviewed the color fundus photographs and FA images to identify eyes with a CRA (A.E. and A.U.). Data from the baseline SD-OCT (Cirrus OCT; Carl Zeiss Meditech, Dublin, CA) were evaluated to determine the volume of SRF and PED. The analysis involved other OCT features that could affect SRF volume, such as the presence of subretinal hyperreflective material (SHRM), CME, PED, and CNV subtypes. The inclusion and exclusion criteria are listed in Table 1.

The study was approved by the institutional review board of the David Geffen School of Medicine at the University of California, Los Angeles. The research project adhered to the tenets of the Declaration of Helsinki and complied with the regulations set forth by the Health Insurance Portability and Accountability Act. Informed consent was obtained from participants.

Grading Protocol

Color fundus photographs, FA images, and SD-OCT images of study eyes were reviewed for qualitative features and were analyzed for quantitative measures by 2 certified reading center graders (A.E. and A.U.) using the Cirrus Macular Thickness Analysis software (version 7.0). We identified eyes with a CRA (designated as cases) and eyes without CRA (designated as controls). Reproducibility analysis was performed because each grader identified case and control groups and evaluated the OCT features independently.

Baseline visit SD-OCT data were evaluated to determine the presence and volume of SRF and PED. All 128 B-scans of the volume cube also were reviewed for other pathologic features, aside from the typical CNV membrane. Specifically, we evaluated for features that could affect SRF volume, such as presence of SHRM, CME, PED, and CNV subtypes.

Subretinal fluid and PED volumes were calculated using a modified version of the technique described by Heussen et al.[16] The vertical extent of the SRF or PED was calculated by multiplying the number of B-scans involved by the spacing between B-scans (6 mm divided by 128 B-scans). The horizontal distance was calculated by multiplying the number of A-scans involved by the spacing between A-scans (6 mm divided by 512 A-scans). This area then was multiplied by the maximal thickness of the SRF or PED to generate an estimate of the SRF or PED volume (Fig 3).

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