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## BRIEF COMMUNICATION



## TIME to discuss the optic nerve?

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The recent large-scale randomized control trial 'Treatment in Morning versus Evening' (TIME) clearly demonstrated that the time of antihypertensive dosing administration does not affect the occurrence of adverse cardiovascular outcomes in patients suffering from arterial hypertension (AHT) [1].

Accumulating evidence implicates nocturnal blood pressure dipping in glaucoma progression, especially in glaucoma patients with normal intraocular pressure [2, 3]. The TIME trial reports no significant difference between evening and morning dosing, with regards to hospitalization due to glaucoma. However, glaucoma is essentially treated in an outpatient setting, i.e., without hospitalization. Even glaucoma surgery is usually performed in an outpatient setting and, if hospitalization is needed, this is often related to comorbidity. Therefore, using hospitalization as a glaucoma proxy could result in underreporting and bias.

Additionally, dipping cannot be easily linked to a dosing time, indicating the need for personalized workup to establish the optimal time for antihypertensive administration. Ophthalmologists have been reluctant to suggest that glaucoma patients with AHT should move their antihypertensive dosing time, for fear of cardiovascular events. Based on the results of the TIME trial, the treating ophthalmologist and cardiologist or internist have more freedom to adjust dosing time for each glaucoma patient, if disease progression asks for a better diurnal blood pressure profile. Importantly, there is room for improvement; even at the level of the general population, recent studies reveal an association between antihypertensive treatment and retinal ganglion cell health [4].

Given that the 2040-projected number of people with glaucoma worldwide exceeds 110 million, and the growing burden related to coexisting glaucoma and AHT is understated in clinical practice, physicians should be alert of patients exhibiting both pathologies [5].

## REFERENCES

1. Mackenzie IS, Rogers A, Poulter NR, Williams B, Brown MJ, Webb DJ, et al. Cardiovascular outcomes in adults with hypertension with evening versus morning dosing of usual antihypertensives in the UK (TIME study): a prospective, randomised, open-label, blinded-endpoint clinical trial. *Lancet*. 2022;400:1417–25.

2. Charlson ME, de Moraes CG, Link A, Wells MT, Harmon G, Peterson J, et al. Nocturnal systemic hypotension increases the risk of glaucoma progression. *Ophthalmology*. 2014;121:2004–12.
3. Melgarejo JD, Lee JH, Petitto M, Yépez JB, Murati FA, Jin Z, et al. Glaucomatous optic neuropathy associated with nocturnal dip in blood pressure: findings from the Maracaibo Aging Study. *Ophthalmology*. 2018;125:807–14.
4. Pappelis K, Jansonius NM. U-shaped effect of blood pressure on structural OCT metrics and retinal perfusion in ophthalmologically healthy subjects. *Invest Ophthalmol Vis Sci*. 2021;62:5.
5. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*. 2014;121:2081–90.

## AUTHOR CONTRIBUTIONS

KP: conceptualisation, writing. AA: conceptualisation, review & editing. KK: conceptualisation, review & editing. KT: conceptualisation, review & editing. NJ: conceptualisation, supervision, review & editing.

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## COMPETING INTERESTS

The author declares no competing interests.

## ADDITIONAL INFORMATION

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