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The use of ocular perfusion pressure surrogates in population-based glaucoma studies

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To the editor,

I refer to the published article: Vawda N, Munsamy AJ. A review of ocular perfusion pressure and retinal thickness: A case for the role of systemic hypotension in glaucoma. Afr Vision Eye Health. 2021;80(1):1–9. https://doi.org/10.4102/aveh.v80i1.630

The role of ocular blood flow – and specifically optic nerve head (ONH) perfusion – in glaucoma pathogenesis has been the subject of considerable research interest in recent decades. This has led many studies to explore the relationship between ocular perfusion pressure (OPP) and glaucoma risk. However, true OPP (the difference between arterial and venous pressure in the eye) is difficult to measure and most studies have instead adopted a surrogate measure: OPP = blood pressure (BP) – intraocular pressure (IOP), where brachial BP is used to approximate ocular arterial pressure and IOP is used to approximate ocular venous pressure.

As the authors (N. Vawda and A.J. Munsamy) demonstrate in their Table 2, multiple population-based studies have reported associations between surrogate OPP measures and glaucoma, but I would like to draw the readers' attention to the particular problem of interpreting these associations – a statistical issue which has been well described elsewhere.[1,2,3]

Simply, the inclusion of these surrogates in any regression model does not allow for inferences to be drawn regarding the true effect of ocular perfusion on glaucoma risk. In models without adjustment for IOP (as in some early studies referenced in Table 2),[4,5,6] it has been shown that any association between OPP and glaucoma may be related solely to the IOP component of the surrogate[1] – which is not unsurprising given the strong association between IOP and glaucoma. Similarly, in models with additional adjustment for IOP, any observed associations are attributed entirely to the BP component of the surrogate. This has been substantiated theoretically and demonstrated using simulated data.[2]

These studies clearly implicate BP in glaucoma pathogenesis, and I agree with the authors' hypothesis that systemic hypotension may play an important role in glaucoma. Unfortunately, the role of ocular perfusion remains unclear, and the use of surrogate measures should be discouraged. Future studies should instead aim to provide direct measures of ocular blood flow or ONH perfusion and explore whether these are implicated in glaucoma risk.

References

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Response to Letter to the Editor

After perusal of the references below[1,2] provided by the author (Dr Kelsey V. Stuart) of the *Letter to the Editor* regarding the use of studies cited in Table 2 of our review article, it is clear that the 'simple surrogate for OPP' formula of OPP = BP – IOP is lacking when applied to multivariable regression analysis – thereby challenging the use of the associations found in the located studies listed in Table 2.

The dissuasion from Dr Stuart regarding the use of crude formulae in statistical associations is noted.

Our review attempted to use the associations reported in Table 2 to make a case of reduced OPP as an indication of reduced ocular blood flow being associated with a glaucoma risk. This was within the context of our review providing plausible arguments that systemic hypotension has a role in glaucoma. We understand that using the findings of these studies may be questionable, and we acknowledge the issue raised by the esteemed author. However, despite the surrogate OPP formula's questionable use, glaucoma risk is still associated with reduced OPP and therefore the hypothesis that the chronicity of low BP has a legitimate role to play in compromising ocular blood flow with systemic hypotension as well as possible a risk for glaucoma.

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