Hypertension Research (2025) 48:1208–1210
https://doi.org/10.1038/s41440-024-02038-2

COMMENT

A silent interplay between elevated intraocular pressure, glaucoma, and hypertension

Tatsuya Sato[1,2] · Araya Umetsu[3] · Marenao Tanaka[1] · Hiroshi Ohguro[3] · Masato Furuhashi[1]

Received: 5 November 2024 / Revised: 15 November 2024 / Accepted: 20 November 2024 / Published online: 5 December 2024

Keyword Intraocular pressure · Glaucoma · Fatty acid-binding protein 5 (FABP5) · Lipid metabolism

Intraocular pressure (IOP) is a pressure to keep an approximately spherical shape of the eyeball and it plays a pivotal role in the maintenance of normal visual function and ocular homeostasis. The level of IOP is physiologically controlled by a dynamics of aqueous humor circulation consisting of (1) production by the ciliary body, (2) spread into the anterior chamber and (3) drainage through the trabecular meshwork. However, an imbalance between the production and drainage of aqueous humor can cause a dysregulation of IOP. Abnormally elevated IOP is one of the major causes of glaucoma, which can lead to serious visual impairment. The establishment of effective approaches for controlling IOP has been an important research topic.

It has recently been reported that the risk for the development of glaucoma independent of levels of IOP was significantly higher in patients with hypertension who were taking calcium channel blockers than in those taking other antihypertensive agents [1], suggesting that therapeutic strategies for hypertension can affect eye diseases including glaucoma. Furthermore, in addition to the evidence that chronic elevation of IOP is associated with the development of glaucoma, there have been some studies showing a relationship between IOP and blood pressure. Recent cross-sectional studies showed that patients with hypertension often have a high level of IOP [2] and a high incidence of glaucoma [3]. However, there had been few longitudinal studies on the incidence rate of hypertension based on levels of IOP. Moreover, it remains unclear whether a high level of IOP, even within the normal range, is a risk factor for the development of hypertension. Therefore, we recently investigated the chronological relationship between IOP and new onset of hypertension during a 10-year follow-up period in 7487 Japanese people who underwent medical health checkups [4]. Cox proportional hazards analysis adjusted for confounding factors including age, sex, systolic blood pressure, obesity, habits of current smoking and alcohol drinking, family history of hypertension, estimated glomerular filtration rate, and diagnosis of diabetes and dyslipidemia at baseline showed that the hazard ratio (HR) for newly developed hypertension was significantly higher in subjects with the 3rd tertile of IOP (≥14 mmHg) than in those with the 1st tertile of IOP (≤11 mmHg) (HR [95% confidence interval]: 1.14 [1.01–1.29]) [4]. Furthermore, analysis using a restricted cubic spline curve showed that a gradual but robust increase in HR for new onset of hypertension was accompanied by an increase in IOP at baseline [4]. Our findings suggest that a high level of IOP, even within the normal range, is an independent risk factor for the development of hypertension over a 10-year period. Based on the results, we propose that the presence of high IOP levels should be considered not only as an indicator for diagnosis and management of glaucoma but also as a risk factor for the development of hypertension. Cardiovascular physicians and ophthalmologists should closely collaborate to prevent the development of hypertension by detecting the presence of high IOP levels.

The mechanisms underlying the link between elevated IOP, glaucoma, and hypertension are presumably multifactorial. It has been shown that the production of aqueous humor in the ciliary body is regulated by the sympathetic and parasympathetic nervous systems and humoral factors such as the renin-angiotensin-aldosterone system [5]. Those

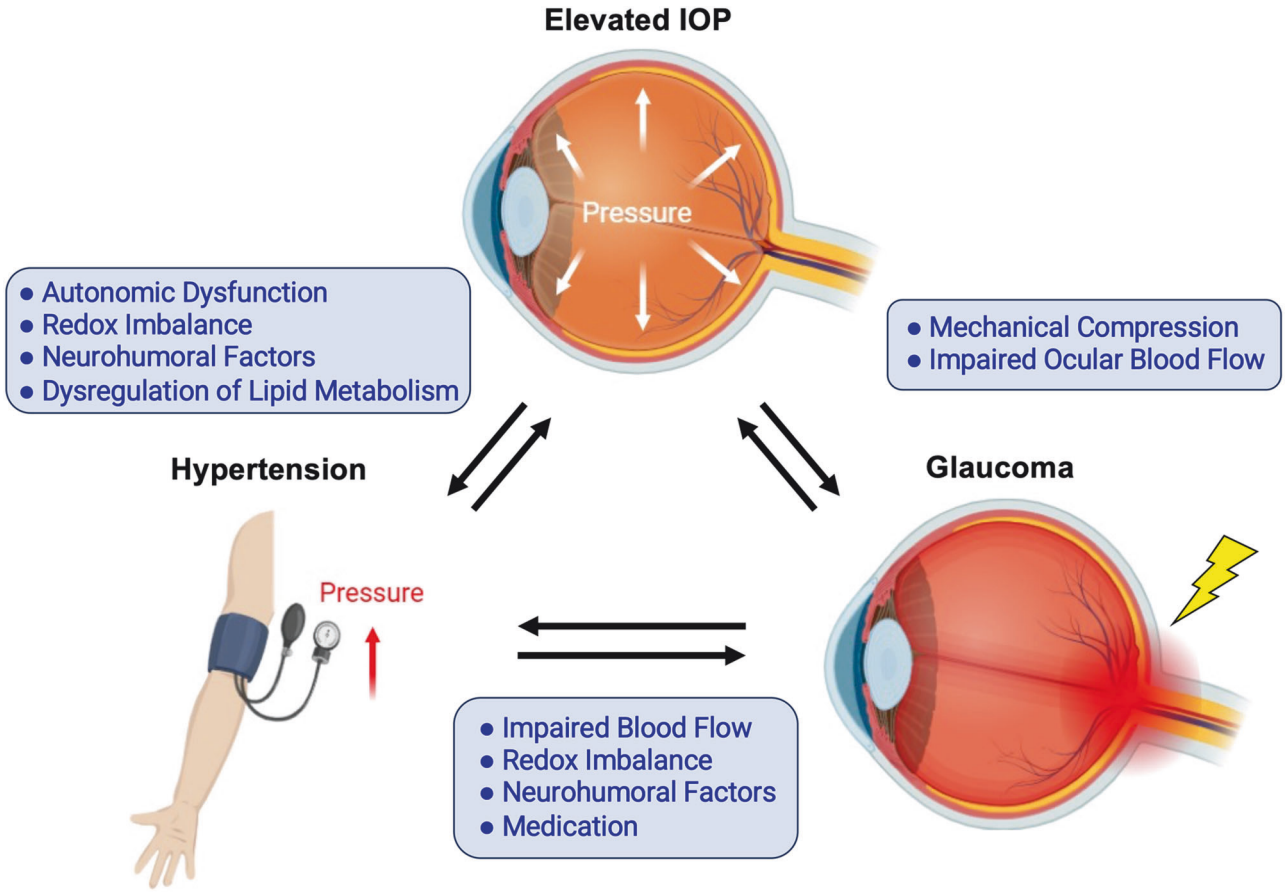
✉ Masato Furuhashi
furuhasi@sapmed.ac.jp

[1] Department of Cardiovascular, Renal and Metabolic Medicine, Sapporo Medical University School of Medicine, Sapporo, Japan

[2] Department of Cellular Physiology and Signal Transduction, Sapporo Medical University School of Medicine, Sapporo, Japan

[3] Department of Ophthalmology, Medical University School of Medicine, Sapporo, Japan

Graphical Opinion



factors may be at least major determinants in the relationship of elevated IOP and glaucoma with hypertension. Indeed, a recent study showed that a high IOP level, even within the normal range, was a risk factor for the development of glaucoma regardless of blood pressure in patients with primary aldosteronism [6]. Several factors including autonomic dysfunction, humoral factors, redox imbalance, and insulin resistance have been shown to be involved in various intraocular physiological dysfunctions including glaucoma [5].

It has been reported that fatty acid-binding protein 5 (FABP5) expressed in adipocytes and macrophages plays significant roles in several aspects of metabolic syndrome, including hypertension and atherosclerosis [7, 8]. We recently demonstrated that FABP5 is abundantly expressed in human non-pigmented ciliary epithelial cells among several ocular cell lines and that FABP5 regulates the expression of aquaporin 1 as an essential regulator in aqueous humor dynamics in human non-pigmented ciliary epithelial cells [9], possibly regulating levels of IOP. Taken together with the results of our previous study showing that FABP5 level in human vitreous tissue was increased in patients with retinal vein occlusion [10], which is induced by atherosclerosis as a mutual relationship between IOP and hypertension, dysregulation of lipid metabolism may be a novel important clue in the relationship between increased levels of IOP and systemic diseases including hypertension. Future studies focusing on the role of lipid metabolism abnormalities linking hypertension and eye diseases are warranted.

In summary, there is a silent but distinct interplay between elevated IOP, glaucoma and hypertension. Possible mechanisms of the interaction are shown in Fig. 1. It should be noted that we need to be more interested in the relationship between hypertension and eye diseases.

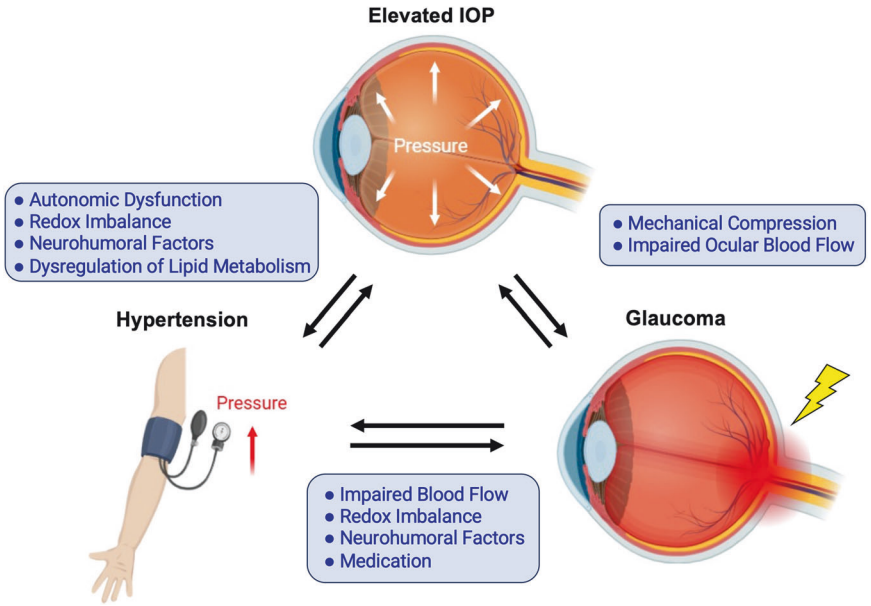


Fig. 1 Schema of the possible link between elevated IOP, glaucoma, and hypertension. IOP intraocular pressure

Funding MT (22K08313) and MF (23K07993) were supported by grants from Japan Society for the Promotion of Science.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Kastner A, Stuart KV, Montesano G, De Moraes CG, Kang JH, Wiggs JL, et al. Calcium channel blocker use and associated glaucoma and related traits among UK Biobank participants. JAMA Ophthalmol. 2023;141:956–64.
2. Yasukawa T, Hanyuda A, Yamagishi K, Yuki K, Uchino M, Ozawa Y, et al. Relationship between blood pressure and intraocular pressure in the JPHC-NEXT eye study. Sci Rep. 2022;12:17493.
3. Kuang TM, Xirasagar S, Kao YW, Shia BC, Lin HC. Association of systemic hypertension with primary open-angle glaucoma: a population-based case-control study. Am J Ophthalmol. 2020;218:99–104.
4. Umetsu A, Tanaka M, Sato T, Akiyama Y, Endo K, Mori K, et al. High intraocular pressure is independently associated with new-onset systemic hypertension over a 10-year period. Circ J. 2024;88:1689–96.
5. Kopp W. Aging and "Age-Related" Diseases—What Is the Relation? Aging Dis. 2024 (e-pub ahead of print 2024/07/16). https://doi.org/10.14336/AD.2024.0570.
6. Hirooka K, Higashide T, Sakaguchi K, Udagawa S, Sugiyama K, Oki K, et al. Prevalence of normal-tension glaucoma in patients with primary aldosteronism. Am J Ophthalmol. 2024;269:339–45.
7. Furuhashi M, Hotamisligil GS. Fatty acid-binding proteins: role in metabolic diseases and potential as drug targets. Nat Rev Drug Discov. 2008;7:489–503.
8. Furuhashi M, Ogura M, Matsumoto M, Yuda S, Muranaka A, Kawamukai M, et al. Serum FABP5 concentration is a potential biomarker for residual risk of atherosclerosis in relation to cholesterol efflux from macrophages. Sci Rep. 2017;7:217.
9. Higashide M, Watanabe M, Sato T, Umetsu A, Nishikiori N, Ogawa T, et al. FABP5 is a possible factor for the maintenance of functions of human non-pigmented ciliary epithelium cells. Int J Mol Sci. 2024;25:9285.
10. Higashide M, Furuhashi M, Watanabe M, Itoh K, Suzuki S, Umetsu A, et al. Fatty acid-binding proteins 4 and 5 are involved in the pathogenesis of retinal vascular diseases in different manners. Life. 2022;12:467.