

Translating Perfusion Pressure

Current evidence on the role of perfusion pressure in glaucoma and future considerations.

BY FOTIS TOPOUZIS, MD

Glaucoma may continue to progress after the reduction of IOP to targeted levels,¹⁻³ which indicates that factors other than pressure affect the pathogenesis of the disease. Research is providing increasing support for the idea that vascular risk factors have a role in glaucoma, with the association between low ocular perfusion pressure and glaucoma being the most consistent finding.

Perfusion pressure is defined as the difference between arterial and venous pressure, which, in the eye, by convention equals IOP. Blood pressure and IOP are therefore the principal components of ocular perfusion pressure (perfusion pressure = blood pressure – IOP), which determines the nutritive delivery of arterial blood to the capillary beds. Ocular hemodynamics in young, healthy individuals are autoregulated to maintain a constant supply of blood to ocular tissues, despite changes in perfusion pressure.⁴ In glaucoma, it has been hypothesized that defective autoregulation results in ischemic damage and reperfusion injury.⁵

PERFUSION PRESSURE AS A RISK FACTOR FOR THE PREVALENCE, INCIDENCE, AND PROGRESSION OF GLAUCOMA

Several population-based studies have suggested that low diastolic perfusion pressure is associated with an increased incidence of open-angle glaucoma (OAG)⁶⁻⁸ or that the prevalence of glaucoma decreases progressively with increased diastolic perfusion pressure.^{9,10} The Barbados Eye Studies, population-based cohort studies of 3,222 participants of African origin with a follow-up of over 9 years, recently reported that all lower perfusion pressures (meaning systolic, diastolic, and mean perfusion pressure) were associated with an increased risk of OAG.¹¹ In addition, the Early Manifest Glaucoma Trial (EMGT)—a prospective, randomized, controlled clinical trial of 255 white participants with a median follow-up of 8 years—found that a baseline systolic per-

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sion pressure of 125 mm Hg or less was a risk factor for OAG progression.¹²

Although the findings from cross-sectional studies and the EMGT consistently demonstrate that low perfusion pressure is a risk factor for glaucoma, clinicians need to be cautious when interpreting these data. The results in the Barbados Eye Studies¹¹ and the EMGT¹² were adjusted for IOP as well as IOP-lowering and blood pressure-lowering treatment. In the cross-sectional studies reporting low perfusion pressure as a risk factor for the prevalence of glaucoma, however, the results were not adjusted.⁶⁻¹⁰

WHICH IS MORE IMPORTANT, IOP OR BLOOD PRESSURE?

Perfusion pressure can be affected by IOP and blood pressure, but which is really “playing the game”? In a given patient, it could be IOP alone, blood pressure alone, or a combination of the two. Even if one assumes the third case, which seems most likely, there is currently no way of knowing the weight of each variable and whether it is the same for the entire spectrum of IOP. For example, the Egna-Neumarkt Study did not find an association between low diastolic perfusion pressure and an increased incidence of normal-tension glaucoma.⁹

Additionally, because there are few reports on how

IOP and blood pressure vary at different time points during the 24-hour period,^{13,14} the impact of fluctuations in IOP and blood pressure on perfusion pressure is unknown.

Further complicating the matter, perfusion pressure can be influenced by high IOP alone or by IOP-lowering treatment. It is possible that the significance of blood pressure varies depending on the IOP. In the EMGT subgroup analyses with regard to IOP, a systolic blood pressure of 160 mm Hg or less was associated with disease progression in patients who had a baseline IOP below 21 mm Hg. In contrast, among patients with a higher baseline IOP, a systolic perfusion pressure of 125 mm Hg or less but not a systolic blood pressure of 160 mm Hg or less was associated with glaucomatous progression.¹² The association was therefore possibly driven by high IOP, leading to a lower systolic perfusion pressure.

PERFUSION PRESSURE AND LOW BLOOD PRESSURE SECONDARY TO BLOOD PRESSURE-LOWERING TREATMENT

Initial evidence of the role of low blood pressure secondary to blood pressure-lowering treatment in glaucoma was provided by the Thessaloniki Eye Study, which found an association between blood pressure and the structure of the optic disc among subjects without glaucoma.¹⁵ In regression models with perfusion and blood pressure as continuous variables, a low diastolic perfusion pressure, a low diastolic blood pressure, and the use of blood pressure-lowering treatment were significantly associated with increased cupping and decreased rim area. The results were adjusted for IOP, the use of blood pressure-lowering treatment, and the duration of this treatment.

In subgroup analysis, the association with the optic disc's structure was observed only in the subject group with a diastolic blood pressure below 90 mm Hg as a result of blood pressure-lowering treatment. There was no difference in the optic disc's structure between the groups with a high diastolic blood pressure (> 90 mm Hg), a high diastolic blood pressure (> 90 mm Hg) under treatment, and a normal diastolic blood pressure (< 90 mm Hg). The results were also adjusted for the aforementioned variables. These findings suggest that, in patients with a compromised vascular bed, lowering the blood pressure below a certain level might induce changes in the optic disc.¹⁵

The Thessaloniki Eye Study helps with interpretation, because no subjects with glaucoma were included in the specific report and IOP therefore was not an issue in the algorithm. The association found was thus not related to IOP and was a direct connection between

blood pressure secondary to blood pressure-lowering treatment and the optic disc's structure.

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The type and duration of blood pressure-lowering treatment may also contribute to patients' risk of developing glaucoma. The Thessaloniki Eye Study included no analysis of the type of blood pressure-lowering treatment. In the European Glaucoma Prevention Study, the use of diuretics was an independent risk factor for OAG,¹⁶ a finding that suggests that the type of blood pressure-lowering treatment may be a variable to consider in addition to the blood pressure level.

CONCLUSION

The findings from cross-sectional studies and the EMGT consistently showed low perfusion pressure to be a risk factor for glaucoma. The weight of IOP and blood pressure in the perfusion-pressure equation, however, remains unknown, as does the effect of their diurnal fluctuation. The role of perfusion pressure in glaucoma remains to be elucidated with regard to low blood pressure secondary to blood pressure-lowering treatment. This information is of particular importance considering that, in the elderly general population, the rate of hypertension is approximately 50%^{17,18} and the percentage of individuals on blood pressure-lowering treatment is nearly 30%.^{8,17,18} At present, the confounding effect of blood pressure-lowering treatment in perfusion pressure is unknown. Based on the results of the Thessaloniki Eye Study, the effect of this therapy may depend on the blood pressure level as a result of the treatment.

All of these issues may partially explain the inconsistent results of research into the role of hypertension in glaucoma. The apparent complexity of the interaction of perfusion pressure with other potential risk factors for glaucoma warrants further research, and it means that physicians cannot currently consider perfusion pressure in their assessment of individual patients. The inclusion of perfusion pressure in clinical practice would entail determining and quantifying the role of perfusion pressure in patients' risk of developing glaucoma. This information would require the establish-

ment of randomized, controlled clinical trials specifically designed to address perfusion pressure. Such investigations would confirm and quantify the risk and should be able to provide data on (1) mean systolic and diastolic perfusion pressure, (2) mean values, peak/trough, and fluctuation of perfusion pressure, and (3) blood pressure level as a result of blood pressure-lowering treatment or not.

Also needed are studies involving the 24-hour assessment of IOP and blood pressure. In addition, future studies assessing perfusion pressure should include the preservation of vision and/or structure as end points and involve long-term follow-up. □

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