Glaucoma is a multifactorial optic neuropathy that affects more than 50 million people and is the second leading cause of blindness worldwide. The role of IOP has been well documented as a major modifiable risk factor for glaucoma, but decreasing IOP does not always stop the progression of the disease. Additionally, many glaucoma patients have a relatively low IOP, while some healthy individuals have a relatively high IOP.

Vascular impairment as a risk for glaucoma has also been well established, especially over the past 2 decades. In 1953, Duke-Elder suggested vascular risk factors in the pathogenesis of open-angle glaucoma. Hundreds of prospective studies have since determined that impaired vascular regulation, lower blood flow in ocular vessels, and lower ocular perfusion pressure (OPP) are some of the main hemodynamic issues contributing to primary open-angle glaucoma. In 2009, the World Glaucoma Association reached a consensus that vascular dysregulation may contribute to the pathogenesis of glaucoma and that impaired OPP is an independent risk factor for glaucoma.

Despite this wealth of evidence, ophthalmologists’ understanding of vascular considerations in glaucoma management remains limited. No gold standard for measuring all relevant ocular vascular beds exists, imaging devices have inherent limitations and assumptions, and experienced technicians are in short supply. Furthermore, vascular contributions as risk factors for glaucoma have largely been studied for disease incidence and prevalence but not fully explored in terms of the risk of disease progression.

**OCULAR PERFUSION PRESSURE**

OPP is the pressure difference between the arterial blood supply that drives blood through the intraocular...
vasculature and IOP. Because there are no direct, reliable techniques by which to measure OPP, values are approximated with brachial arterial pressure (BP) and IOP, often defined as two-thirds of the mean arterial BP-IOP, with additional calculations for systolic OPP (systolic BP-IOP) and diastolic OPP (diastolic BP-IOP). The Early Manifest Glaucoma Trial (EMGT) found that lower systolic OPP and lower diastolic BP were significant predictors for glaucomatous progression. The Low-Pressure Glaucoma Treatment Study (LoGTS) reported that decreased mean OPP is associated with an increased risk of functional progression. In a population-based cohort of black residents of Barbados, a lower OPP at baseline increased relative glaucoma risk approximately threefold.

Measuring OPP is complicated by positional changes, diurnal variation, and circadian rhythm. A single measurement during a patient’s visit may not be an adequate representation due to the diurnal variation of IOP and BP. Choi et al reported that wider circadian OPP fluctuations were associated with excessive nocturnal BP dipping and worse visual field (VF) indices in glaucoma patients, whereas circadian OPP fluctuation was the most consistent clinical risk factor for glaucoma severity. Furthermore, patients with higher levels of 24-hour mean BP and OPP fluctuations have been shown to have a greater cumulative probability of VF progression. Similarly, medically treated eyes with normal-tension glaucoma and greater 24-hour OPP fluctuations had faster paracentral VF defects progression than in eyes with stable 24-hour OPP.

**RETOBULBAR, RETINAL, AND CHOROIDAL BLOOD FLOW**

Dozens of prospective clinical studies have identified blood flow deficiencies in the retrobulbar, retinal, and choroidal circulation of patients with glaucoma. Various imaging methodologies have been used to quantify these ocular vascular deficits including widely used color Doppler imaging (Figure 1) and, more recently, retinal oximetry (Figure 2) to assess different ocular tissue beds. The inability to autoregulate localized blood flow and corresponding tissue oxygenation and toxin removal in changing physiological conditions and/or lower comparative blood flow values have been well established in glaucoma. In the past decade, emerging data have suggested that ocular hemodynamic insults also contribute to glaucomatous progression. In brief, retrobulbar blood flow and vascular resistance have been found to be linked to and predictive of VF deterioration independent of IOP. There remains, however, an immediate need for more predictive modeling and clinical trials to confirm these findings and to further explore retinal and other vascular tissues in terms of glaucomatous progression.

**PATIENT POPULATIONS AT RISK**

Evidence suggests that patients with diabetes and/or patients of African descent who have glaucoma are at significantly elevated risk for glaucomatous damage due to their respective prevalence of systemic vascular disease. Continued exploration of the risk in these patient populations may improve disease screening and management, thereby reducing the disproportionate burden glaucoma has on the African descent population.

**CONCLUSION**

Vascular considerations in glaucoma management are no longer theoretical. A sound foundation of data supports their involvement in this multifactorial disease. OPP is an established independent risk factor, and localized
ocular circulation deficits have been identified in the retrobulbar, retinal, and choroidal circulation, with preliminary data showing retrobulbar blood flow to be predictive of glaucomatous progression. Certain patient populations may also be at elevated risk, including those with diabetes and/or glaucoma patients of African descent.

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