Retinal and choroidal vascular abnormalities contribute to the conversion from dry to wet age-related macular degeneration: a theoretical approach

Rowe, Lucas[1]; Harris, Alon[1]; Ciulla, Thomas[2]; Chiaravialli, Greta[3]; Verticchio Vercellin, Alice Chandra[4,5]; Siesky, Brent[1]; Guidoboni, Giovanna[6]

1. Ophthalmology, Indiana University School of Medicine, Indianapolis, IN, United States.
2. Midwest Eye Institute, Indianapolis, IN, United States.
3. Politecnico di Milano, Milano, Italy.
4. Ophthalmology, University of Pavia, Pavia, Italy.
5. IRCCS – Fondazione Bietti, Rome, Italy.
6. University of Missouri, Columbia, MO, United States.

Background and Hypothesis: Age-related macular degeneration (AMD) is the leading cause of adult blindness in the developed world, and can be classified as one of two types: dry or wet. Abnormalities in retinal and choroidal vasculature may influence dry-to-wet conversion. This study represents a first attempt to use mathematical modeling to characterize the impact of retinal and choroidal blood flow on the oxygenation of retinal layers at various distances from the macula, in healthy individuals and AMD patients.

Experimental Design or Project Methods: The macula is modeled as 7 layers: ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), photoreceptors layer (PH), retinal pigmented epithelium (RPE). Oxygen supply is provided by the vitreous, the choroid, and by three retinal capillary plexi. Oxygen profiles through the macular tissue are calculated by simulating the balance between O_2 supply, consumption and diffusion in: physiological baseline conditions; AMD conditions.

Results: Choroidal vasculature impairment affects tissue more proximal to the macular center, retinal blood flow impairment affects tissue more proximal to the macular periphery, and oxygenation of the foveal avascular zone is not affected by retinal vasculature impairment. The decrease in oxygenation due to retinal and choroidal blood flow impairment in AMD is more prominent in the RPE, PH and ONL in all three anatomical zones of the macula.

Conclusion and Potential Impact: Our mathematical model revealed that reduced choroidal and retinal oxygenation in AMD patients mostly affects the RPE and PH layers, regardless of the distance from the macula. This finding may explain hypoxia inducible factor-1 (HIF-1) production in these layers, which leads to enhanced vascular endothelial growth factor (VEGF) production, causing neovascularization and conversion to wet AMD. Our model suggests that treatment modalities aimed at maintaining stable oxygenation in dry AMD patients may prevent conversion to wet AMD, and reduce vision loss in these patients.