

Age-Based Association of Glaucoma with the Prevalence of Diabetes and Hypertension at a National Hospital in Seoul

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Abstract: Glaucoma can have profound consequences on vision. Although diabetes and hypertension have been suggested as risk factors for glaucoma, their relevance in epidemiological studies remains controversial. Accordingly, we investigated whether diabetes and hypertension, as well as factors such as age and sex, affected the risk of glaucoma. From May 30, 2022, to June 24, 2022, 1152 patients were selected from a national hospital (Seoul, Korea) to analyze the association among visual field test results, diabetes, and hypertension. Patients who visited the hospital for glaucoma treatment or those referred for glaucoma were randomly selected. The mean deviation value, obtained from visual field test results, is an index of the overall change in the visual field. Based on the mean deviation value, patients with glaucoma were classified into early- ($-6 < MD < 0$), middle- ($-12 < MD < -6$), and late-stage ($MD < -12$) glaucoma groups. Among the 1152 patients, 110 (10%) had diabetes co-occurring with hypertension and 997 (87%) had glaucoma. Among the patients with glaucoma, those with early glaucoma were the most represented and most of them did not have comorbid diabetes or hypertension. Moreover, the incidence of glaucoma was higher in older adults aged ≥ 60 years. No major sex-based changes in the occurrence of diabetes and hypertension were detected in patients with glaucoma. This retrospective study suggests that diabetes and hypertension may affect glaucoma risk; however, other factors such as age may also play a role in glaucoma progression. Regular medical and ophthalmic examinations are necessary to diagnose and manage glaucoma.

Keywords: Glaucoma, Diabetes, Hypertension, Visual Field Test, Mean Deviation Value

Introduction

Glaucoma is the next global main reason for blindness (Sevastopolsky, 2017). Chronic eye disease known as glaucoma causes irreversible vision field abnormalities due to increasing optic nerve damage (Zhou *et al.*, 2022). Loss to the optic nerve and retinal nerve fiber layers characterizes the chronic, progressive optic neuropathy known as glaucoma, which may cause a persistent injury of peripheral or central vision (Stein *et al.*, 2021). Different sections of the optic nerve and retinal nerve fiber are affected by additional optic disorders, such as inflammatory or compressive neuropathies, to variable

degrees, in contrast to glaucoma and comparable ischemic optic neuropathies. Optic neuropathies, including optic neuritis, neuroretinitis, and optic nerve head drusen, can present with different visual field defects (Phu *et al.*, 2017). An important method for identifying and tracking vision loss in glaucoma patients is visual field testing (Wu and Medeiros, 2018).

The region where a stimulus can be visually detected is often referred to as the visual field (Phu *et al.*, 2017). The identification of progressive glaucoma still heavily relies on functional glaucoma testing along with visual field testing (Aref and Budenz, 2017). An automated perimetry tool known as the Humphrey Field Analyzer (HFA; Carl

Zeiss Meditec, Dublin, CA) is being widely used to identify and track potential Visual Field (VF) deterioration (Goukon *et al.*, 2019).

Diabetes can indirectly contribute to the development of glaucoma optic neuropathy through elevated intraocular pressure and angiopathy or direct loss of the optic nerve (Li *et al.*, 2021). When anatomical and functional loss is taken into account, people with diabetes, hypertension, or both have much more severe glaucoma than those who do not (Khatri *et al.*, 2018). Although diabetes and hypertension are putative reasons for glaucoma, their relevance in epidemiological studies is controversial (Zhao *et al.*, 2014). However, several reports have confirmed that glaucoma risk increases with age (McMonnies, 2017). A study conducted in Iran showed that the occurrence of glaucoma was low in those younger than 50 years, suggesting that attention to this vital reason of blindness is warranted in individuals aged 55 years (Hashemi *et al.*, 2019). In addition, a study conducted in Australia suggested an association between glaucoma and diabetes in those aged over 45 years, providing a chance for a main preclusion of glaucoma (Jiang *et al.*, 2022). The occurrence of glaucoma increases with age and other characteristics such as high myopia, raised intraocular pressure, and an affirmative family antiquity of glaucoma, according to a review of glaucoma studies (Schuster *et al.*, 2020).

There are many distinct factors that can cause glaucoma; accordingly, the results of our study were formulated from data obtained from an ophthalmology department at a national hospital in Korea and the results of the VF tests in relation to diabetes and hypertension were statistically analyzed. Therefore, we aimed to determine whether glaucoma was affected by other factors, such as age and sex, in addition to diabetes and hypertension.

Materials and Methods

Ethical Approval

The Dankook University institutional review board approved the protocol (approval number: 2022-08-010). The declaration of Helsinki's principles were followed to conduct this study. Because the study used de-identified data from tests run by medical institutions to make a diagnosis, the need for patient permission was avoided.

Study Population

Patients who visited a national hospital (Seoul, Korea) from May 30, 2022, to June 24, 2022, for glaucoma treatment or those referred for glaucoma were randomly selected for inclusion in our study. Data from 1152 patients were obtained to analyze the association between VF test results and the prevalence rates of diabetes and

hypertension. Results that could not be analyzed because of very low-test reliability and cases referred by neuro ophthalmologists were excluded because they were not related to the mechanisms of glaucoma.

VF Test Strategy

Full-threshold VF testing, Swedish Interactive Threshold Algorithm (SITA) standard VF testing, and SITA fast fields were acknowledged. Only patients who underwent the Humphrey Automated VF test were included in the study.

VF Tests and Threshold Test Patterns

The following types of VF tests were accepted in the study:

- 1) 30-2: A 30° range threshold check and the most common threshold test for glaucoma
- 2) 24-2: A pattern that reduces the temporal, superior, and inferior VFs by 6° except for the nasal VF in 30-2. It is a faster test than 30-2
- 3) 10-2: Inspects the central 10° and is suitable for end-stage glaucoma screening

Classification of Glaucoma by Stages

The Mean Deviation (MD) value is an index of overall VF change. The number of differences in the VF sensitivity of patients compared to the normal sensitivity in healthy individuals from the same age group after age adjustment was calculated and averaged. Based on the MD value on the VF test result sheet, patients were classified into early- ($-6 < MD < 0$), middle- ($-12 < MD < -6$), and late-stage ($MD < -12$) glaucoma.

Statistical Analyses

Data were analyzed using the MedCalc software package (MedCalc software, Ostend, Belgium) after matching for age, sex, duration of diabetes and hypertension, and VF test results among the participants. The collected VF results were divided into stages according to the MD standard values and the relationships between diabetes, hypertension, age, and sex were statistically analyzed.

Results

From May 30, 2022, to June 24, 2022, 1152 patients were enrolled in the study, among whom 110 (10%) had co-occurring diabetes and hypertension and 997 (87%) had glaucoma based on the inclusion and exclusion criteria.

First, among the results obtained from the VF test, the MD values were divided into early-stage ($-6 < MD < 0$), middle-stage ($-12 < MD < -6$), and late-stage ($MD < -12$) glaucoma (Fig. 1).

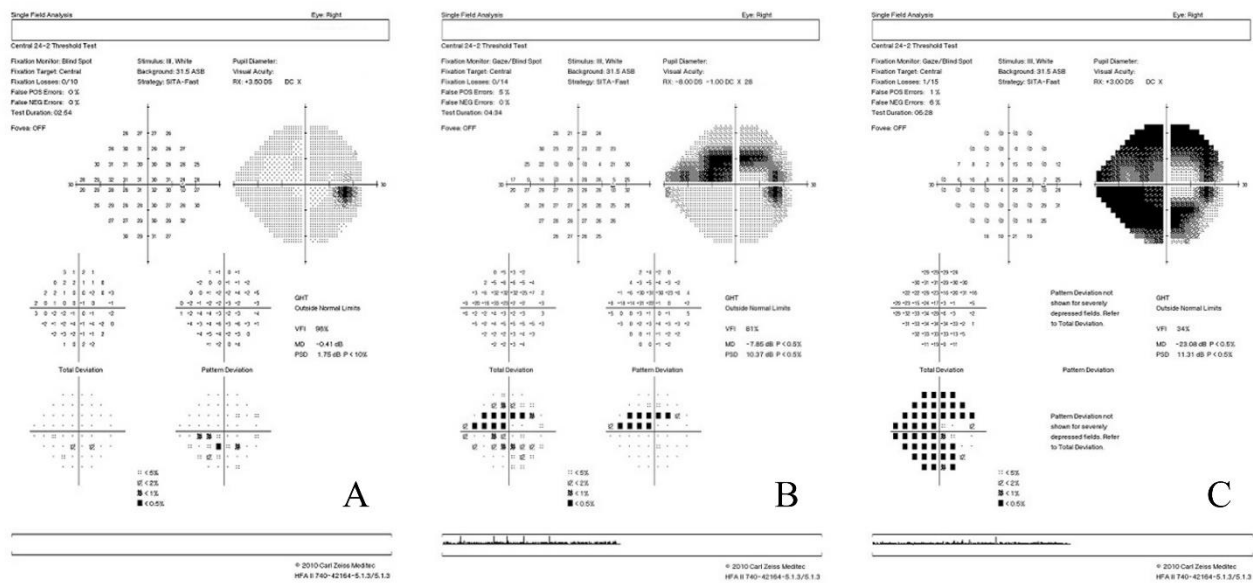


Fig. 1: Visual field test sheets showing the gradual progression of glaucoma. (A) Early-stage glaucoma. (B) Middle-stage glaucoma. (C) Late-stage glaucoma. VFI: Visual Field Index, MD: Mean Deviation, PSD: Pattern Standard Deviation

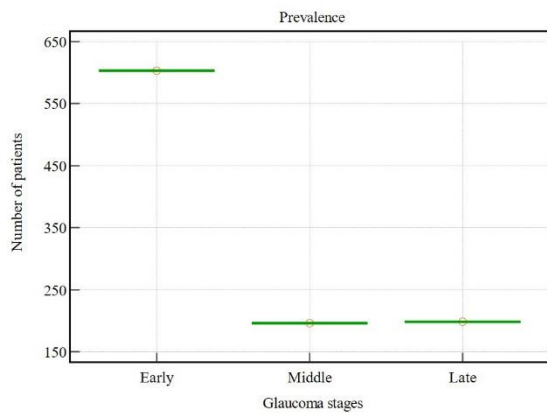


Fig. 2: Prevalence of patients by glaucoma stage

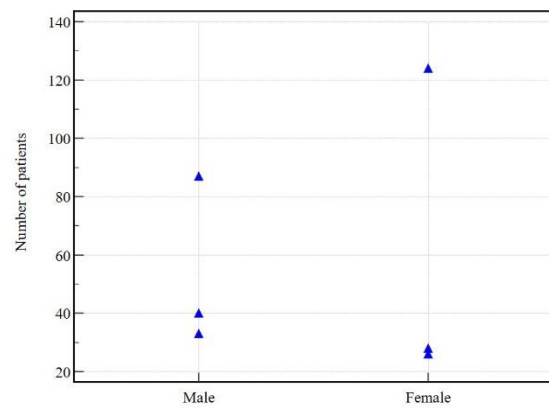
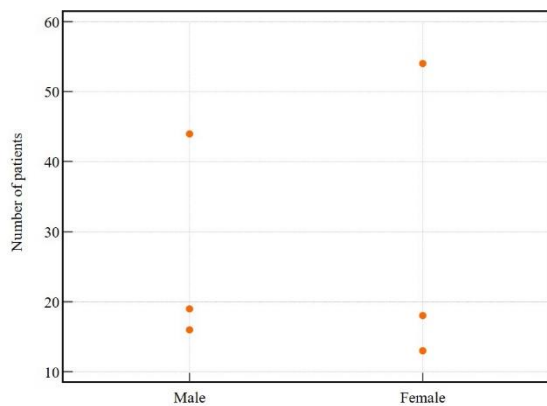


Fig. 3: Patients with diabetes and hypertension were stratified by sex. Orange circles indicate the number of patients with diabetes, and blue triangles indicate the number of patients with hypertension



Among patients with glaucoma, early glaucoma (603/997) was the most prevalent and most participants did not have diabetes (833/997) or hypertension (569/997) (Fig. 2).

There were more patients free of diabetes or hypertension aged <60 years; however, in participants aged >60 years, the proportions of the outpatients with diabetes and hypertension matched those of outpatients without diabetes and hypertension. Additionally, there were more outpatients with diabetes and hypertension in the 70-90-year age group.

Table 1: Percentage of patients with diabetes and hypertension stratified by age in early-stage glaucoma

Age group	10s (%)	20s (%)	30s (%)	40s (%)	50s (%)	60s (%)	70s (%)	80s (%)	90s (%)	p-value
Diabetes	0	0	0	2	7	32	48	11	0	0.0888
Healthy	1	5	6	12	21	30	19	6	0	0.0121
Hypertension	0	1	0	5	13	25	45	12	0	0.0587
Healthy	1	6	8	13	22	33	13	4	0	0.0148

Table 2: Percentage of patients with diabetes and hypertension stratified by age in middle-stage glaucoma

Age group	10s (%)	20s (%)	30s (%)	40s (%)	50s (%)	60s (%)	70s (%)	80s (%)	90s (%)	p-value
Diabetes	0	0	0	0	7	31	34	28	0	0.0597
Healthy	1	3	7	10	15	31	23	10	0	0.0132
Hypertension	0	0	0	6	12	32	35	15	0	0.0446
Healthy	1	4	9	10	15	30	20	11	0	0.0087

Table 3: Percentage of patients with diabetes and hypertension stratified by age in late-stage glaucoma

Age group	10s (%)	20s (%)	30s (%)	40s (%)	50s (%)	60s (%)	70s (%)	80s (%)	90s (%)	p-value
Diabetes	0	0	0	0	11	14	46	27	3	0.0701
Healthy	1	2	0	8	21	32	17	18	0	0.0207
Hypertension	0	0	0	5	7	15	41	31	2	0.0560
Healthy	1	3	0	7	24	35	15	15	0	0.0260

When examining the early, middle, and late stages of glaucoma in detail, the proportion of diabetes was higher in participants with early glaucoma (60-80 years old) and the proportion of hypertension was higher among participants with early glaucoma aged 70-80 years. In the case of mid-stage glaucoma, the values of patients with diabetes and hypertension in their 60s gradually equaled those of patients without diabetes and hypertension; however, for those in their 80s, the values of patients with diabetes and hypertension were higher than those of patients without diabetes or hypertension. The incidence of end-stage glaucoma was greater in patients in their 70s and 90s for both diabetes and hypertension. Therefore, the incidence of glaucoma was higher in older adults over the age of 60 years (Table 1-3). Lastly, when patients were divided by sex at each glaucoma stage, there were slightly more females than those among the healthy, diabetes, and hypertension groups. However, there were no important changes based on sex in the occurrence of diabetes or hypertension (Fig. 3).

Discussion

The primary universal cause of persistent blindness is glaucoma (Stein *et al.*, 2021). By 2040, there will likely be 111.8 million glaucoma patients between the ages of 40 and 80 years (Yang *et al.*, 2021). Age, smoking status, African heritage, family history, genetics, hypertension, hypotension (especially lowered nocturnal blood pressure), atherosclerosis, lipid dysregulation, and diabetes are all risk factors for developing glaucoma (Schuster *et al.*, 2020). In our study, we found that early stage glaucoma was the most common stage of glaucoma among patients. The incidence of diabetes, hypertension, and glaucoma

increased with age; however, there were no important changes in their incidence among males and females.

When glaucoma was divided into stages based on severity, the proportion of patients with early stage glaucoma was greater than that of those with middle and late stage glaucoma and there were more patients without diabetes or hypertension at each stage of glaucoma. Diabetes is linked to microvascular damage and possibly impacts the vascular autoregulation of the retina and optic nerve (Yang *et al.*, 2021). One study found that those with diabetes had a higher risk of increasing glaucoma than people without diabetes, but another found no correlation between the prevalence of glaucoma and diabetes (Rim *et al.*, 2018; Grzybowski *et al.*, 2020). The length of hypertension and the extent of vascular damage could theoretically be linked to glaucoma risk (Grzybowski *et al.*, 2020). However, although significant data suggest an association between hypertension and glaucoma, no studies have shown this association (Grzybowski *et al.*, 2020).

Age is also a major threat to all types of glaucoma due to certain age-related changes that affect the optic nerve (Zhang *et al.*, 2021). Because there are many mitochondria near the optic disc, age-related mitochondrial malfunction may limit energy supply and hasten the development of glaucoma (Grzybowski *et al.*, 2020). As we age, the lens ages and thickens and the center shifts forward, which compresses the iris and pushes it forward. This results in a shallow anterior chamber, which narrows or even closes the anterior chamber angle, leading to the acute onset of glaucoma (Yang *et al.*, 2021). Additionally, each decade of aging is correlated with an increase in mean ocular perfusion pressure, intraocular pressure, and corneal thickness (Grzybowski *et al.*, 2020).

The assessment of aging requires the accumulation of data on medical conditions, such as high blood pressure, hypotension, diabetes, migraine, obstructive sleep apnea, cataracts, glaucoma, and medications taken (Schuster *et al.*, 2020). Herein, the incidence of diabetes and hypertension gradually increased in patients older than 60 years and the occurrence of glaucoma was greater in the older adult group.

When patients were divided by sex, the proportion of females with diabetes, hypertension, and glaucoma was higher than that of males, but the difference was not statistically significant. One study found that the effects of estrogen and testosterone on intraocular heaviness, ocular blood movement, and neuroprotection may contribute to the risk of developing glaucoma in some individuals (Patel *et al.*, 2018). The authors also reported that estrogen was related to the onset and development of glaucoma in females, particularly in those who were premenopausal (Qiu *et al.*, 2021). In contrast, one study observed that sex hormone level in postmenopausal females was not considerably related to primary open angle glaucoma; however, higher testosterone levels were significantly associated with glaucoma (Kang *et al.*, 2018).

This study has some limitations. First, it was conducted in only one region of Korea and additional research is needed in other regions and countries. Second, genetic diseases (such as retinitis pigmentosa, which causes night blindness) were not considered when analyzing the test results. The results were not examined considering the patients' clinical features because this was a retrospective study.

In our study, VF test results, and diabetes and hypertension data provided by a national hospital in Korea were collected, compared, and analyzed based on age, sex, and the stage of glaucoma progression. Thus, it was possible to examine the trend in the incidence of diabetes and hypertension in each age group. Additionally, our study demonstrated the possible association between glaucoma and diabetes, and hypertension through statistical analysis, especially in patients aged over 60 years. There has been significant evidence linking the frequency of glaucoma to other chronic illnesses (Sun *et al.*, 2022). Early detection is essential to stop the progression of glaucoma (Allison *et al.*, 2020). Therefore, other regular medical examinations may be necessary for diagnosing and managing glaucoma in addition to ophthalmic examinations (Sun *et al.*, 2022). Our study indicated that not only diabetes and hypertension but also age could affect the incidence of glaucoma. Additional studies should be conducted to determine if the levels of hypertension and diabetes are related to the progression of glaucoma.

Conclusion

This study presented data through statistical analysis to understand the prevalence of glaucoma according to diabetes and hypertension in patients. We found that most glaucoma patients had early-stage glaucoma, and

most did not have diabetes or hypertension. In addition, the incidence of glaucoma was higher in the elderly over 60 years of age. Also, no major sex-specific changes were found in the incidence of diabetes and hypertension in patients with glaucoma. This retrospective study suggests that diabetes and hypertension may affect glaucoma risk. However, other factors such as age may also play a role in glaucoma progression. Therefore, regular internal and ophthalmic examinations are recommended to diagnose and manage glaucoma.

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Author's Contributions

Sun Jung Lee: Made substantial contributions to the conception or designed of the study. Made substantial contributions to the acquisition and analysis of data.

Tae Su Jang: Made substantial contributions to the conception or designed of the study.

Jaе Kyung Kim: Made substantial contributions to the acquisition and analysis of data.

Ethics

This study was approved by the Dankook University Institutional Review Board (IRB No. 2022-08-010).

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