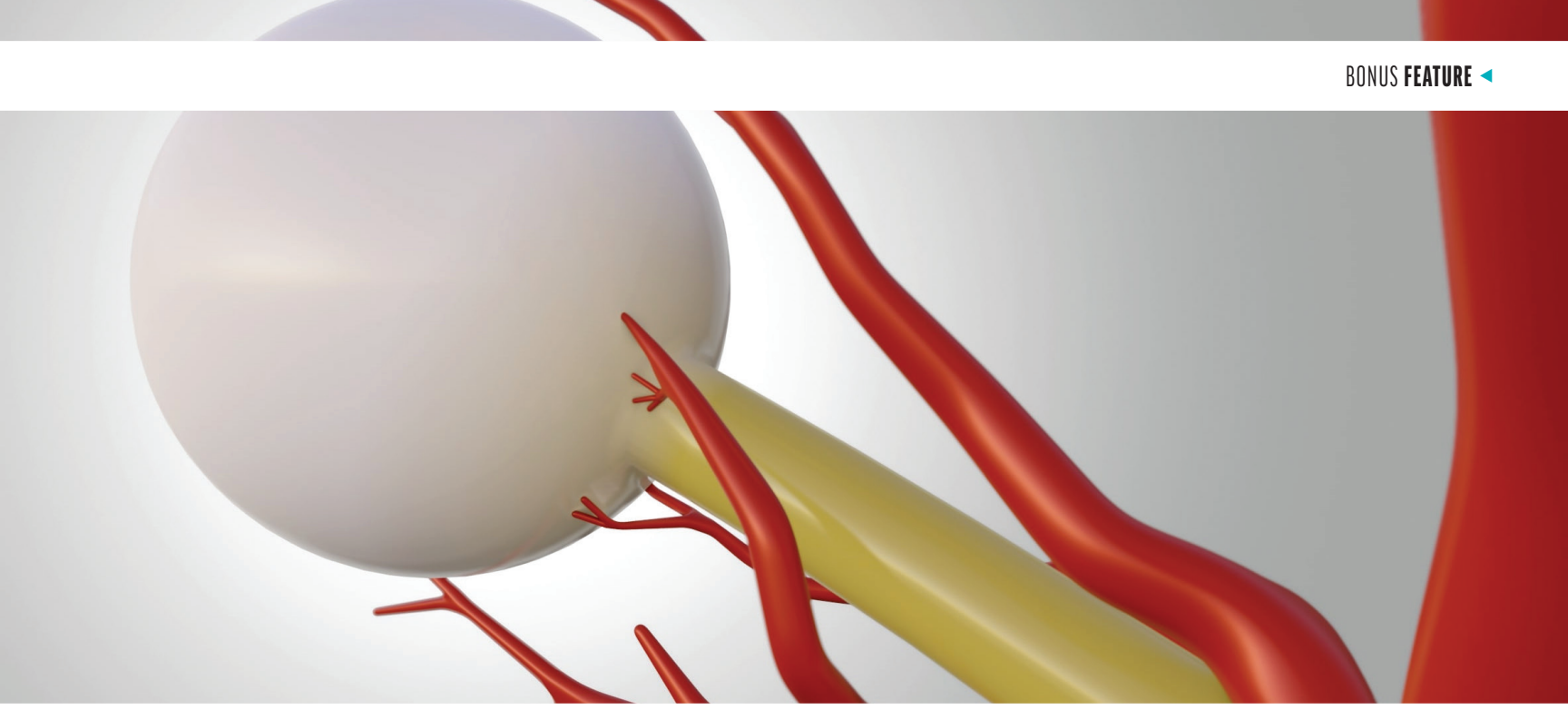

THE MYSTERY OF CILIORETINAL ARTERIES AND AMD

Research is beginning to unravel the role these arteries play in the pathogenesis of neovascularization.

BY ADEL EBRAHEEM, MD, MS, OD

Age-related macular degeneration (AMD) is a multifactorial condition characterized by dysregulation of the inflammatory, complement, lipid, and angiogenic pathways. AMD is classified as either dry or wet based on the absence or presence of choroidal neovascularization (CNV), respectively. Dry (nonexudative) AMD represents most of the total number of AMD cases.[1] The hallmark of dry AMD is the presence of drusen, which can progress to geographic atrophy. Wet (exudative) AMD is characterized by invasion of the outer retina by new, immature blood vessels, or CNV, from the underlying choroid. The pathogenesis of wet AMD is the secretion of vascular endothelial growth factor (VEGF), which promotes the growth of these abnormal blood vessels.

CNV can manifest as a retinal pigment epithelial detachment (PED), cystoid macular edema, hemorrhage, disciform scar, subretinal fluid (SRF), or a combination of these clinical features.

IDENTIFYING CILIORETINAL ARTERIES

The outer retina receives its blood supply from the choroid; the nutrients take a path through Bruch membrane and the retinal pigment epithelium to the neural retina. The central retinal artery is the main blood supply to the inner retina. The inner layers of the macula may receive a second blood supply from cilioretinal arteries, which emerge from the choroidal vascular bed (Figure). Cilioretinal arteries typically originate from the temporal margin of the optic disc, although they can also occasionally originate near the nasal border. Multiple cases in the literature have shown evidence of two or more cilioretinal arteries.[2]

In the general population, the prevalence of a cilioretinal artery varies from 7% to 50%.[3] The most accurate imaging modality for

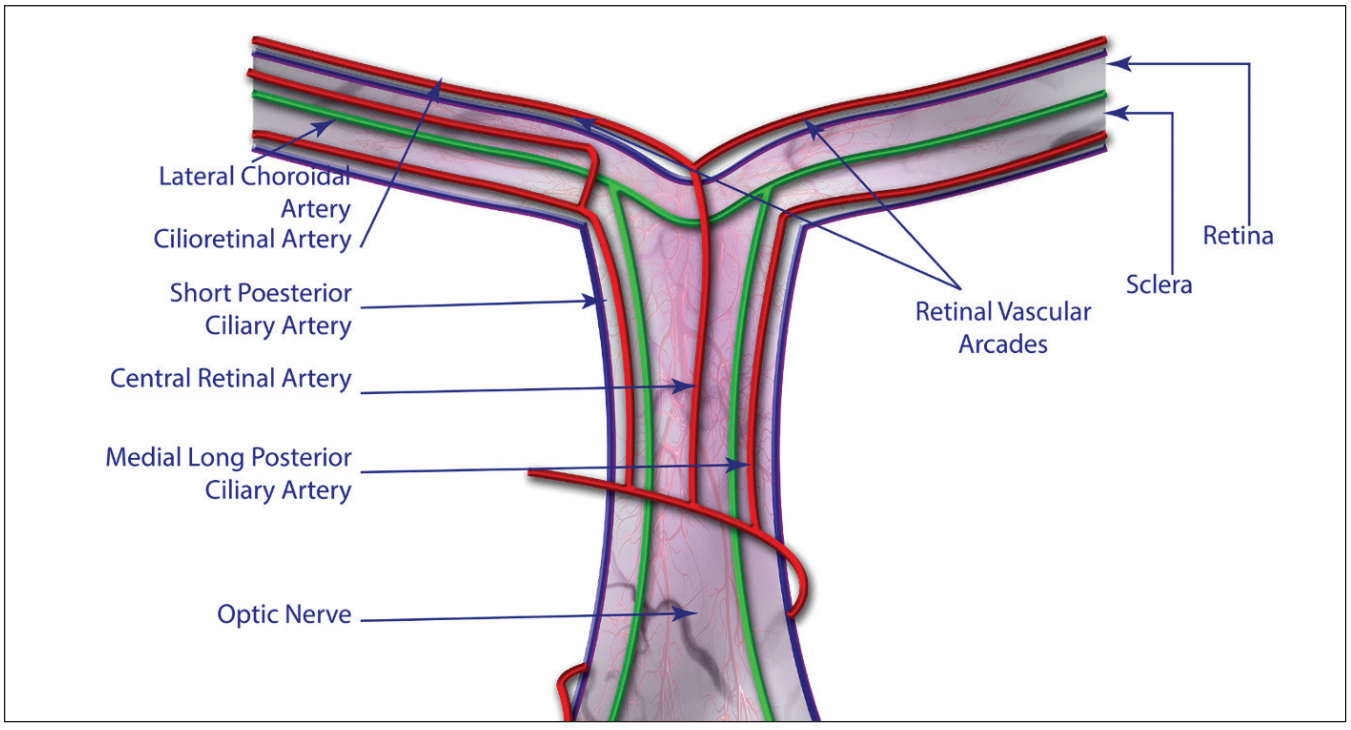

Figure. Diagram of the retinal blood supply reveals the cilioretinal artery.

detecting the existence of cilioretinal arteries is fluorescein angiography; however, some clinicians also employ biomicroscopic fundus examinations or fundus imaging to confirm the presence of cilioretinal arteries.

THE LINK BETWEEN CILIORETINAL ARTERIES AND AMD

Many researchers have explored the connection between cilioretinal arteries and the clinical characteristics of AMD. For example, Inan et al found that cilioretinal arteries inhibit the development of drusen,[4] and Meister et al noted that AMD was more common in eyes lacking cilioretinal arteries.[5]

The team at Doheny Eye Institute and I evaluated the relationship between the extent of SRF and the presence of a cilioretinal artery in the eyes of 212 patients with treatment-naïve wet AMD. Spectral-domain OCT images were graded by two independent physicians to identify and calculate SRF volume. We concluded that the presence of a cilioretinal artery correlated negatively with SRF volume, and we speculated that this is due to the hemodynamic effect of cilioretinal arteries.[6]

To further characterize the relationship between cilioretinal arteries and wet AMD, Snyder et al performed a secondary analysis of the Age-Related Eye Disease Study (AREDS).[7] The retrospective analysis of data from 3,647 AREDS patients showed that a cilioretinal artery was negatively correlated with the prevalence of CNV.

However, Bavinger et al conducted a secondary data analysis of the Comparison of Age-Related Macular Degeneration Treatment Trials and found no relationship between wet AMD and the presence of cilioretinal arteries. The researchers noted the uncertainty of such a discrepancy between their results and other study outcomes.[8]

ADDITIONAL CORRELATIONS

Researchers are working on ways to better characterize the hemodynamic effect of cilioretinal arteries, beginning with a calculation of blood flow to the inner retina.[9] For example, at least two studies have identified a variation in the diameter of the central retinal artery.[10,11] Dorner et al found that the mean diameter of the central retinal artery in humans was 163 µm with a standard deviation of 17 µm.[11] The diameter of blood vessels plays a crucial role in determining the pressure and velocity of blood flow. The same equation these researchers used could be employed to calculate the volume of blood that deviates from the outer retina to the inner retina in the presence of cilioretinal arteries. The presence of a cilioretinal artery has the potential to modify the circulation of blood within the eye, consequently affecting the features of macular edema or subretinal fluid.

Landa et al studied the correlation between diabetic macular edema (DME) and the presence of cilioretinal arteries. The OCT data analysis demonstrated that DME was observed in 87% of patients

AT A GLANCE

- Research shows a link between the presence of cilioretinal arteries and inhibited drusen development, possibly suggesting a protective effect against age-related macular degeneration.
- The presence of cilioretinal arteries has an effect on the hemodynamics of retinal blood flow and is linked to the development of choroidal neovascularization and the volume of subretinal fluid.
- Because patients with cilioretinal arteries should have a lower rate of subretinal fluid accumulation than patients without cilioretinal arteries, the author suggests patients with cilioretinal arteries be studied separately in clinical trials that investigate anti-VEGF treatment outcomes.

with a cilioretinal artery compared with less than 30% in the control group without a cilioretinal artery. In addition, the researchers observed that the average blood velocity in the cilioretinal arteries was significantly higher compared with the mean arterial blood velocity.[12] By integrating insights from various research endeavors, it is apparent that the identification of a cilioretinal artery represents a significant biomarker that can influence the prognosis of macular edema and subretinal fluid.

Leclaire et al analyzed the influence of cilioretinal arteries on peripapillary and macula vascular density.[13] They concluded that the capillary plexus density was significantly higher in the cilioretinal artery group compared with controls. The anatomic distribution of retinal blood vessel density during embryogenesis may be modified by the presence of a cilioretinal artery. However, the optic nerve blood perfusion was lower in the study group.

WHAT'S NEXT FOR RESEARCH

Based on the data discussed above, it is clear that cilioretinal arteries affect the retinal blood flow hemodynamics and correlate with the presence of CNV and SRF volume. These findings require further investigation to better understand the relationships between cilioretinal artery diameter, CNV, SRF volume, and the presence and volume of PED, which might explain the difference between the Bavinger et al study and other study results.

In addition, the presence of CNV and SRF volume may be affected by other factors, such as cardiac output, blood pressure, and the diameter of carotid arteries.

The presence of a cilioretinal artery is an important biologic marker that clinicians should screen for when managing patients with AMD, as it may affect the treatment regimen and prognosis. The majority of retina specialists administer a loading dose of anti-VEGF followed by a maintenance dose when implementing the treat-and-extend regimen. Caution might be exercised when applying the loading dose to patients with a cilioretinal artery, as these individuals are at a higher risk of progressing to macular atrophy at a quicker pace compared with those without a cilioretinal artery. A study conducted by a team of researchers at the University of California, Los Angeles and Doheny Eye Institute showed that substantial but moderate positive associations were found between the existence of a cilioretinal artery and macular atrophy.[14]

In my opinion, patients who have cilioretinal arteries should be studied separately in clinical trials that investigate anti-VEGF treatment outcomes to avoid bias within the data. ■

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